Table SI. Detailed information of 443 differential proteins in BDE  $4^{th}$  and  $8^{th}$  Ger and HOC group (filtered with threshold value of expression fold change >2 or < 0.5 and P<0.05).

Dunda in	and 8 <sup>th</sup> C	P-value BDE 4 <sup>th</sup> Ger/HOCs Ratio	Regulated	Length (kDa)
Protein		1 0001	type	
Poly(U)-binding-splicing factor PUF60	1.432	0.001	UP	564
Formin-binding protein 4	1.819	0.001	UP	1031
Ubiquitin carboxyl-terminal hydrolase 10	1.529	0.001	UP	792
Nuclear inhibitor of protein phosphatase 1	1.670	0.002	UP	351
Glutamate-rich WD repeat-containing protein 1	1.977	0.002	UP	446
28S ribosomal protein S28, mitochondrial	1.379	0.002	UP	186
TGF-beta-activated kinase 1 and MAP3K7-binding protein 1	2.795	0.002	UP	502
28S ribosomal protein S26, mitochondrial	1.890	0.003	UP	200
N-terminal Xaa-Pro-Lys N-methyltransferase 1	1.641	0.003	UP	223
Ubiquitin thioesterase otulin	9.714	0.004	UP	352
Vacuolar protein sorting-associated protein 37B	2.087	0.005	UP	285
MKI67 FHA domain-interacting nucleolar phosphoprotein	1.390	0.005	UP	317
Ubiquitin-conjugating enzyme E2 variant 1	1.688	0.005	UP	147
Phosphatidate cytidylyltransferase, mitochondrial	2.778	0.005	UP	337
28S ribosomal protein S23, mitochondrial	1.800	0.006	UP	177
H/ACA ribonucleoprotein complex non-core subunit NAF1	3.349	0.006	UP	489
Signal-induced proliferation-associated protein 1	1.303	0.007	UP	1037
THO complex subunit 6 homolog	1.422	0.007	UP	341
Cystatin-B	2.182	0.007	UP	98
Suppressor of SWI4 1 homolog	1.546	0.008	UP	470
TATA box-binding protein-like protein 1	4.638	0.008	UP	186
Diphosphoinositol polyphosphate phosphohydrolase 1	1.339	0.008	UP	168
Polyglutamine-binding protein 1	12.375	0.009	UP	263
MalonateCoA ligase ACSF3, mitochondrial	25.564	0.009	UP	583
Phosphatidylinositol 4-phosphate 3-kinase C2 domain-containing subunit alpha	1.482	0.009	UP	1686
28S ribosomal protein S16, mitochondrial	2.353	0.010	UP	135
Ubiquitin-associated protein 2-like	1.228	0.010	UP	1107
Ribosomal protein S6 kinase beta-2	11.010	0.010	UP	485
6-phosphogluconolactonase	1.580	0.010	UP	257
Arpin	2.269	0.010	UP	226
Pantothenate kinase 4	1.386	0.010	UP	820
Activator of 90 kDa heat shock protein ATPase homolog 1	1.471	0.011	UP	338
60S ribosome subunit biogenesis protein NIP7 homolog	1.738	0.012	UP	180
40S ribosomal protein S17	1.459	0.012	UP	135
Ubiquitin carboxyl-terminal hydrolase 25	1.675	0.012	UP	1055
Forkhead box protein K1	2.265	0.013	UP	719
Hydroxymethylglutaryl-CoA synthase, cytoplasmic	1.788	0.014	UP	520
Transportin-2	1.260	0.014	UP	887
Barrier-to-autointegration factor	10.379	0.014	UP	89

Transcription elongation factor SPT5	1.414	0.014	UP	1082
Mediator of RNA polymerase II transcription subunit 20	1.572	0.014	UP	212
Cleavage and polyadenylation specificity factor subunit 3	1.886	0.015	UP	684
Mitogen-activated protein kinase 1	1.358	0.015	UP	358
60S ribosomal protein L23	1.916	0.015	UP	140
ATP-dependent RNA helicase DHX8	6.542	0.015	UP	1244
Structural maintenance of chromosomes protein 2	3.565	0.015	UP	1191
Methionine aminopeptidase 2	1.584	0.015	UP	478
Peptidyl-prolyl cis-trans isomerase FKBP3	1.313	0.015	UP	224
Ribonuclease P protein subunit p29	1.835	0.015	UP	221
Testis-expressed protein 10	1.468	0.016	UP	928
WD repeat-containing protein 75	1.901	0.016	UP	830
Jupiter microtubule associated homolog 2	2.163	0.016	UP	190
Torsin-1A-interacting protein 2, isoform IFRG15	1.914	0.017	UP	131
Probable ATP-dependent RNA helicase DDX49	1.359	0.017	UP	480
RNA-binding protein 15	1.548	0.018	UP	962
Peroxisomal membrane protein PMP34	2.030	0.018	UP	307
Probable ATP-dependent RNA helicase DDX46	1.605	0.018	UP	1032
ADP-ribosylation factor-like protein 2	1.305	0.018	UP	184
Neuroguidin	2.632	0.018	UP	315
Flap endonuclease 1	7.703	0.018	UP	378
DNA repair protein RAD50	3.415	0.019	UP	1312
Gem-associated protein 5	3.363	0.019	UP	1502
Signal recognition particle 19 kDa protein	1.589	0.019	UP	144
ARF GTPase-activating protein GIT2	1.477	0.020	UP	708
DCN1-like protein 1	1.432	0.020	UP	259
Glutaredoxin-1	5.100	0.021	UP	107
Protein phosphatase 1G	1.554	0.021	UP	542
Rapamycin-insensitive companion of mTOR	1.238	0.021	UP	1708
Annexin A5	1.413	0.022	UP	319
Activating signal cointegrator 1	1.925	0.023	UP	581
Splicing factor U2AF 35 kDa subunit	1.517	0.023	UP	239
Heat shock protein 105 kDa	1.884	0.023	UP	858
Cleavage and polyadenylation specificity factor subunit 7	1.349	0.023	UP	471
Annexin A3	1.285	0.024	UP	323
Mediator of DNA damage checkpoint protein 1	14.740	0.025	UP	1707
Histone acetyltransferase type B catalytic subunit	63.701	0.025	UP	416
Zinc finger C2HC domain-containing protein 1A	1.624	0.025	UP	324
tRNA methyltransferase 10 homolog A	6.149	0.025	UP	328
Armadillo repeat-containing X-linked protein 3	1.465	0.026	UP	379
28S ribosomal protein S11, mitochondrial	2.116	0.026	UP	191
Cytochrome c oxidase subunit 4 isoform 1, mitochondrial	1.435	0.026	UP	169

28S ribosomal protein S10, mitochondrial	2.254	0.026	UP	160
Josephin-2	7.328	0.026	UP	188
Regulatory-associated protein of mTOR	1.430	0.027	UP	1335
Cyclin-dependent kinase inhibitor 2A	4.528	0.028	UP	168
Nucleoredoxin	1.257	0.028	UP	435
28S ribosomal protein S18b, mitochondrial	1.440	0.029	UP	254
Peptidyl-prolyl cis-trans isomerase A	1.446	0.029	UP	164
CAD protein [Includes: Glutamine-dependent	1.828	0.029	UP	2225
carbamoyl-phosphate synthase	1.828	0.029	O1	2223
SUN domain-containing protein 2	2.178	0.029	UP	731
Methylated-DNAprotein-cysteine methyltransferase	3.573	0.030	UP	211
Muscleblind-like protein 1	1.213	0.030	UP	341
Tyrosine-protein kinase Fer	1.247	0.030	UP	823
Nascent polypeptide-associated complex subunit alpha	1.463	0.030	UP	215
Signal-induced proliferation-associated 1-like protein 3	1.452	0.030	UP	1776
Metastasis-associated protein MTA3	2.218	0.031	UP	591
Cordon-bleu protein-like 1	1.425	0.034	UP	1273
Uncharacterized protein C6orf203 homolog	1.946	0.034	UP	240
La-related protein 1	1.665	0.034	UP	1072
N-alpha-acetyltransferase 50	1.918	0.034	UP	169
40S ribosomal protein S24	1.609	0.034	UP	133
ADP-sugar pyrophosphatase	1.607	0.034	UP	218
Negative elongation factor A	8.183	0.034	UP	530
THO complex subunit 3	1.217	0.034	UP	351
Ankyrin-2	2.989	0.035	UP	3898
Exportin-T	1.209	0.035	UP	963
Mitogen-activated protein kinase 14	1.592	0.035	UP	360
Intraflagellar transport protein 122 homolog	3.296	0.035	UP	1182
Histone-lysine N-methyltransferase SETD2	4.826	0.035	UP	2537
Protein Red	1.444	0.035	UP	557
Mitotic spindle assembly checkpoint protein MAD2A	3.441	0.035	UP	205
Protein quaking	1.426	0.035	UP	341
Homer protein homolog 3	1.247	0.036	UP	356
Nuclear factor 1 C-type	9.460	0.037	UP	439
Protein MEMO1	1.608	0.037	UP	297
RNA-binding protein 39	1.461	0.037	UP	530
Symplekin	1.613	0.037	UP	1284
Phospholipid hydroperoxide glutathione peroxidase	1.395	0.037	UP	197
DNA topoisomerase 2-alpha	1.959	0.038	UP	1528
Phosphatidylinositol transfer protein alpha isoform	1.333	0.038	UP	271
DDB1- and CUL4-associated factor 7	1.521	0.039	UP	342
Protein arginine N-methyltransferase 7	5.703	0.040	UP	692
		0	1	1

Nucleoporin Nup37	1.568	0.040	UP	326
TBC1 domain family member 1	1.242	0.040	UP	1255
Arginine/serine-rich coiled-coil protein 2	5.981	0.040	UP	376
Something about silencing protein 10	2.498	0.041	UP	469
Glomulin	1.370			
		0.041	UP	596
WD repeat domain phosphoinositide-interacting protein 3	1.275	0.041	UP	344
Cyclin-dependent kinase 13	10.995	0.041	UP	1511
Deoxyhypusine hydroxylase	1.770	0.042	UP	302
Elongin-B	1.633	0.043	UP	118
Armadillo repeat-containing protein 6	3.204	0.043	UP	468
RWD domain-containing protein 1	1.936	0.044	UP	243
Peptidyl-prolyl cis-trans isomerase F, mitochondrial	2.235	0.044	UP	206
Bystin	1.674	0.045	UP	436
Mesenteric estrogen-dependent adipogenesis protein	1.513	0.045	UP	303
26S proteasome non-ATPase regulatory subunit 13	1.314	0.045	UP	376
28S ribosomal protein S7, mitochondrial	1.388	0.045	UP	242
Splicing factor 3A subunit 3	1.293	0.046	UP	501
Nuclear cap-binding protein subunit 2	1.722	0.046	UP	156
Probable ATP-dependent RNA helicase DDX27	1.815	0.046	UP	760
Guanine nucleotide exchange factor MSS4	1.947	0.047	UP	123
rRNA 2'-O-methyltransferase fibrillarin	2.401	0.047	UP	327
Casein kinase II subunit alpha'	1.275	0.047	UP	350
Transcription termination factor 2	12.113	0.047	UP	1138
SWI/SNF complex subunit SMARCC2	1.550	0.047	UP	1213
Polymerase delta-interacting protein 3	1.512	0.048	UP	420
A-kinase anchor protein 8	1.946	0.048	UP	687
Serine/threonine-protein kinase PRP4 homolog	2.092	0.048	UP	1007
Charged multivesicular body protein 3	1.346	0.048	UP	224
Ferredoxin-2, mitochondrial	4.193	0.048	UP	174
Large proline-rich protein BAG6	1.526	0.048	UP	1154
28S ribosomal protein S24, mitochondrial	23.185	0.048	UP	167
Exosome complex component RRP4	1.465	0.048	UP	293
Eukaryotic translation elongation factor 1 epsilon-1	1.317	0.048	UP	174
Protein phosphatase 1 regulatory subunit 12B	1.666	0.048	UP	976
Protein prune homolog 2	4.592	0.049	UP	3084
Fas apoptotic inhibitory molecule 1	1.652	0.049	UP	179
Serine/arginine repetitive matrix protein 2	1.969	0.049	UP	2703
U4/U6 small nuclear ribonucleoprotein Prp3	1.439	0.049	UP	683
E3 ubiquitin-protein ligase TRIM47	1.223	0.049	UP	641
ATP-dependent RNA helicase DDX18	2.178	0.050	UP	660
Macrophage-expressed gene 1 protein	0.083	0.030	DOWN	713
Oxysterol-binding protein-related protein 9	0.648	0.010	DOWN	736
Oxysteror-ornaing protein-related protein 9	0.048	0.021	DOWN	/30

Endoplasmic reticulum mannosyl-oligosaccharide	0.492	0.048	DOWN	658
1,2-alpha-mannosidase				
Probable 2-oxoglutarate dehydrogenase E1 component DHKTD1, mitochondrial	0.604	0.013	DOWN	921
Adenylyltransferase and sulfurtransferase MOCS3	0.164	0.027	DOWN	460
Exocyst complex component 6B	0.747	0.023	DOWN	810
Canalicular multispecific organic anion transporter 2	0.125	0.015	DOWN	1523
A-kinase anchor protein 5	0.009	0.001	DOWN	745
FERM, ARHGEF and pleckstrin domain-containing protein 1	0.184	0.017	DOWN	1048
Calpain-2 catalytic subunit	0.750	0.028	DOWN	700
Syntenin-1	0.338	0.042	DOWN	299
Collagen alpha-1(XV) chain	0.055	0.006	DOWN	1367
Tyrosine-protein phosphatase non-receptor type 9	0.630	0.042	DOWN	593
Exocyst complex component 7	0.511	0.017	DOWN	697
Sialidase-1	0.149	0.034	DOWN	409
Mitochondrial import inner membrane translocase subunit	0.1.,	0.02.	20111	.0,
TIM44	0.233	0.017	DOWN	452
Neutral amino acid transporter A	0.318	0.005	DOWN	532
Syndecan-4	0.397	0.001	DOWN	198
Rho GTPase-activating protein 6	0.094	0.033	DOWN	987
OX-2 membrane glycoprotein	0.263	0.032	DOWN	278
Ninjurin-1	0.120	0.040	DOWN	152
Integrin beta-5	0.405	0.035	DOWN	798
Cathepsin S	0.005	0.001	DOWN	340
14-3-3 protein sigma	0.424	0.003	DOWN	248
Electrogenic sodium bicarbonate cotransporter 1	0.212	0.004	DOWN	1079
Palmitoyl-protein thioesterase 1	0.326	0.036	DOWN	306
Target of Myb protein 1	0.378	0.009	DOWN	492
Signal transducing adapter molecule 2	0.767	0.030	DOWN	523
Tripeptidyl-peptidase 1	0.443	0.027	DOWN	562
Coronin-1A	0.014	0.004	DOWN	461
Collagen alpha-1(IV) chain	0.420	0.022	DOWN	1669
Fructose-bisphosphate aldolase C	0.075	0.036	DOWN	363
cAMP-dependent protein kinase catalytic subunit alpha	0.668	0.001	DOWN	351
Integrin alpha-M	0.011	0.005	DOWN	1153
Ectonucleotide pyrophosphatase/phosphodiesterase family				
member 1	0.507	0.010	DOWN	906
Low affinity immunoglobulin gamma Fc region receptor II	0.057	0.006	DOWN	330
Apolipoprotein E	0.025	0.003	DOWN	311
Lysozyme C-2	0.027	0.003	DOWN	148
Superoxide dismutase	0.770	0.009	DOWN	222
Small integral membrane protein 1	0.577	0.039	DOWN	78
Fibronectin	0.076	0.030	DOWN	2477

Keratin, type II cytoskeletal 8	0.086	0.048	DOWN	490
Integrin beta-2	0.004	0.000	DOWN	771
Inositol 1,4,5-trisphosphate receptor type 1	0.386	0.046	DOWN	2749
Beta-glucuronidase	0.108	0.008	DOWN	648
Intercellular adhesion molecule 1	0.060	0.025	DOWN	537
Complement C1q subcomponent subunit B	0.016	0.002	DOWN	253
CD44 antigen	0.231	0.033	DOWN	778
Interleukin-4 receptor subunit alpha	0.066	0.008	DOWN	810
Lysosomal protective protein	0.436	0.020	DOWN	474
Methanethiol oxidase	0.064	0.029	DOWN	472
Receptor-type tyrosine-protein phosphatase alpha	0.821	0.027	DOWN	829
Cathepsin D	0.282	0.049	DOWN	410
Syndecan-1	0.207	0.031	DOWN	311
Lysosomal acid phosphatase	0.398	0.018	DOWN	423
Myristoylated alanine-rich C-kinase substrate	0.750	0.049	DOWN	309
Alpha-mannosidase 2	0.613	0.047	DOWN	1150
Sodium- and chloride-dependent glycine transporter 1	0.567	0.047	DOWN	692
Adenylosuccinate synthetase isozyme 1	0.012	0.001	DOWN	457
Macrophage scavenger receptor types I and II	0.005	0.001	DOWN	458
Dipeptidase 1	0.158	0.042	DOWN	410
Macrosialin	0.002	0.000	DOWN	326
Protein NEDD1	0.668	0.020	DOWN	660
Thromboxane-A synthase	0.009	0.001	DOWN	533
Fibulin-2	0.079	0.032	DOWN	1221
Natural resistance-associated macrophage protein 1	0.028	0.003	DOWN	548
Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA	0.031	0.003	DOWN	655
Glutathione peroxidase 3	0.134	0.030	DOWN	226
Programmed cell death protein 2	0.442	0.009	DOWN	343
Aldehyde dehydrogenase, mitochondrial	0.769	0.019	DOWN	519
Tyrosine-protein kinase SYK	0.095	0.015	DOWN	629
Rab GDP dissociation inhibitor alpha	0.725	0.006	DOWN	447
Arylsulfatase A	0.431	0.007	DOWN	506
V-type proton ATPase catalytic subunit A	0.516	0.035	DOWN	617
V-type proton ATPase subunit d 1	0.608	0.048	DOWN	351
Alpha-2-macroglobulin receptor-associated protein	0.494	0.036	DOWN	360
Ectonucleoside triphosphate diphosphohydrolase 1	0.012	0.001	DOWN	510
Toll-like receptor 7	0.074	0.009	DOWN	1050
VIP36-like protein	0.595	0.022	DOWN	347
Protein transport protein Sec61 subunit gamma	0.748	0.023	DOWN	68
Ras-related protein Rab-8B	0.438	0.012	DOWN	207
4-aminobutyrate aminotransferase, mitochondrial	0.066	0.015	DOWN	500
Ras-related protein Rab-1A	0.812	0.039	DOWN	205

V-type proton ATPase 16 kDa proteolipid subunit	0.477	0.037	DOWN	155
Serine/threonine-protein phosphatase 2B catalytic subunit	0.775	0.022	DOWN	521
alpha isoform	0.775	0.032	DOWN	521
Acid sphingomyelinase-like phosphodiesterase 3a	0.012	0.004	DOWN	445
3-beta-hydroxysteroid-Delta	0.831	0.006	DOWN	230
Ena/VASP-like protein	0.051	0.021	DOWN	414
Isochorismatase domain-containing protein 2A	0.586	0.017	DOWN	206
Vacuolar protein sorting-associated protein 45	0.624	0.033	DOWN	570
Aminopeptidase N	0.007	0.002	DOWN	966
Bone morphogenetic protein 1	0.130	0.035	DOWN	991
Complement C1q subcomponent subunit A	0.075	0.009	DOWN	245
Collagen alpha-1(VIII) chain	0.124	0.000	DOWN	744
Aquaporin-1	0.033	0.011	DOWN	269
Complement C1q subcomponent subunit C	0.137	0.029	DOWN	246
Ras-related C3 botulinum toxin substrate 2	0.017	0.002	DOWN	192
Basement membrane-specific heparan sulfate proteoglycan	0.120	0.001	DOWN	2505
core protein	0.130	0.001	DOWN	3707
Platelet glycoprotein 4	0.020	0.007	DOWN	472
Neutrophil cytosol factor 1	0.051	0.006	DOWN	390
SLAM family member 5	0.096	0.011	DOWN	329
Scavenger receptor cysteine-rich type 1 protein M130	0.028	0.003	DOWN	1121
Zinc transporter SLC39A7	0.643	0.004	DOWN	476
Putative phospholipase B-like 2	0.588	0.045	DOWN	594
NLR family member X1	0.253	0.017	DOWN	975
Hexokinase-3	0.004	0.000	DOWN	922
Ceroid-lipofuscinosis neuronal protein 5 homolog	0.229	0.010	DOWN	341
Divergent protein kinase domain 2A	0.441	0.027	DOWN	430
Phosphofurin acidic cluster sorting protein 2	0.098	0.012	DOWN	862
Transmembrane anterior posterior transformation protein 1	0.450	0.010	DOWN	564
N-acetylgalactosamine-6-sulfatase	0.078	0.017	DOWN	520
Zinc transporter 9	0.145	0.038	DOWN	567
Palmitoyltransferase ZDHHC20	0.644	0.011	DOWN	380
Ganglioside GM2 activator	0.548	0.023	DOWN	193
Glutaryl-CoA dehydrogenase, mitochondrial	0.622	0.032	DOWN	438
Lymphocyte antigen 75	0.250	0.018	DOWN	1723
Syntaxin-binding protein 3	0.739	0.035	DOWN	592
Glutathione S-transferase theta-2	0.173	0.028	DOWN	244
Arginase-1	0.002	0.000	DOWN	323
Plastin-2	0.010	0.002	DOWN	627
Adhesion G protein-coupled receptor E1	0.027	0.003	DOWN	931
Fibrillin-1	0.038	0.011	DOWN	2873
NADPH:adrenodoxin oxidoreductase, mitochondrial	0.629	0.036	DOWN	494
Growth arrest-specific protein 6	0.189	0.031	DOWN	674

Macrophage mannose receptor 1	0.006	0.001	DOWN	1456
Pregnancy zone protein	0.116	0.019	DOWN	1495
Versican core protein	0.023	0.002	DOWN	3357
Serum paraoxonase/lactonase 3	0.508	0.048	DOWN	354
Retinal dehydrogenase 2	0.061	0.024	DOWN	518
Dystroglycan	0.300	0.027	DOWN	893
Sialoadhesin	0.009	0.004	DOWN	1695
ADP-ribosyl cyclase/cyclic ADP-ribose hydrolase 2	0.034	0.022	DOWN	311
UDP-glucuronosyltransferase 1-6	0.729	0.023	DOWN	531
C-type mannose receptor 2	0.700	0.002	DOWN	1479
Tyrosine-protein phosphatase non-receptor type 13	0.121	0.036	DOWN	2453
Endothelial protein C receptor	0.079	0.028	DOWN	242
All-trans-retinol 13,14-reductase	0.266	0.008	DOWN	609
Raftlin	0.825	0.006	DOWN	554
Protein wntless homolog	0.492	0.004	DOWN	541
Protein CASC4	0.516	0.001	DOWN	435
Nucleoporin NUP188 homolog	0.727	0.013	DOWN	1759
Nesprin-1	0.718	0.011	DOWN	8799
Ubiquitin carboxyl-terminal hydrolase MINDY-1	0.216	0.031	DOWN	468
F-box only protein 22	0.429	0.013	DOWN	402
Echinoderm microtubule-associated protein-like 2	0.274	0.001	DOWN	649
Coiled-coil domain-containing protein 93	0.717	0.043	DOWN	629
Tumor necrosis factor ligand superfamily member 18	0.139	0.017	DOWN	173
Ubiquitin-protein ligase E3C	0.732	0.007	DOWN	1083
Phosphatidylinositol 5-phosphate 4-kinase type-2 beta	0.466	0.010	DOWN	416
Calcium-transporting ATPase type 2C member 1	0.163	0.043	DOWN	918
Uroplakin-3b	0.026	0.015	DOWN	275
ADP-ribosylation factor-like protein 5A	0.389	0.043	DOWN	179
N-acetylglucosamine-6-sulfatase	0.514	0.014	DOWN	544
Phospholipase D4	0.010	0.001	DOWN	503
Mitochondrial Rho GTPase 1	0.690	0.045	DOWN	631
Transmembrane 9 superfamily member 4	0.580	0.036	DOWN	643
Calcium-binding mitochondrial carrier protein Aralar1	0.742	0.018	DOWN	677
Coagulation factor XIII A chain	0.012	0.002	DOWN	732
Protein FAM49A	0.244	0.030	DOWN	323
Exopolyphosphatase PRUNE1	0.654	0.001	DOWN	454
Neutral cholesterol ester hydrolase 1	0.271	0.035	DOWN	408
LHFPL tetraspan subfamily member 6 protein	0.451	0.041	DOWN	200
Golgi resident protein GCP60	0.482	0.050	DOWN	525
Trifunctional enzyme subunit alpha, mitochondrial	0.674	0.016	DOWN	763
Copine-3	0.532	0.022	DOWN	533
T-complex protein 11-like protein 1	0.627	0.011	DOWN	509

Complex I assembly factor TIMMDC1, mitochondrial	0.594	0.029	DOWN	285
ADP-ribosylation factor-related protein 1	0.419	0.032	DOWN	201
RAD50-interacting protein 1	0.491	0.016	DOWN	792
Chondroitin sulfate N-acetylgalactosaminyltransferase 2	0.389	0.010	DOWN	542
Endonuclease domain-containing 1 protein	0.029	0.003	DOWN	501
Vacuolar protein sorting-associated protein 52 homolog	0.664	0.045	DOWN	723
E3 ubiquitin-protein ligase Itchy	0.588	0.005	DOWN	864
Latent-transforming growth factor beta-binding protein 1	0.068	0.032	DOWN	1712
Synaptojanin-1 (EC 3.1.3.36)	0.660	0.049	DOWN	1574
Myosin light chain 6B	0.037	0.004	DOWN	207
Membralin	0.042	0.005	DOWN	574
BMP-binding endothelial regulator protein	0.134	0.046	DOWN	685
Rho GTPase-activating protein 18	0.810	0.041	DOWN	663
Fermitin family homolog 3	0.016	0.002	DOWN	665
Dynamin-1-like protein	0.727	0.034	DOWN	742
Serine/threonine-protein kinase Nek9	0.581	0.039	DOWN	984
Leucine-rich repeat-containing protein 25	0.032	0.004	DOWN	297
Nck-associated protein 1-like	0.044	0.005	DOWN	1134
Very-long-chain (3R)-3-hydroxyacyl-CoA dehydratase 3	0.537	0.022	DOWN	362
Shootin-1	0.086	0.023	DOWN	631
EMILIN-2	0.008	0.001	DOWN	1074
ATP-dependent RNA helicase DDX54	0.603	0.029	DOWN	874
SEC14-like protein 4	0.094	0.011	DOWN	403
Exocyst complex component 1	0.616	0.007	DOWN	894
TBC1 domain family member 22A	0.591	0.036	DOWN	516
Apolipoprotein B receptor	0.052	0.027	DOWN	942
Fibrinogen gamma chain	0.031	0.019	DOWN	436
39S ribosomal protein L50, mitochondrial	0.034	0.004	DOWN	159
Solute carrier family 35 member F6	0.417	0.023	DOWN	372
Coiled-coil domain-containing protein 115	0.140	0.034	DOWN	180
Group XV phospholipase A2	0.623	0.018	DOWN	412
Translocating chain-associated membrane protein 1	0.762	0.003	DOWN	374
RUS1 family protein C16orf58 homolog	0.599	0.048	DOWN	466
Haloacid dehalogenase-like hydrolase domain-containing 5	0.339	0.012	DOWN	419
Transmembrane protein 205	0.481	0.007	DOWN	189
Egl nine homolog 1	0.658	0.046	DOWN	400
Acyl-CoA:lysophosphatidylglycerol acyltransferase 1	0.581	0.039	DOWN	370
Serotransferrin	0.004	0.000	DOWN	697
cGMP-dependent 3',5'-cyclic phosphodiesterase	0.060	0.007	DOWN	939
Endothelial cell-selective adhesion molecule	0.092	0.050	DOWN	394
Tubulointerstitial nephritis antigen-like	0.064	0.008	DOWN	466
Serine/threonine-protein kinase 26	0.315	0.050	DOWN	416

GTPase IMAP family member 4	0.130	0.016	DOWN	328
EMILIN-1	0.061	0.011	DOWN	1017
N-acylneuraminate cytidylyltransferase	0.297	0.014	DOWN	432
Transmembrane glycoprotein NMB	0.004	0.002	DOWN	574
Histone chaperone ASF1A	0.236	0.008	DOWN	204
Prenylcysteine oxidase	0.483	0.003	DOWN	505
39S ribosomal protein L20, mitochondrial	0.617	0.025	DOWN	149
Exosome complex component RRP46	0.522	0.015	DOWN	235
Vitamin K epoxide reductase complex subunit 1	0.630	0.023	DOWN	161
IST1 homolog	0.674	0.045	DOWN	362
EEF1A lysine methyltransferase 1	0.209	0.047	DOWN	214
Phosphoacetylglucosamine mutase	0.750	0.046	DOWN	542
Transmembrane emp24 domain-containing protein 10	0.559	0.023	DOWN	219
Plasminogen receptor	0.628	0.034	DOWN	147
GRIP and coiled-coil domain-containing protein 1	0.298	0.009	DOWN	778
SUN domain-containing protein 1	0.606	0.004	DOWN	913
Nitric oxide synthase-interacting protein	0.436	0.003	DOWN	301
Esterase OVCA2	0.557	0.045	DOWN	225
Adipocyte plasma membrane-associated protein	0.533	0.012	DOWN	415
LysM and putative peptidoglycan-binding domain-containing protein 2	0.043	0.001	DOWN	215
Coiled-coil domain-containing protein 91	0.599	0.025	DOWN	442
Glycine amidinotransferase, mitochondrial	0.077	0.023	DOWN	423
Trimeric intracellular cation channel type B	0.077	0.003	DOWN	292
AP-2 complex subunit beta	0.703	0.012	DOWN	937
Armadillo repeat-containing protein 8	0.763	0.040	DOWN	673
Matrix remodeling-associated protein 8	0.707	0.000	DOWN	442
Sushi domain-containing protein 2	0.707	0.016	DOWN	820
Pre-mRNA-splicing factor SYF1	0.130	0.027	DOWN	855
	0.423	0.048		
N-acetylneuraminate lyase  ATP synthase subunit d, mitochondrial	0.829	0.001	DOWN	320 161
MICOS complex subunit Mic26	0.829	0.042	DOWN	198
Fibroblast growth factor 23	0.112	0.042	DOWN	251
Sciellin	0.018	0.002	DOWN	652
Allograft inflammatory factor 1-like	0.470	0.020	DOWN	150
Secretory carrier-associated membrane protein 2	0.570	0.043	DOWN	329
Decreum y carrier-associated inclifficially Divident 4	0.570			219
	0.721	0.026		
Trafficking protein particle complex subunit 4	0.721	0.026	DOWN	
Trafficking protein particle complex subunit 4 Reticulon-3	0.761	0.031	DOWN	964
Trafficking protein particle complex subunit 4 Reticulon-3 Hematopoietic prostaglandin D synthase	0.761 0.121	0.031 0.015	DOWN DOWN	964 199
Trafficking protein particle complex subunit 4  Reticulon-3  Hematopoietic prostaglandin D synthase  Glycosylated lysosomal membrane protein  Pleckstrin	0.761	0.031	DOWN	964

			1	
P2X purinoceptor 4	0.070	0.042	DOWN	388
Sphingomyelin phosphodiesterase 3	0.057	0.012	DOWN	655
Prolargin	0.019	0.006	DOWN	378
Ras GTPase-activating-like protein IQGAP1	0.712	0.043	DOWN	1657
Sacsin	0.639	0.018	DOWN	4582
Peroxisomal biogenesis factor 3	0.662	0.010	DOWN	372
Spastin	0.250	0.034	DOWN	614
Microfibrillar-associated protein 5	0.056	0.032	DOWN	164
Tumor necrosis factor receptor superfamily member 10B	0.049	0.006	DOWN	381
A disintegrin and metalloproteinase with thrombospondin motifs 5	0.036	0.006	DOWN	930
Interferon-activable protein 202	0.477	0.028	DOWN	445
Thymidine kinase 2, mitochondrial	0.763	0.004	DOWN	270
Zinc finger E-box-binding homeobox 2	0.496	0.046	DOWN	1215
Transmembrane emp24 domain-containing protein 2	0.638	0.036	DOWN	201
Serine protease HTRA1	0.071	0.042	DOWN	480
Periplakin	0.597	0.031	DOWN	1755
Glycosylphosphatidylinositol anchor attachment 1 protein	0.584	0.037	DOWN	621
MAGUK p55 subfamily member 2	0.026	0.003	DOWN	552
Prostaglandin F2 receptor negative regulator	0.164	0.019	DOWN	879
Type-1 angiotensin II receptor-associated protein	0.575	0.011	DOWN	161
Maleylacetoacetate isomerase	0.389	0.017	DOWN	216
Exostosin-like 3	0.089	0.010	DOWN	918
Reversion-inducing cysteine-rich protein with Kazal motifs	0.093	0.041	DOWN	971
Pantetheinase	0.021	0.007	DOWN	512
Platelet factor 4	0.018	0.002	DOWN	105
Glycogen	0.693	0.018	DOWN	738
Angiopoietin-related protein 4	0.052	0.031	DOWN	410
General vesicular transport factor p115	0.666	0.035	DOWN	959
Myotubularin	0.405	0.012	DOWN	603
Uroplakin-1b	0.040	0.021	DOWN	260
Oxidoreductase HTATIP2	0.595	0.009	DOWN	242
Cytokine receptor-like factor 3	0.712	0.005	DOWN	442

BDEs, bile duct epithelial cells; Ger, generation; HOCs, hepatic oval cells; LFQ, label-free quantification.

Table SII. Functional annotation of 30 differential proteins with cell differentiation in BDE  $4^{th}$  and  $8^{th}$  Ger and HOCs group by NCBI.

Protein name	Length (kDa)	Function
Ninjurin-1	152	FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion molecule involved in various processes such as inflammation, cell death, axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008, PubMed:24347169, PubMed:24917672, PubMed:31526566, PubMed:33472215). Promotes cell adhesion by mediating homophilic interactions via its extracellular N-terminal adhesion motif (N-NAM) (PubMed:24917672, PubMed:30510259). Involved in the progression of the inflammatory stress by promoting cell-to-cell interactions between immune cells and endothelial cells (PubMed:24917672, PubMed:30510259). Involved in leukocyte migration during inflammation by promoting transendothelial migration of macrophages via homotypic binding (PubMed:24917672). Promotes the migration of monocytes across the brain endothelium to central nervous system inflammatory lesions (By similarity). Acts as a regulator of Toll-like receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during systemic inflammation; directly binds LPS (PubMed:25860173). Acts as a mediator of both programmed and necrotic cell death (PubMed:19557008, PubMed:33472215). Plays a key role in the induction of plasma membrane rupture during programmed and necrotic cell death: oligomerizes in response to death stimuli to mediate plasma membrane rupture (cytolysis), leading to release intracellular molecules named damage-associated molecular patterns (DAMPs) that propagate the inflammatory response (PubMed:33472215). Plays a role in nerve regeneration by promoting maturation of Schwann cells (PubMed:31526566). Acts as a regulator of angiogenesis (PubMed:25766274, PubMed:30354207). Promotes the formation of new vessels by mediating the interaction between capillary pericyte cells and endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates vascular functions in penile tissue as well as vascular formation (PubMed:24979788). Promotes osteoclasts development by enhancing the survival of prefusion osteoclasts (PubMed:30700695). Also involved in cell senescence in a

		ECO:0000269 PubMed:30354207, ECO:0000269 PubMed:30510259,
		ECO:0000269 PubMed:30700695, ECO:0000269 PubMed:31091274,
		ECO:0000269 PubMed:31526566, ECO:0000269 PubMed:33472215}.;
		FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage,
		which has chemotactic activity (PubMed:23142597). Acts as an
		anti-inflammatory mediator by promoting monocyte recruitment, thereby
		ameliorating atherosclerosis (PubMed:32883094).
		{ECO:0000269 PubMed:23142597, ECO:0000269 PubMed:32883094}.
		FUNCTION: Phosphorylates a large number of substrates in the
		cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B,
		ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9
		and VASP (PubMed:10805756, PubMed:19223768). Regulates the
		abundance of compartmentalized pools of its regulatory subunits through
		phosphorylation of PJA2 which binds and ubiquitinates these subunits,
		leading to their subsequent proteolysis (By similarity). RORA is activated
		by phosphorylation. Required for glucose-mediated adipogenic
		differentiation increase and osteogenic differentiation inhibition from
		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
		circulating platelets in a resting state by phosphorylating proteins in
		numerous platelet inhibitory pathways when in complex with
		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
		thrombin and collagen disrupt these complexes and free active PRKACA
	351	stimulates platelets and leads to platelet aggregation by phosphorylating
cAMP-dependent protein		VASP. RYR2 channel activity is potentiated by phosphorylation in
kinase catalytic subunit		presence of luminal Ca(2+), leading to reduced amplitude and increased
alpha		frequency of store overload-induced Ca(2+) release (SOICR)
		characterized by an increased rate of Ca(2+) release and propagation
		`
		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
	1	(

Interleukin-4 receptor subunit alpha	810	ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.; FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm flagellum to promote spermatozoa capacitation.  {ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.  FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in promoting Th2 differentiation. The IL4/IL13 responses are involved in regulating IgE production and, chemokine and mucus production at sites of allergic inflammation. In certain cell types, can signal through activation of insulin receptor substrates, IRS1/IRS2.  FUNCTION: Required for mitosis progression. Promotes the nucleation
Protein NEDD1	660	of microtubules from the spindle (By similarity). May play an important role during the embryonic development and differentiation of the central nervous system (PubMed:1378265).  {ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
Protein phosphatase 3 catalytic subunit alpha	521	FUNCTION: Calcium-dependent, calmodulin-stimulated protein phosphatase which plays an essential role in the transduction of intracellular Ca(2+)-mediated signals (PubMed:7791792, PubMed:26794871). Many of the substrates contain a PxIxIT motif and/or a LxVP motif (By similarity). In response to increased Ca(2+) levels, dephosphorylates and activates phosphatase SSH1 which results in cofilin dephosphorylation (By similarity). In response to increased Ca(2+) levels following mitochondrial depolarization, dephosphorylates DNM1L inducing DNM1L translocation to the mitochondrion (By similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+) release probability at hippocampal neuronal soma and synaptic terminals (By similarity). Dephosphorylates heat shock protein HSPB1 (By similarity). Dephosphorylates and activates transcription factor NFATC1 (By similarity). Dephosphorylates and inactivates transcription factor ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation from 14-3-3 proteins (By similarity). Required for postnatal development of the nephrogenic zone and superficial glomeruli in the kidneys, cell cycle homeostasis in the nephrogenic zone, and ultimately normal kidney function (PubMed:15509543). Plays a role in intracellular AQP2 processing and localization to the apical membrane in the kidney, may thereby be required for efficient kidney filtration (PubMed:16735444). Required for secretion of salivary enzymes amylase, peroxidase, lysozyme and sialic acid via formation of secretory vesicles in the submandibular glands (PubMed:21435446). Required for calcineurin activity and homosynaptic depotentiation in the hippocampus (PubMed:10200317). Required for normal differentiation and survival of keratinocytes and therefore required for epidermis superstructure formation (PubMed:19626032). Positively regulates osteoblastic bone

		formation, via promotion of osteoblast differentiation
		(PubMed:16286645). Positively regulates osteoclast differentiation,
		potentially via NFATC1 signaling (PubMed:16968888). May play a role
		in skeletal muscle fiber type specification, potentially via NFATC1
		signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK
		signaling via inhibition of nuclear translocation of the transcription
		factors RELA and RELB (PubMed:26029823). Required for
		antigen-specific T-cell proliferation response (PubMed:8627154).
		{ECO:0000250 UniProtKB:P48452, ECO:0000250 UniProtKB:P63329,
		ECO:0000250 UniProtKB:Q08209, ECO:0000269 PubMed:10200317,
		ECO:0000269 PubMed:12773574, ECO:0000269 PubMed:15509543,
		ECO:0000269 PubMed:16286645, ECO:0000269 PubMed:16735444,
		ECO:0000269 PubMed:16968888, ECO:0000269 PubMed:19626032,
		ECO:0000269 PubMed:21435446, ECO:0000269 PubMed:26029823,
		ECO:0000269 PubMed:26794871, ECO:0000269 PubMed:7791792,
		ECO:0000269 PubMed:8627154}.
		FUNCTION: Self-ligand receptor of the signaling lymphocytic activation
		molecule (SLAM) family. SLAM receptors triggered by homo- or
		heterotypic cell-cell interactions are modulating the activation and
		differentiation of a wide variety of immune cells and thus are involved in
		the regulation and interconnection of both innate and adaptive immune
		response. Activities are controlled by presence or absence of small
		cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2
		(PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity
		dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases
		proliferative responses of activated T-cells and SH2D1A/SAP does not
		seen be required for this process. Homophilic interactions enhance
		interferon gamma/IFNG secretion in lymphocytes and induce platelet
		stimulation via a SH2D1A/SAP-dependent pathway. May serve as a
		marker for hematopoietic progenitor cells (By similarity). Required for a
SLAM family member 5	329	prolonged T-cell:B-cell contact, optimal T follicular helper function, and
		germinal center formation (PubMed:20153220). In germinal centers
		involved in maintaining B cell tolerance and in preventing autoimmunity
		(PubMed:25801429). In mast cells negatively regulates high affinity
		immunoglobulin epsilon receptor signaling; independent of SH2D1A and
		SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In
		macrophages enhances LPS-induced MAPK phosphorylation and
		NF-kappaB activation and modulates LPS-induced cytokine secretion;
		involving ITSM 2 (PubMed:20628063). Positively regulates
		macroautophagy in primary dendritic cells via stabilization of IRF8;
		inhibits TRIM21-mediated proteasomal degradation of IRF8 (By
		similarity). {ECO:0000250 UniProtKB:Q9UIB8,
		ECO:0000269 PubMed:16037392, ECO:0000269 PubMed:20153220,
		ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259,
	<u> </u>	<u>'</u>

		ECO:0000269 PubMed:25801429, ECO:0000305}.
		FUNCTION: Plays a role in primary cilia formation (By similarity). May
		act as a downstream effector of HOXC8 possibly by transducing or
		transmitting extracellular information required for axial skeletal
Transmembrane anterior		patterning during development (By similarity). May be involved in
posterior transformation	564	cartilage and bone development (By similarity). May play a role in the
protein 1		differentiation of cranial neural crest cells (By similarity).
		{ECO:0000250 UniProtKB:A2BIE7,
		ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
		FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm
		diameter microfibrils of the extracellular matrix, which conveys both
		structural and regulatory properties to load-bearing connective tissues.
		Fibrillin-1-containing microfibrils provide long-term force bearing
		structural support. In tissues such as the lung, blood vessels and skin,
		microfibrils form the periphery of the elastic fiber, acting as a scaffold for
		the deposition of elastin. In addition, microfibrils can occur as
		elastin-independent networks in tissues such as the ciliary zonule, tendon,
		cornea and glomerulus where they provide tensile strength and have
		, , , , , , , , , , , , , , , , , , ,
		anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis
		through specific interactions with growth factors, such as the bone
		morphogenetic proteins (BMPs), growth and differentiation factors
		(GDFs) and latent transforming growth factor-beta-binding proteins
		(LTBPs), cell-surface integrins and other extracellular matrix protein and
		proteoglycan components (By similarity). Regulates osteoblast
		maturation by controlling TGF-beta bioavailability and calibrating
E.1 .11. 1	2072	TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively
Fibrillin-1	2873	regulates osteoclastogenesis by binding and sequestering an osteoclast
		differentiation and activation factor TNFSF11. This leads to disruption of
		TNFSF11-induced Ca(2+) signaling and impairment of
		TNFSF11-mediated nuclear translocation and activation of transcription
		factor NFATC1 which regulates genes important for osteoclast
		differentiation and function (PubMed:24039232). Mediates cell adhesion
		via its binding to cell surface receptors integrins ITGAV:ITGB3 and
		ITGA5:ITGB1. Binds heparin and this interaction plays an important role
		in the assembly of microfibrils (By similarity).
		{ECO:0000250 UniProtKB:P35555, ECO:0000269 PubMed:20855508,
		ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine
		secreted by white adipose tissue that plays an important regulatory role in
		the glucose metabolism of liver, muscle and pancreas
		(PubMed:31230984, PubMed:30997682). Hormone that targets the liver
		in response to fasting to increase plasma glucose levels
		(PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface
		of hepatocytes and promotes hepatocyte glucose release by activating the
		protein kinase A activity in the liver, resulting in rapid glucose release

		into the circulation (PubMed:31230984). May act as a regulator of adaptive thermogenesis by inhibiting browning and energy consumption, while increasing lipid deposition in white adipose tissue (PubMed:33705351). Also acts as an orexigenic hormone that increases appetite: crosses the blood brain barrier and exerts effects on the hypothalamus (PubMed:29106398). In the arcuate nucleus of the hypothalamus, asprosin directly activates orexigenic AgRP neurons and indirectly inhibits anorexigenic POMC neurons, resulting in appetite stimulation (PubMed:29106398, PubMed:32337066). Activates orexigenic AgRP neurons via binding to the olfactory receptor Olfr734 (PubMed:32337066). May also play a role in sperm motility in testis via
		interaction with Olfr734 receptor (PubMed:31798959).  {ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682, ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959, ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.  FUNCTION: May play a role in intercellular signaling and in connecting
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cell motility, growth and differentiation. Binds hyaluronic acid.
All-trans-retinol 13,14-reductase	609	FUNCTION: Catalyzes the saturation of all-trans-retinol to all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779, PubMed:19139408). Does not exhibit any activity toward all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers (PubMed:15358783). May play a role in the metabolism of vitamin A (PubMed:15358783, PubMed:17253779). Independently of retinol conversion, may regulate liver metabolism upstream of MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This effect seems not to mimic the in vivo situation in which animals show increased adiposity in the absence of RETSAT (PubMed:19940255). {ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255}, ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
Calcium-transporting ATPase type 2C member 1	918	FUNCTION: ATP-driven pump that supplies the Golgi apparatus with Ca(2+) and Mn(2+) ions, both essential cofactors for processing and trafficking of newly synthesized proteins in the secretory pathway (By similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on the cytoplasmic side of the membrane and delivers them to the lumenal side. The transfer of ions across the membrane is coupled to ATP hydrolysis and is associated with a transient phosphorylation that shifts the pump conformation from inward-facing to outward-facing state (By similarity). Plays a primary role in the maintenance of Ca(2+) homeostasis in the trans-Golgi compartment with a functional impact on Golgi and post-Golgi protein sorting as well as a structural impact on cisternae morphology. Responsible for loading the Golgi stores with

		Ca(21) in a in lambin and a second tracking to 1.
		Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation
		and epidermis integrity (By similarity). Participates in Ca(2+) and
		Mn(2+) ions uptake into the Golgi store of hippocampal neurons and
		regulates protein trafficking required for neural polarity
		(PubMed:19793975). May also play a role in the maintenance of Ca(2+)
		and Mn(2+) homeostasis and signaling in the cytosol while preventing
		cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194,
		ECO:0000269 PubMed:19793975}.
		FUNCTION: Phosphodiesterase (PDE) that has higher activity toward
Evanalembasubatasa		cAMP than cGMP, as substrate. Plays a role in cell proliferation,
Exopolyphosphatase	454	migration and differentiation, and acts as a negative regulator of NME1.
PRUNE1		Plays a role in the regulation of neurogenesis. Involved in the regulation
		of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma		FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl
membrane-associated	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte
protein		differentiation. {ECO:0000250}.
F		FUNCTION: Regulator of phosphate homeostasis (By similarity).
		Inhibits renal tubular phosphate transport by reducing SLC34A1 levels
		(By similarity). Acts directly on the parathyroid to decrease PTH
Fibroblast growth factor	251	secretion (By similarity). Regulator of vitamin-D metabolism (By
23	231	similarity). Negatively regulates osteoblasts differentiation and matrix
		mineralization (By similarity). Up-regulates EGR1 expression in the
		presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
		FUNCTION: Receptor for extracellularly released ATP acting as a
		ligand-gated ion channel that plays multiple role in immunity and central
		nervous system physiology (PubMed:26456657, PubMed:35119925).
		Plays a key role in initial steps of T-cell activation and Ca(2+)
		microdomain formation (PubMed:35119925). Participates also in basal
P2X purinoceptor 4	388	T-cell activity without TCR/CD3 stimulation (PubMed:35119925).
1 211 parmocopior 1	200	Promotes the differentiation and activation of Th17 cells via expression
		of retinoic acid-related orphan receptor C/RORC (By similarity). Upon
		activation, drives microglia motility via the PI3K/Akt pathway
		(PubMed:17299767). {ECO:0000250 UniProtKB:Q99571,
		ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:26456657,
		ECO:0000269 PubMed:35119925}.
		FUNCTION: Glycosyltransferase which regulates the biosynthesis of
Exostosin-like 3		heparan sulfate (HS). Important for both skeletal development and
	918	hematopoiesis, through the formation of HS proteoglycans (HSPGs).
		Required for the function of REG3A in regulating keratinocyte
		proliferation and differentiation (By similarity).
		{ECO:0000250 UniProtKB:O43909}.
Vacuolar protein		FUNCTION: Component of the ESCRT-I complex, a regulator of
sorting-associated protein	285	vesicular trafficking process. Required for the sorting of endocytic
37B	203	ubiquitinated cargos into multivesicular bodies. May be involved in cell
עונ		abiquitinated eargos into multivestediai bodies. May be involved in cen

		growth and differentiation (By similarity). {ECO:0000250}.
Ubiquitin-conjugating enzyme E2 variant 1	147	FUNCTION: Has no ubiquitin ligase activity on its own. The UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical poly-ubiquitin chains that are linked through 'Lys-63'. This type of poly-ubiquitination activates IKK and does not seem to involve protein degradation by the proteasome. Plays a role in the activation of NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates transcriptional activation of target genes. Plays a role in the control of progress through the cell cycle and differentiation (By similarity). Plays a role in the error-free DNA repair pathway and contributes to the survival of cells after DNA damage. Promotes TRIM5 capsid-specific restriction activity and the UBE2V1-UBE2N heterodimer acts in concert with TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate the MAP3K7/TAK1 complex which in turn results in the induction and expression of NF-kappa-B and MAPK-responsive inflammatory genes (By similarity). Together with RNF135 and UBE2N, catalyzes the viral RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to activate the downstream signaling pathway that leads to interferon beta production (By similarity). UBE2V1-UBE2N together with TRAF3IP2 E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6, a component of IL17A-mediated signaling pathway. {ECO:0000250,
Ubiquitin carboxyl-terminal hydrolase 25	1055	ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.  FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties conjugated to substrates and thus, functions to process newly synthesized Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains and prevents proteasomal degradation of substrates. Hydrolyzes both 'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity). {ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m) may have a role in the regulation of muscular differentiation and function.
Forkhead box protein K1	719	FUNCTION: Transcriptional regulator involved in different processes such as glucose metabolism, aerobic glycolysis, muscle cell differentiation and autophagy (PubMed:25402684, PubMed:29861159, PubMed:30700909). Recognizes and binds the forkhead DNA sequence motif (5'-GTAAACA-3') and can both act as a transcription activator or repressor, depending on the context (PubMed:25402684, PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a key regulator of metabolic reprogramming towards aerobic glycolysis, a process in which glucose is converted to lactate in the presence of oxygen (PubMed:30700909). Acts by promoting expression of enzymes for glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate kinase (PKLR) and lactate dehydrogenase), while suppressing further oxidation of pyruvate in the mitochondria by up-regulating pyruvate dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably plays a role in gluconeogenesis during overnight fasting, when lactate

		from white adipose tissue and muscle is the main substrate
		(PubMed:30700909). Involved in mTORC1-mediated metabolic
		reprogramming: in response to mTORC1 signaling, translocates into the
		nucleus and regulates the expression of genes associated with glycolysis
		and downstream anabolic pathways, such as HIF1A, thereby regulating
		glucose metabolism (PubMed:29861159). Together with FOXK2, acts as
		a negative regulator of autophagy in skeletal muscle: in response to
		starvation, enters the nucleus, binds the promoters of autophagy genes
		and represses their expression, preventing proteolysis of skeletal muscle
		proteins (PubMed:25402684). Acts as a transcriptional regulator of the
		myogenic progenitor cell population in skeletal muscle
		(PubMed:8007964, PubMed:9271401, PubMed:12446708,
		PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
		of myoglobin (MB) gene, regulating the myogenic progenitor cell
		population (PubMed:8007964, PubMed:9271401). Promotes muscle
		progenitor cell proliferation by repressing the transcriptional activity of
		FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
		PubMed:22956541). Involved in remodeling processes of adult muscles
		that occur in response to physiological stimuli (PubMed:9271401,
		PubMed:22956541). Required to correct temporal orchestration of
		molecular and cellular events necessary for muscle repair
		(PubMed:10792059). Represses myogenic differentiation by inhibiting
		MEFC activity (PubMed:22956541). Positively regulates
		Wnt/beta-catenin signaling by translocating DVL into the nucleus (By
		similarity). Reduces virus replication, probably by binding the interferon
		stimulated response element (ISRE) to promote antiviral gene expression
		(By similarity). {ECO:0000250 UniProtKB:P85037,
		ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:12446708,
		ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:25402684,
		ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:30700909,
		ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.
		FUNCTION: Component of the cleavage and polyadenylation specificity
		factor (CPSF) complex that plays a key role in pre-mRNA 3'-end
		formation, recognizing the AAUAAA signal sequence and interacting
		with poly(A) polymerase and other factors to bring about cleavage and
Cleavage and		poly(A) addition. Has endonuclease activity, and functions as mRNA
•		3'-end-processing endonuclease. Also involved in the histone 3'-end
polyadenylation specificity factor subunit 3	684	pre-mRNA processing. U7 snRNP-dependent protein that induces both
		the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a
		5' to 3' exonuclease for degrading the subsequent downstream cleavage
		product (DCP) of mature histone mRNAs. Cleavage occurs after the
		5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl
		group on the upstream fragment containing the stem loop (SL) and 5'
		phosphate on the downstream cleavage product (DCP) starting with CU

	ı	T
		nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive
		and degrades the DCP RNA substrate even after complete removal of the
		U7-binding site. Binds to the downstream cleavage product (DCP) of
		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
		(miRNAs) during embryonic stem cell differentiation via its interaction
		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
		primary transcript except miR-92a (PubMed:26255770). Only required
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
		pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
		ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
		FUNCTION: Serine/threonine kinase which acts as an essential
		component of the MAP kinase signal transduction pathway.
		MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an
		important role in the MAPK/ERK cascade. They participate also in a
		signaling cascade initiated by activated KIT and KITLG/SCF. Depending
		on the cellular context, the MAPK/ERK cascade mediates diverse
		biological functions such as cell growth, adhesion, survival and
		differentiation through the regulation of transcription, translation,
		cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role
		in initiation and regulation of meiosis, mitosis, and postmitotic functions
		in differentiated cells by phosphorylating a number of transcription
		factors. About 160 substrates have already been discovered for ERKs.
	358	Many of these substrates are localized in the nucleus, and seem to
		participate in the regulation of transcription upon stimulation. However,
Mitogen-activated protein		other substrates are found in the cytosol as well as in other cellular
kinase 1		organelles, and those are responsible for processes such as translation,
		mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also
		involved in the regulation of the endosomal dynamics, including
		lysosome processing and endosome cycling through the perinuclear
		recycling compartment (PNRC); as well as in the fragmentation of the
		Golgi apparatus during mitosis. The substrates include transcription
		factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1),
		cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT,
		PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD,
		BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of
		translation (such as EIF4EBP1) and a variety of other signaling-related
		molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases
		(such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3,
		RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2,

		RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and
		phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other
		substrates which enable the propagation the MAPK/ERK signal to
		additional cytosolic and nuclear targets, thereby extending the specificity
		of the cascade. Mediates phosphorylation of TPR in response to EGF
		stimulation. May play a role in the spindle assembly checkpoint.
		Phosphorylates PML and promotes its interaction with PIN1, leading to
		PML degradation. Phosphorylates CDK2AP2 (By similarity).
		{ECO:0000250 UniProtKB:P28482, ECO:0000250 UniProtKB:P63086,
		ECO:0000269 PubMed:10753946, ECO:0000269 PubMed:11702783,
		ECO:0000269 PubMed:12134156, ECO:0000303 PubMed:16393692,
		ECO:0000303 PubMed:19565474, ECO:0000303 PubMed:21779493}.;
		FUNCTION: Acts as a transcriptional repressor. Binds to a
		[GC]AAA[GC] consensus sequence. Repress the expression of interferon
		gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1,
		IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1.
		Transcriptional activity is independent of kinase activity.
		{ECO:0000250 UniProtKB:P28482}.
		FUNCTION: RNA-binding protein that acts as a key regulator of
		N6-methyladenosine (m6A) methylation of RNAs, thereby regulating
		different processes, such as hematopoietic cell homeostasis, alternative
		splicing of mRNAs and X chromosome inactivation mediated by Xist
		RNA (PubMed:29535189). Associated component of the WMM
		complex, a complex that mediates N6-methyladenosine (m6A)
		methylation of RNAs, a modification that plays a role in the efficiency of
		mRNA splicing and RNA processing (PubMed:29535189). Plays a key
		role in m6A methylation, possibly by binding target RNAs and recruiting
		the WMM complex (PubMed:29535189). Involved in random X
		inactivation mediated by Xist RNA: acts by binding Xist RNA and
		recruiting the WMM complex, which mediates m6A methylation, leading
		to target YTHDC1 reader on Xist RNA and promoting transcription
RNA-binding protein 15	962	repression activity of Xist (By similarity). Required for the development
		of multiple tissues, such as the maintenance of the homeostasis of
		long-term hematopoietic stem cells and for megakaryocyte (MK) and
		B-cell differentiation (PubMed:17283045, PubMed:17376872,
		PubMed:18981216, PubMed:25468569). Regulates megakaryocyte
		differentiation by regulating alternative splicing of genes important for
		megakaryocyte differentiation; probably regulates alternative splicing via
		m6A regulation (By similarity). Required for placental vascular
		branching morphogenesis and embryonic development of the heart and
		spleen (PubMed:18981216). Acts as a regulator of thrombopoietin
		response in hematopoietic stem cells by regulating alternative splicing of
		MPL (PubMed:25468569). May also function as an mRNA export factor,
		stimulating export and expression of RTE-containing mRNAs which are

		present in many retrotransposons that require to be exported prior to
		splicing (By similarity). High affinity binding of pre-mRNA to RBM15
		may allow targeting of the mRNP to the export helicase DBP5 in a
		manner that is independent of splicing-mediated NXF1 deposition,
		resulting in export prior to splicing (By similarity). May be implicated in
		HOX gene regulation (By similarity).
		{ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:17283045,
		ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18981216,
		ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29535189}.
		FUNCTION: Transcription coactivator which associates with nuclear
		receptors, transcriptional coactivators including EP300, CREBBP and
		NCOA1, and basal transcription factors like TBP and TFIIA to facilitate
		nuclear receptors-mediated transcription. May thereby play an important
		role in establishing distinct coactivator complexes under different cellular
		conditions. Plays a role in thyroid hormone receptor and estrogen
		receptor transactivation (By similarity). Also involved in androgen
		receptor transactivation (PubMed:12077347). Plays a pivotal role in the
Activating signal		transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of
cointegrator 1	581	transrepression between nuclear receptor and either AP1 or NF-kappa-B.
connegrator 1		
		May play a role in the development of neuromuscular junction (By
		similarity). May play a role in late myogenic differentiation
		(PubMed:27008887). Also functions as part of the RQC trigger (RQT)
		complex that activates the ribosome quality control (RQC) pathway, a
		pathway that degrades nascent peptide chains during problematic
		translation (By similarity). {ECO:0000250 UniProtKB:Q15650,
		ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
		ECO:0000269 PubMed:27008887}.
		FUNCTION: Histone methyltransferase that specifically trimethylates
		'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36'
		(H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is
		capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
		similarity). Represents the main enzyme generating H3K36me3, a
		specific tag for epigenetic transcriptional activation (PubMed:18157086,
		PubMed:20133625). Plays a role in chromatin structure modulation
Histone-lysine		during elongation by coordinating recruitment of the FACT complex and
N-methyltransferase	2537	by interacting with hyperphosphorylated POLR2A (By similarity). Acts
SETD2		as a key regulator of DNA mismatch repair in G1 and early S phase by
		generating H3K36me3, a mark required to recruit MSH6 subunit of the
		MutS alpha complex: early recruitment of the MutS alpha complex to
		chromatin to be replicated allows a quick identification of mismatch
		DNA to initiate the mismatch repair reaction (By similarity). Required for
		DNA double-strand break repair in response to DNA damage: acts by
		mediating formation of H3K36me3, promoting recruitment of RAD51
		and DNA repair via homologous recombination (HR) (By similarity).
	l	and Diva repair via nomologous recombination (TIK) (by similarity).

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		Acts as a tumor suppressor (By similarity). H3K36me3 also plays an
		essential role in the maintenance of a heterochromatic state, by recruiting
		DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also
		enhanced in intron-containing genes, suggesting that SETD2 recruitment
		is enhanced by splicing and that splicing is coupled to recruitment of
		elongating RNA polymerase (By similarity). Required during
		angiogenesis (PubMed:20133625). Required for endoderm development
		by promoting embryonic stem cell differentiation toward endoderm: acts
		by mediating formation of H3K36me3 in distal promoter regions of
		FGFR3, leading to regulate transcription initiation of FGFR3
		(PubMed:25242323). In addition to histones, also mediates methylation
		of other proteins, such as tubulins and STAT1 (PubMed:27518565).
		Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B
		(alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis
		and cytokinesis and may be a specific tag in cytoskeletal remodeling
		(PubMed:27518565). Involved in interferon-alpha-induced antiviral
		defense by mediating both monomethylation of STAT1 at 'Lys-525' and
		catalyzing H3K36me3 on promoters of some interferon-stimulated genes
		(ISGs) to activate gene transcription (By similarity).
		{ECO:0000250 UniProtKB:Q9BYW2,
		ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625,
		ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.
		FUNCTION: RNA-binding protein that plays a central role in
		myelinization (PubMed:10864952, PubMed:11917126). Also required for
		visceral endoderm function and blood vessel development
		(PubMed:11892011, PubMed:16470614). Binds to the
		5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence
		(PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA
		export, mRNA stability and protein translation, as well as cellular
		processes including apoptosis, cell cycle, glial cell fate and development
		(PubMed:10535969, PubMed:12467586, PubMed:11297509,
		PubMed:11917126, PubMed:15568022). Required to protect and promote
		stability of mRNAs such as MBP and CDKN1B which promotes
Protein quaking	341	oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022).
		Participates in mRNA transport by regulating the nuclear export of MBP
		mRNA (PubMed:12467586). May also play a role in smooth muscle
		development (PubMed:14706070). {ECO:0000269 PubMed:10535969,
		ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509,
		ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126,
		ECO:0000269 PubMed:12467586, ECO:0000269 PubMed:14706070,
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388,
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388, ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388, ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved in regulation of mRNA splicing of MAG pre-mRNA by acting as a
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388, ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved

TBC1 domain family member 1	1255	{ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can induce apoptosis, while heterodimerization with other isoforms results in nuclear translocation of isoform 3 and suppression of apoptosis.  {ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.  FUNCTION: May act as a GTPase-activating protein for Rab family protein(s). May play a role in the cell cycle and differentiation of various tissues. Involved in the trafficking and translocation of GLUT4-containing vesicles and insulin-stimulated glucose uptake into cells. {ECO:0000269 PubMed:19740738}.
Mesenteric estrogen-dependent adipogenesis protein	303	FUNCTION: Involved in processes that promote adipocyte differentiation, lipid accumulation, and glucose uptake in mature adipocytes. {ECO:0000269 PubMed:22510272}.
SWI/SNF complex subunit SMARCC2	1213	FUNCTION: Involved in transcriptional activation and repression of select genes by chromatin remodeling (alteration of DNA-nucleosome topology). Component of SWI/SNF chromatin remodeling complexes that carry out key enzymatic activities, changing chromatin structure by altering DNA-histone contacts within a nucleosome in an ATP-dependent manner. Can stimulate the ATPase activity of the catalytic subunit of these complexes. May be required for CoREST dependent repression of neuronal specific gene promoters in non-neuronal cells. Belongs to the neural progenitors-specific chromatin remodeling complex (npBAF complex) and the neuron-specific chromatin remodeling complex (nBAF complex). During neural development a switch from a stem/progenitor to a postmitotic chromatin remodeling mechanism occurs as neurons exit the cell cycle and become committed to their adult state. The transition from proliferating neural stem/progenitor cells to postmitotic neurons requires a switch in subunit composition of the npBAF and nBAF complexes. As neural progenitors exit mitosis and differentiate into neurons, npBAF complexes which contain ACTL6A/BAF53A and PHF10/BAF45A, are exchanged for homologous alternative ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in neuron-specific complexes (nBAF). The npBAF complex is essential for the self-renewal/proliferative capacity of the multipotent neural stem cells. The nBAF complex along with CREST plays a role regulating the activity of genes essential for dendrite growth (PubMed:17640523). Critical regulator of myeloid differentiation, controlling granulocytopoiesis and the expression of genes involved in neutrophil granule formation (PubMed:28369036). {ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240, ECO:0000303 PubMed:26601204}.
Protein prune homolog 2	3084	FUNCTION: May play an important role in regulating differentiation, survival and aggressiveness of the tumor cells. {ECO:0000250}.

FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion molecule involved in various processes such as inflammation, cell death, axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008, PubMed:24347169, PubMed:24917672, PubMed:31526566, PubMed:33472215). Promotes cell adhesion by mediating homophilic interactions via its extracellular N-terminal adhesion motif (N-NAM) (PubMed:24917672, PubMed:30510259). Involved in the progression of the inflammatory stress by promoting cell-to-cell interactions between immune cells and endothelial cells (PubMed:24917672, PubMed:30510259). Involved in leukocyte migration during inflammation by promoting transendothelial migration of macrophages via homotypic binding (PubMed:24917672). Promotes the migration of monocytes across the brain endothelium to central nervous system inflammatory lesions (By similarity). Acts as a regulator of Toll-like receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during systemic inflammation; directly binds LPS (PubMed:25860173). Acts as a mediator of both programmed and necrotic cell death (PubMed:19557008, PubMed:33472215). Plays a key role in the induction of plasma membrane rupture during programmed and necrotic cell death: oligomerizes in response to death stimuli to mediate plasma membrane rupture (cytolysis), leading to release intracellular molecules named damage-associated molecular patterns (DAMPs) that propagate Ninjurin-1 152 the inflammatory response (PubMed:33472215). Plays a role in nerve regeneration by promoting maturation of Schwann cells (PubMed:31526566). Acts as a regulator of angiogenesis (PubMed:25766274, PubMed:30354207). Promotes the formation of new vessels by mediating the interaction between capillary pericyte cells and endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates vascular functions in penile tissue as well as vascular formation (PubMed:24979788). Promotes osteoclasts development by enhancing the survival of prefusion osteoclasts (PubMed:30700695). Also involved in striated muscle growth and differentiation (PubMed:31091274). Also involved in cell senescence in a p53/TP53 manner, possibly by acting as an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620, PubMed:29073078). {ECO:0000250|UniProtKB:Q92982, ECO:0000269|PubMed:19557008, ECO:0000269|PubMed:23690620, ECO:0000269|PubMed:24347169, ECO:0000269|PubMed:24917672, ECO:0000269|PubMed:24979788, ECO:0000269|PubMed:25766274, ECO:0000269|PubMed:25860173, ECO:0000269|PubMed:29073078, ECO:0000269|PubMed:30354207, ECO:0000269|PubMed:30510259, ECO:0000269|PubMed:30700695, ECO:0000269|PubMed:31091274, ECO:0000269|PubMed:31526566, ECO:0000269|PubMed:33472215}.; FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage,

which has chemotactic activity (PubMed:23142597). Acts as an

		anti-inflammatory mediator by promoting monocyte recruitment, thereby
		ameliorating atherosclerosis (PubMed:32883094).
		{ECO:0000269 PubMed:23142597, ECO:0000269 PubMed:32883094}.
		FUNCTION: Phosphorylates a large number of substrates in the
		cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B,
		ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9
		and VASP (PubMed:10805756, PubMed:19223768). Regulates the
		abundance of compartmentalized pools of its regulatory subunits through
		phosphorylation of PJA2 which binds and ubiquitinates these subunits,
		leading to their subsequent proteolysis (By similarity). RORA is activated
		by phosphorylation. Required for glucose-mediated adipogenic
		differentiation increase and osteogenic differentiation inhibition from
		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
		circulating platelets in a resting state by phosphorylating proteins in
		numerous platelet inhibitory pathways when in complex with
		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
		thrombin and collagen disrupt these complexes and free active PRKACA
		stimulates platelets and leads to platelet aggregation by phosphorylating
		VASP. RYR2 channel activity is potentiated by phosphorylation in
cAMP-dependent protein		presence of luminal Ca(2+), leading to reduced amplitude and increased
kinase catalytic subunit	351	frequency of store overload-induced Ca(2+) release (SOICR)
alpha	351	characterized by an increased rate of Ca(2+) release and propagation
атрпа		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
		ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.;
		FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm
		flagellum to promote spermatozoa capacitation.
		{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.
Interleukin-4 receptor	810	FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples
		1 Souples

subunit alpha		to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in
Subunit aipna		promoting Th2 differentiation. The IL4/IL13 responses are involved in
		regulating IgE production and, chemokine and mucus production at sites
		of allergic inflammation. In certain cell types, can signal through
		activation of insulin receptor substrates, IRS1/IRS2.
		<u> </u>
		FUNCTION: Required for mitosis progression. Promotes the nucleation
D ( NEDD1	660	of microtubules from the spindle (By similarity). May play an important
Protein NEDD1	660	role during the embryonic development and differentiation of the central
		nervous system (PubMed:1378265).
		{ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
		FUNCTION: Calcium-dependent, calmodulin-stimulated protein
		phosphatase which plays an essential role in the transduction of
		intracellular Ca(2+)-mediated signals (PubMed:7791792,
		PubMed:26794871). Many of the substrates contain a PxIxIT motif
		and/or a LxVP motif (By similarity). In response to increased Ca(2+)
		levels, dephosphorylates and activates phosphatase SSH1 which results in
		cofilin dephosphorylation (By similarity). In response to increased
		Ca(2+) levels following mitochondrial depolarization, dephosphorylates
		DNM1L inducing DNM1L translocation to the mitochondrion (By
		similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+)
		release probability at hippocampal neuronal soma and synaptic terminals
		(By similarity). Dephosphorylates heat shock protein HSPB1 (By
		similarity). Dephosphorylates and activates transcription factor NFATC1
		(By similarity). Dephosphorylates and inactivates transcription factor
		ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May
		dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation
Protein phosphatase 3		from 14-3-3 proteins (By similarity). Required for postnatal development
catalytic subunit alpha	521	of the nephrogenic zone and superficial glomeruli in the kidneys, cell
caming the sac aims are in		cycle homeostasis in the nephrogenic zone, and ultimately normal kidney
		function (PubMed:15509543). Plays a role in intracellular AQP2
		processing and localization to the apical membrane in the kidney, may
		thereby be required for efficient kidney filtration (PubMed:16735444).
		Required for secretion of salivary enzymes amylase, peroxidase,
		lysozyme and sialic acid via formation of secretory vesicles in the
		submandibular glands (PubMed:21435446). Required for calcineurin
		activity and homosynaptic depotentiation in the hippocampus
		(PubMed:10200317). Required for normal differentiation and survival of
		keratinocytes and therefore required for epidermis superstructure
		formation (PubMed:19626032). Positively regulates osteoblastic bone
		formation, via promotion of osteoblast differentiation
		(PubMed:16286645). Positively regulates osteoclast differentiation,
		potentially via NFATC1 signaling (PubMed:16968888). May play a role
		in skeletal muscle fiber type specification, potentially via NFATC1
		signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK

		signaling via inhibition of nuclear translocation of the transcription factors RELA and RELB (PubMed:26029823). Required for antigen-specific T-cell proliferation response (PubMed:8627154). {ECO:0000250 UniProtKB:P48452, ECO:0000250 UniProtKB:P63329, ECO:0000250 UniProtKB:Q08209, ECO:0000269 PubMed:10200317, ECO:0000269 PubMed:12773574, ECO:0000269 PubMed:15509543, ECO:0000269 PubMed:16286645, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16968888, ECO:0000269 PubMed:19626032, ECO:0000269 PubMed:21435446, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:26794871, ECO:0000269 PubMed:7791792, ECO:0000269 PubMed:8627154}.
SLAM family member 5	329	FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell:B-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling; independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretion; involving ITSM 2 (PubMed:20628063). Positively regulates macroautophagy in primary dendritic cells via stabilization of IRF8; inhibits TRIM21-mediated proteasomal degradation of IRF8 (By similarity). {ECO:0000259 PubMed:20628063, ECO:0000269 PubMed:20153220, ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259, ECO:0000269 PubMed:25801429, ECO:0000365 .
Transmembrane anterior posterior transformation protein 1	564	FUNCTION: Plays a role in primary cilia formation (By similarity). May act as a downstream effector of HOXC8 possibly by transducing or transmitting extracellular information required for axial skeletal patterning during development (By similarity). May be involved in

	T	T
		cartilage and bone development (By similarity). May play a role in the
		differentiation of cranial neural crest cells (By similarity).
		{ECO:0000250 UniProtKB:A2BIE7,
		ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
		FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm
		diameter microfibrils of the extracellular matrix, which conveys both
		structural and regulatory properties to load-bearing connective tissues.
		Fibrillin-1-containing microfibrils provide long-term force bearing
		structural support. In tissues such as the lung, blood vessels and skin,
		microfibrils form the periphery of the elastic fiber, acting as a scaffold for
		the deposition of elastin. In addition, microfibrils can occur as
		elastin-independent networks in tissues such as the ciliary zonule, tendon,
		cornea and glomerulus where they provide tensile strength and have
		anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis
		through specific interactions with growth factors, such as the bone
		morphogenetic proteins (BMPs), growth and differentiation factors
		(GDFs) and latent transforming growth factor-beta-binding proteins
		(LTBPs), cell-surface integrins and other extracellular matrix protein and
		proteoglycan components (By similarity). Regulates osteoblast
		maturation by controlling TGF-beta bioavailability and calibrating
		TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively
		regulates osteoclastogenesis by binding and sequestering an osteoclast
		differentiation and activation factor TNFSF11. This leads to disruption of
F" 'II' 1	2072	TNFSF11-induced Ca(2+) signaling and impairment of
Fibrillin-1	2873	TNFSF11-mediated nuclear translocation and activation of transcription
		factor NFATC1 which regulates genes important for osteoclast
		differentiation and function (PubMed:24039232). Mediates cell adhesion
		via its binding to cell surface receptors integrins ITGAV:ITGB3 and
		ITGA5:ITGB1. Binds heparin and this interaction plays an important role
		in the assembly of microfibrils (By similarity).
		{ECO:0000250 UniProtKB:P35555, ECO:0000269 PubMed:20855508,
		ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine
		secreted by white adipose tissue that plays an important regulatory role in
		the glucose metabolism of liver, muscle and pancreas
		(PubMed:31230984, PubMed:30997682). Hormone that targets the liver
		in response to fasting to increase plasma glucose levels
		(PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface
		of hepatocytes and promotes hepatocyte glucose release by activating the
		protein kinase A activity in the liver, resulting in rapid glucose release
		into the circulation (PubMed:31230984). May act as a regulator of
		adaptive thermogenesis by inhibiting browning and energy consumption,
		while increasing lipid deposition in white adipose tissue
		(PubMed:33705351). Also acts as an orexigenic hormone that increases
		appetite: crosses the blood brain barrier and exerts effects on the
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		hypothalamus (PubMed:29106398). In the arcuate nucleus of the
		hypothalamus, asprosin directly activates orexigenic AgRP neurons and
		indirectly inhibits anorexigenic POMC neurons, resulting in appetite
		stimulation (PubMed:29106398, PubMed:32337066). Activates
		orexigenic AgRP neurons via binding to the olfactory receptor Olfr734
		(PubMed:32337066). May also play a role in sperm motility in testis via
		interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682,
		ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959,
		ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
		FUNCTION: May play a role in intercellular signaling and in connecting
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cell
•		motility, growth and differentiation. Binds hyaluronic acid.
		FUNCTION: Catalyzes the saturation of all-trans-retinol to
		all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779,
		PubMed:19139408). Does not exhibit any activity toward
		all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers
		(PubMed:15358783). May play a role in the metabolism of vitamin A
		(PubMed:15358783, PubMed:17253779). Independently of retinol
All-trans-retinol		conversion, may regulate liver metabolism upstream of
	609	
13,14-reductase		MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte
		differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This
		effect seems not to mimic the in vivo situation in which animals show
		increased adiposity in the absence of RETSAT (PubMed:19940255).
		{ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779,
		ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255,
		ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
		FUNCTION: ATP-driven pump that supplies the Golgi apparatus with
		Ca(2+) and Mn(2+) ions, both essential cofactors for processing and
		trafficking of newly synthesized proteins in the secretory pathway (By
		similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on
		the cytoplasmic side of the membrane and delivers them to the lumenal
		side. The transfer of ions across the membrane is coupled to ATP
		hydrolysis and is associated with a transient phosphorylation that shifts
Calcium-transporting		the pump conformation from inward-facing to outward-facing state (By
ATPase type 2C member	918	similarity). Plays a primary role in the maintenance of Ca(2+)
1		homeostasis in the trans-Golgi compartment with a functional impact on
		Golgi and post-Golgi protein sorting as well as a structural impact on
		cisternae morphology. Responsible for loading the Golgi stores with
		Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation
		and epidermis integrity (By similarity). Participates in Ca(2+) and
		Mn(2+) ions uptake into the Golgi store of hippocampal neurons and
		regulates protein trafficking required for neural polarity
		(PubMed:19793975). May also play a role in the maintenance of Ca(2+)
		(r unividually 1939/3). Iviay also play a role in the maintenance of $Ca(2+)$

and Mn(2+) homeostasis and signaling in the cytosol while preventing cytotoxicity (By similarity). [ECO:0000250]UniProtKB:P98194, ECO:0000269]PubMed:19793975}.  FUNCTION: Phosphodiesterase (PDE) that has higher activity toward cAMP than cGMP, as substrate. Plays a role in cell proliferation, migration and differentiation, and acts as a negative regulator of NME1. Plays a role in the regulation of neurogenesis. Involved in the regulation of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.  Adipocyte plasma
Exopolyphosphatase PRUNE1  454  Exopolyphosphatase PRUNE1  Adipocyte plasma membrane-associated protein  Fibroblast growth factor 23  251  FUNCTION: Regulator of phosphate homeostasis (By similarity). Inhibits renal tubular phosphate transport by regulates of decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. (ECC:0000250) ECC:0000269 PubMed:35119925). Plays a key role in initial steps of T-cell activation activation, drives microglia motility via the P13K/Akt pathway (PubMed:17299767). (ECC:0000269 PubMed:26456657, ECC:0000269 PubMed:26456657, ECC:0000269 PubMed:25119925). FUNCTION: Glycosyltransferase which regulates the biosynthesis of heparan sulfate (HS). Important for both skeletal development and hematonogies is through the formation of HS protecelycans (HSPGs)
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Exostosin-like 3 918 — — — — — — — — — — — — — — — — — — —
Required for the function of REG3A in regulating keratinocyte
proliferation and differentiation (By similarity).
{ECO:0000250 UniProtKB:O43909}.
Vacuolar protein  FUNCTION: Component of the ESCRT-I complex, a regulator of
vesicular trafficking process. Required for the sorting of endocytic
sorting-associated protein 37B  285  ubiquitinated cargos into multivesicular bodies. May be involved in cell
growth and differentiation (By similarity). {ECO:0000250}.
FUNCTION: Has no ubiquitin ligase activity on its own. The
Ubiquitin-conjugating UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical
enzyme E2 variant 1 poly-ubiquitin chains that are linked through 'Lys-63'. This type of
poly-ubiquitination activates IKK and does not seem to involve protein

		degradation by the proteasome. Plays a role in the activation of
		NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates
		transcriptional activation of target genes. Plays a role in the control of
		progress through the cell cycle and differentiation (By similarity). Plays a
		role in the error-free DNA repair pathway and contributes to the survival
		of cells after DNA damage. Promotes TRIM5 capsid-specific restriction
		activity and the UBE2V1-UBE2N heterodimer acts in concert with
		TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate
		the MAP3K7/TAK1 complex which in turn results in the induction and
		expression of NF-kappa-B and MAPK-responsive inflammatory genes
		(By similarity). Together with RNF135 and UBE2N, catalyzes the viral
		RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to
		activate the downstream signaling pathway that leads to interferon beta
		production (By similarity). UBE2V1-UBE2N together with TRAF3IP2
		E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6,
		a component of IL17A-mediated signaling pathway. {ECO:0000250,
		ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
		FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties
		conjugated to substrates and thus, functions to process newly synthesized
Ubiquitin		Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains
carboxyl-terminal	1055	and prevents proteasomal degradation of substrates. Hydrolyzes both
hydrolase 25	1000	'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
ny droidso 25		{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
		may have a role in the regulation of muscular differentiation and function.
		FUNCTION: Transcriptional regulator involved in different processes
		such as glucose metabolism, aerobic glycolysis, muscle cell
		differentiation and autophagy (PubMed:25402684, PubMed:29861159,
		PubMed:30700909). Recognizes and binds the forkhead DNA sequence
		motif (5'-GTAAACA-3') and can both act as a transcription activator or
		repressor, depending on the context (PubMed:25402684,
		PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
		, -
		key regulator of metabolic reprogramming towards aerobic glycolysis, a
		process in which glucose is converted to lactate in the presence of oxygen
Forkhead box protein K1	719	(PubMed:30700909). Acts by promoting expression of enzymes for
		glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
		kinase (PKLR) and lactate dehydrogenase), while suppressing further
		oxidation of pyruvate in the mitochondria by up-regulating pyruvate
		dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
		plays a role in gluconeogenesis during overnight fasting, when lactate
		from white adipose tissue and muscle is the main substrate
		(PubMed:30700909). Involved in mTORC1-mediated metabolic
		reprogramming: in response to mTORC1 signaling, translocates into the
		nucleus and regulates the expression of genes associated with glycolysis
		and downstream anabolic pathways, such as HIF1A, thereby regulating

		glucose metabolism (PubMed:29861159). Together with FOXK2, acts as
		a negative regulator of autophagy in skeletal muscle: in response to
		starvation, enters the nucleus, binds the promoters of autophagy genes
		and represses their expression, preventing proteolysis of skeletal muscle
		proteins (PubMed:25402684). Acts as a transcriptional regulator of the
		myogenic progenitor cell population in skeletal muscle
		(PubMed:8007964, PubMed:9271401, PubMed:12446708,
		PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
		of myoglobin (MB) gene, regulating the myogenic progenitor cell
		population (PubMed:8007964, PubMed:9271401). Promotes muscle
		progenitor cell proliferation by repressing the transcriptional activity of
		FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
		PubMed:22956541). Involved in remodeling processes of adult muscles
		that occur in response to physiological stimuli (PubMed:9271401,
		PubMed:22956541). Required to correct temporal orchestration of
		molecular and cellular events necessary for muscle repair
		(PubMed:10792059). Represses myogenic differentiation by inhibiting
		MEFC activity (PubMed:22956541). Positively regulates
		Wnt/beta-catenin signaling by translocating DVL into the nucleus (By
		similarity). Reduces virus replication, probably by binding the interferon
		stimulated response element (ISRE) to promote antiviral gene expression
		(By similarity). {ECO:0000250 UniProtKB:P85037,
		ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:12446708,
		ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:25402684,
		ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:30700909,
		ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.
		FUNCTION: Component of the cleavage and polyadenylation specificity
		factor (CPSF) complex that plays a key role in pre-mRNA 3'-end
		formation, recognizing the AAUAAA signal sequence and interacting
		with poly(A) polymerase and other factors to bring about cleavage and
		poly(A) addition. Has endonuclease activity, and functions as mRNA
		3'-end-processing endonuclease. Also involved in the histone 3'-end
	684	pre-mRNA processing. U7 snRNP-dependent protein that induces both
Cleavage and polyadenylation specificity factor subunit		the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a
		5' to 3' exonuclease for degrading the subsequent downstream cleavage
		product (DCP) of mature histone mRNAs. Cleavage occurs after the
3		5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl
		group on the upstream fragment containing the stem loop (SL) and 5'
		phosphate on the downstream cleavage product (DCP) starting with CU
		nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive
		and degrades the DCP RNA substrate even after complete removal of the
		U7-binding site. Binds to the downstream cleavage product (DCP) of
		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
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		(miRNAs) during embryonic stem cell differentiation via its interaction
		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
		primary transcript except miR-92a (PubMed:26255770). Only required
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
		pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
		ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
		FUNCTION: Serine/threonine kinase which acts as an essential
		component of the MAP kinase signal transduction pathway.
		MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an
		important role in the MAPK/ERK cascade. They participate also in a
		signaling cascade initiated by activated KIT and KITLG/SCF. Depending
		on the cellular context, the MAPK/ERK cascade mediates diverse
		biological functions such as cell growth, adhesion, survival and
		differentiation through the regulation of transcription, translation,
		cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role
		in initiation and regulation of meiosis, mitosis, and postmitotic functions
		in differentiated cells by phosphorylating a number of transcription
		factors. About 160 substrates have already been discovered for ERKs.
		Many of these substrates are localized in the nucleus, and seem to
		participate in the regulation of transcription upon stimulation. However,
		other substrates are found in the cytosol as well as in other cellular
		organelles, and those are responsible for processes such as translation,
Mitogen-activated protein	• •	mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also
kinase 1	358	involved in the regulation of the endosomal dynamics, including
		lysosome processing and endosome cycling through the perinuclear
		recycling compartment (PNRC); as well as in the fragmentation of the
		Golgi apparatus during mitosis. The substrates include transcription
		factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1),
		cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT,
		PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD,
		BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of
		translation (such as EIF4EBP1) and a variety of other signaling-related
		molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases
		(such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3,
		RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2,
		RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and
		phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other
		substrates which enable the propagation the MAPK/ERK signal to
		additional cytosolic and nuclear targets, thereby extending the specificity
		of the cascade. Mediates phosphorylation of TPR in response to EGF
		of the caseade. Mediates phospholylation of 11 K in response to EOF

		stimulation. May play a role in the spindle assembly checkpoint.
		Phosphorylates PML and promotes its interaction with PIN1, leading to
		PML degradation. Phosphorylates CDK2AP2 (By similarity).
		{ECO:0000250 UniProtKB:P28482, ECO:0000250 UniProtKB:P63086,
		ECO:0000269 PubMed:10753946, ECO:0000269 PubMed:11702783,
		ECO:0000269 PubMed:12134156, ECO:0000303 PubMed:16393692,
		ECO:0000303 PubMed:19565474, ECO:0000303 PubMed:21779493}.;
		FUNCTION: Acts as a transcriptional repressor. Binds to a
		[GC]AAA[GC] consensus sequence. Repress the expression of interferon
		gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1,
		IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1.
		Transcriptional activity is independent of kinase activity.
		{ECO:0000250 UniProtKB:P28482}.
		FUNCTION: RNA-binding protein that acts as a key regulator of
		N6-methyladenosine (m6A) methylation of RNAs, thereby regulating
		different processes, such as hematopoietic cell homeostasis, alternative
		splicing of mRNAs and X chromosome inactivation mediated by Xist
		RNA (PubMed:29535189). Associated component of the WMM
		complex, a complex that mediates N6-methyladenosine (m6A)
		methylation of RNAs, a modification that plays a role in the efficiency of
		mRNA splicing and RNA processing (PubMed:29535189). Plays a key
		role in m6A methylation, possibly by binding target RNAs and recruiting
		the WMM complex (PubMed:29535189). Involved in random X
		inactivation mediated by Xist RNA: acts by binding Xist RNA and
		recruiting the WMM complex, which mediates m6A methylation, leading
		to target YTHDC1 reader on Xist RNA and promoting transcription
		repression activity of Xist (By similarity). Required for the development
		of multiple tissues, such as the maintenance of the homeostasis of
RNA-binding protein 15	962	long-term hematopoietic stem cells and for megakaryocyte (MK) and
		B-cell differentiation (PubMed:17283045, PubMed:17376872,
		PubMed:18981216, PubMed:25468569). Regulates megakaryocyte
		differentiation by regulating alternative splicing of genes important for
		megakaryocyte differentiation; probably regulates alternative splicing via
		m6A regulation (By similarity). Required for placental vascular
		branching morphogenesis and embryonic development of the heart and
		spleen (PubMed:18981216). Acts as a regulator of thrombopoietin
		response in hematopoietic stem cells by regulating alternative splicing of
		MPL (PubMed:25468569). May also function as an mRNA export factor,
		stimulating export and expression of RTE-containing mRNAs which are
		present in many retrotransposons that require to be exported prior to
		splicing (Ry similarity) High affinity hinding of are mDNA to DDM15
		splicing (By similarity). High affinity binding of pre-mRNA to RBM15
		may allow targeting of the mRNP to the export helicase DBP5 in a

		HOV can a regulation (Dy give !lavite)
		HOX gene regulation (By similarity).
		{ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:17283045,
		ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18981216,
		ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29535189}.
		FUNCTION: Transcription coactivator which associates with nuclear
		receptors, transcriptional coactivators including EP300, CREBBP and
		NCOA1, and basal transcription factors like TBP and TFIIA to facilitate
		nuclear receptors-mediated transcription. May thereby play an important
		role in establishing distinct coactivator complexes under different cellular
		conditions. Plays a role in thyroid hormone receptor and estrogen
		receptor transactivation (By similarity). Also involved in androgen
		receptor transactivation (PubMed:12077347). Plays a pivotal role in the
Activating signal	<b>701</b>	transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of
cointegrator 1	581	transrepression between nuclear receptor and either AP1 or NF-kappa-B.
		May play a role in the development of neuromuscular junction (By
		similarity). May play a role in late myogenic differentiation
		(PubMed:27008887). Also functions as part of the RQC trigger (RQT)
		complex that activates the ribosome quality control (RQC) pathway, a
		pathway that degrades nascent peptide chains during problematic
		translation (By similarity). {ECO:0000250 UniProtKB:Q15650,
		ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
		ECO:0000269 PubMed:27008887}.
		FUNCTION: Histone methyltransferase that specifically trimethylates
		'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36'
		(H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is
		capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
		similarity). Represents the main enzyme generating H3K36me3, a
		specific tag for epigenetic transcriptional activation (PubMed:18157086,
		PubMed:20133625). Plays a role in chromatin structure modulation
		during elongation by coordinating recruitment of the FACT complex and
		by interacting with hyperphosphorylated POLR2A (By similarity). Acts
		as a key regulator of DNA mismatch repair in G1 and early S phase by
Histone-lysine		generating H3K36me3, a mark required to recruit MSH6 subunit of the
N-methyltransferase	2537	1
SETD2		MutS alpha complex: early recruitment of the MutS alpha complex to
		chromatin to be replicated allows a quick identification of mismatch
		DNA to initiate the mismatch repair reaction (By similarity). Required for
		DNA double-strand break repair in response to DNA damage: acts by
		mediating formation of H3K36me3, promoting recruitment of RAD51
		and DNA repair via homologous recombination (HR) (By similarity).
		Acts as a tumor suppressor (By similarity). H3K36me3 also plays an
		essential role in the maintenance of a heterochromatic state, by recruiting
		DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also
		enhanced in intron-containing genes, suggesting that SETD2 recruitment
1	1	is enhanced by splicing and that splicing is coupled to recruitment of

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		elongating RNA polymerase (By similarity). Required during
		angiogenesis (PubMed:20133625). Required for endoderm development
		by promoting embryonic stem cell differentiation toward endoderm: acts
		by mediating formation of H3K36me3 in distal promoter regions of
		FGFR3, leading to regulate transcription initiation of FGFR3
		(PubMed:25242323). In addition to histones, also mediates methylation
		of other proteins, such as tubulins and STAT1 (PubMed:27518565).
		Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B
		(alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis
		and cytokinesis and may be a specific tag in cytoskeletal remodeling
		(PubMed:27518565). Involved in interferon-alpha-induced antiviral
		defense by mediating both monomethylation of STAT1 at 'Lys-525' and
		catalyzing H3K36me3 on promoters of some interferon-stimulated genes
		(ISGs) to activate gene transcription (By similarity).
		{ECO:0000250 UniProtKB:Q9BYW2,
		ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625,
		ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.
		FUNCTION: RNA-binding protein that plays a central role in
		myelinization (PubMed:10864952, PubMed:11917126). Also required for
		visceral endoderm function and blood vessel development
		(PubMed:11892011, PubMed:16470614). Binds to the
		5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence
		(PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA
		export, mRNA stability and protein translation, as well as cellular
		processes including apoptosis, cell cycle, glial cell fate and development
		(PubMed:10535969, PubMed:12467586, PubMed:11297509,
		PubMed:11917126, PubMed:15568022). Required to protect and promote
		stability of mRNAs such as MBP and CDKN1B which promotes
		oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022).
		Participates in mRNA transport by regulating the nuclear export of MBP
Protein quaking	341	mRNA (PubMed:12467586). May also play a role in smooth muscle
1 Totem quaking	541	development (PubMed:14706070). {ECO:0000269 PubMed:10535969,
		ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509,
		ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126,
		ECO:0000269 PubMed:12467586, ECO:0000269 PubMed:14706070,
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388,
		ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved
		in regulation of mRNA splicing of MAG pre-mRNA by acting as a
		negative regulator of MAG exon 12 alternative splicing.
		{ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can induce
		apoptosis, while heterodimerization with other isoforms results in nuclear
		translocation of isoform 3 and suppression of apoptosis.
		{ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a
		translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.

		FUNCTION: May act as a GTPase-activating protein for Rab family
TD C1 1 : 0 !!		protein(s). May play a role in the cell cycle and differentiation of various
TBC1 domain family	1255	tissues. Involved in the trafficking and translocation of
member 1		GLUT4-containing vesicles and insulin-stimulated glucose uptake into
		cells. {ECO:0000269 PubMed:19740738}.
Mesenteric		FUNCTION: Involved in processes that promote adipocyte
estrogen-dependent	303	differentiation, lipid accumulation, and glucose uptake in mature
adipogenesis protein		adipocytes. {ECO:0000269 PubMed:22510272}.
		FUNCTION: Involved in transcriptional activation and repression of
		select genes by chromatin remodeling (alteration of DNA-nucleosome
		topology). Component of SWI/SNF chromatin remodeling complexes
		that carry out key enzymatic activities, changing chromatin structure by
		altering DNA-histone contacts within a nucleosome in an ATP-dependent
		manner. Can stimulate the ATPase activity of the catalytic subunit of
		these complexes. May be required for CoREST dependent repression of
		neuronal specific gene promoters in non-neuronal cells. Belongs to the
		neural progenitors-specific chromatin remodeling complex (npBAF
		complex) and the neuron-specific chromatin remodeling complex (nBAF
		complex). During neural development a switch from a stem/progenitor to
		a postmitotic chromatin remodeling mechanism occurs as neurons exit
	1213	the cell cycle and become committed to their adult state. The transition
		from proliferating neural stem/progenitor cells to postmitotic neurons
SWI/SNF complex		requires a switch in subunit composition of the npBAF and nBAF
subunit SMARCC2		complexes. As neural progenitors exit mitosis and differentiate into
		neurons, npBAF complexes which contain ACTL6A/BAF53A and
		PHF10/BAF45A, are exchanged for homologous alternative
		ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in
		neuron-specific complexes (nBAF). The npBAF complex is essential for
		the self-renewal/proliferative capacity of the multipotent neural stem
		cells. The nBAF complex along with CREST plays a role regulating the
		activity of genes essential for dendrite growth (PubMed:17640523).
		Critical regulator of myeloid differentiation, controlling
		granulocytopoiesis and the expression of genes involved in neutrophil
		granule formation (PubMed:28369036).
		{ECO:0000269 PubMed:17640523, ECO:0000269 PubMed:28369036,
		ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240,
		ECO:0000303 PubMed:26601204}.
		FUNCTION: May play an important role in regulating differentiation,
Protein prune homolog 2	3084	survival and aggressiveness of the tumor cells. {ECO:0000250}.
		FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion
		molecule involved in various processes such as inflammation, cell death,
Ninjurin-1	152	axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008,
,		PubMed:24347169, PubMed:24917672, PubMed:31526566,
		PubMed:33472215). Promotes cell adhesion by mediating homophilic
		1 delited 5 1/2215). I follows cen adhesion by mediating nontophine

interactions via its extracellular N-terminal adhesion motif (N-NAM) (PubMed:24917672, PubMed:30510259). Involved in the progression of the inflammatory stress by promoting cell-to-cell interactions between immune cells and endothelial cells (PubMed:24917672, PubMed:30510259). Involved in leukocyte migration during inflammation by promoting transendothelial migration of macrophages via homotypic binding (PubMed:24917672). Promotes the migration of monocytes across the brain endothelium to central nervous system inflammatory lesions (By similarity). Acts as a regulator of Toll-like receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during systemic inflammation; directly binds LPS (PubMed:25860173). Acts as a mediator of both programmed and necrotic cell death (PubMed:19557008, PubMed:33472215). Plays a key role in the induction of plasma membrane rupture during programmed and necrotic cell death: oligomerizes in response to death stimuli to mediate plasma membrane rupture (cytolysis), leading to release intracellular molecules named damage-associated molecular patterns (DAMPs) that propagate the inflammatory response (PubMed:33472215). Plays a role in nerve regeneration by promoting maturation of Schwann cells (PubMed:31526566). Acts as a regulator of angiogenesis (PubMed:25766274, PubMed:30354207). Promotes the formation of new vessels by mediating the interaction between capillary pericyte cells and endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates vascular functions in penile tissue as well as vascular formation (PubMed:24979788). Promotes osteoclasts development by enhancing the survival of prefusion osteoclasts (PubMed:30700695). Also involved in striated muscle growth and differentiation (PubMed:31091274). Also involved in cell senescence in a p53/TP53 manner, possibly by acting as an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620, PubMed:29073078). {ECO:0000250|UniProtKB:Q92982, ECO:0000269|PubMed:19557008, ECO:0000269|PubMed:23690620, ECO:0000269|PubMed:24347169, ECO:0000269|PubMed:24917672, ECO:0000269|PubMed:24979788, ECO:0000269|PubMed:25766274, ECO:0000269|PubMed:25860173, ECO:0000269|PubMed:29073078, ECO:0000269|PubMed:30354207, ECO:0000269|PubMed:30510259, ECO:0000269|PubMed:30700695, ECO:0000269|PubMed:31091274, ECO:0000269|PubMed:31526566, ECO:0000269|PubMed:33472215}.; FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage, which has chemotactic activity (PubMed:23142597). Acts as an anti-inflammatory mediator by promoting monocyte recruitment, thereby ameliorating atherosclerosis (PubMed:32883094).  $\{ECO: 0000269 | PubMed: 23142597, ECO: 0000269 | PubMed: 32883094\}.$ FUNCTION: Phosphorylates a large number of substrates in the

cAMP-dependent protein kinase catalytic subunit FUNCTION: Phosphorylates a large number of substrates in the cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B,

alpha		ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9
aipiia		and VASP (PubMed:10805756, PubMed:19223768). Regulates the
		, , , , , , , , , , , , , , , , , , , ,
		abundance of compartmentalized pools of its regulatory subunits through
		phosphorylation of PJA2 which binds and ubiquitinates these subunits,
		leading to their subsequent proteolysis (By similarity). RORA is activated
		by phosphorylation. Required for glucose-mediated adipogenic
		differentiation increase and osteogenic differentiation inhibition from
		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
		circulating platelets in a resting state by phosphorylating proteins in
		numerous platelet inhibitory pathways when in complex with
		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
		thrombin and collagen disrupt these complexes and free active PRKACA
		stimulates platelets and leads to platelet aggregation by phosphorylating
		VASP. RYR2 channel activity is potentiated by phosphorylation in
		presence of luminal Ca(2+), leading to reduced amplitude and increased
		frequency of store overload-induced Ca(2+) release (SOICR)
		characterized by an increased rate of Ca(2+) release and propagation
		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
		ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.;
		FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm
		flagellum to promote spermatozoa capacitation.
		{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.
		FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples
		to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in
Interleukin-4 receptor	810	promoting Th2 differentiation. The IL4/IL13 responses are involved in
subunit alpha	810	regulating IgE production and, chemokine and mucus production at sites
		of allergic inflammation. In certain cell types, can signal through
		activation of insulin receptor substrates, IRS1/IRS2.
	1	<u>-</u>

		FINICEIONI D. 110 14 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
		FUNCTION: Required for mitosis progression. Promotes the nucleation
		of microtubules from the spindle (By similarity). May play an important
Protein NEDD1	660	role during the embryonic development and differentiation of the central
		nervous system (PubMed:1378265).
		{ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
		FUNCTION: Calcium-dependent, calmodulin-stimulated protein
		phosphatase which plays an essential role in the transduction of
		intracellular Ca(2+)-mediated signals (PubMed:7791792,
		PubMed:26794871). Many of the substrates contain a PxIxIT motif
		and/or a LxVP motif (By similarity). In response to increased Ca(2+)
		levels, dephosphorylates and activates phosphatase SSH1 which results in
		cofilin dephosphorylation (By similarity). In response to increased
		Ca(2+) levels following mitochondrial depolarization, dephosphorylates
		DNM1L inducing DNM1L translocation to the mitochondrion (By
		similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+)
		release probability at hippocampal neuronal soma and synaptic terminals
		(By similarity). Dephosphorylates heat shock protein HSPB1 (By
		similarity). Dephosphorylates and activates transcription factor NFATC1
		(By similarity). Dephosphorylates and inactivates transcription factor
		ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May
	521	dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation
		from 14-3-3 proteins (By similarity). Required for postnatal development
		of the nephrogenic zone and superficial glomeruli in the kidneys, cell
Protein phosphatase 3		cycle homeostasis in the nephrogenic zone, and ultimately normal kidney
catalytic subunit alpha		function (PubMed:15509543). Plays a role in intracellular AQP2
catarytic subunit aipna		processing and localization to the apical membrane in the kidney, may
		thereby be required for efficient kidney filtration (PubMed:16735444).
		Required for secretion of salivary enzymes amylase, peroxidase,
		lysozyme and sialic acid via formation of secretory vesicles in the
		submandibular glands (PubMed:21435446). Required for calcineurin
		activity and homosynaptic depotentiation in the hippocampus
		(PubMed:10200317). Required for normal differentiation and survival of
		keratinocytes and therefore required for epidermis superstructure
		formation (PubMed:19626032). Positively regulates osteoblastic bone
		formation, via promotion of osteoblast differentiation
		(PubMed:16286645). Positively regulates osteoclast differentiation,
		potentially via NFATC1 signaling (PubMed:16968888). May play a role
		in skeletal muscle fiber type specification, potentially via NFATC1
		signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK
		signaling via inhibition of nuclear translocation of the transcription
		factors RELA and RELB (PubMed:26029823). Required for
		antigen-specific T-cell proliferation response (PubMed:8627154).
		{ECO:0000250 UniProtKB:P48452, ECO:0000250 UniProtKB:P63329,
		ECO:0000250 UniProtKB:Q08209, ECO:0000269 PubMed:10200317,

		ECO:0000269 PubMed:12773574, ECO:0000269 PubMed:15509543, ECO:0000269 PubMed:16286645, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16968888, ECO:0000269 PubMed:19626032, ECO:0000269 PubMed:21435446, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:26794871, ECO:0000269 PubMed:7791792, ECO:0000269 PubMed:8627154}.  FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homoor heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune
SLAM family member 5	329	response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell:B-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling; independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretion; involving ITSM 2 (PubMed:20628063). Positively regulates macroautophagy in primary dendritic cells via stabilization of IRF8; inhibits TRIM21-mediated proteasomal degradation of IRF8 (By similarity). {ECO:0000269 PubMed:16037392, ECO:0000269 PubMed:20153220, ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259, ECO:0000269 PubMed:25801429, ECO:0000269 PubMed:20962259, ECO:0000269 PubMed:25801429, ECO:0000305}.
Transmembrane anterior posterior transformation protein 1	564	FUNCTION: Plays a role in primary cilia formation (By similarity). May act as a downstream effector of HOXC8 possibly by transducing or transmitting extracellular information required for axial skeletal patterning during development (By similarity). May be involved in cartilage and bone development (By similarity). May play a role in the differentiation of cranial neural crest cells (By similarity). {ECO:0000250 UniProtKB:A2BIE7, ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
Fibrillin-1	2873	FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm

diameter microfibrils of the extracellular matrix, which conveys both structural and regulatory properties to load-bearing connective tissues. Fibrillin-1-containing microfibrils provide long-term force bearing structural support. In tissues such as the lung, blood vessels and skin, microfibrils form the periphery of the elastic fiber, acting as a scaffold for the deposition of elastin. In addition, microfibrils can occur as elastin-independent networks in tissues such as the ciliary zonule, tendon, cornea and glomerulus where they provide tensile strength and have anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis through specific interactions with growth factors, such as the bone morphogenetic proteins (BMPs), growth and differentiation factors (GDFs) and latent transforming growth factor-beta-binding proteins (LTBPs), cell-surface integrins and other extracellular matrix protein and proteoglycan components (By similarity). Regulates osteoblast maturation by controlling TGF-beta bioavailability and calibrating TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively regulates osteoclastogenesis by binding and sequestering an osteoclast differentiation and activation factor TNFSF11. This leads to disruption of TNFSF11-induced Ca(2+) signaling and impairment of TNFSF11-mediated nuclear translocation and activation of transcription factor NFATC1 which regulates genes important for osteoclast differentiation and function (PubMed:24039232). Mediates cell adhesion via its binding to cell surface receptors integrins ITGAV:ITGB3 and ITGA5:ITGB1. Binds heparin and this interaction plays an important role in the assembly of microfibrils (By similarity). {ECO:0000250|UniProtKB:P35555, ECO:0000269|PubMed:20855508, ECO:0000269|PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine secreted by white adipose tissue that plays an important regulatory role in the glucose metabolism of liver, muscle and pancreas (PubMed:31230984, PubMed:30997682). Hormone that targets the liver in response to fasting to increase plasma glucose levels (PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface of hepatocytes and promotes hepatocyte glucose release by activating the protein kinase A activity in the liver, resulting in rapid glucose release into the circulation (PubMed:31230984). May act as a regulator of adaptive thermogenesis by inhibiting browning and energy consumption, while increasing lipid deposition in white adipose tissue (PubMed:33705351). Also acts as an orexigenic hormone that increases appetite: crosses the blood brain barrier and exerts effects on the hypothalamus (PubMed:29106398). In the arcuate nucleus of the hypothalamus, asprosin directly activates orexigenic AgRP neurons and indirectly inhibits anorexigenic POMC neurons, resulting in appetite stimulation (PubMed:29106398, PubMed:32337066). Activates orexigenic AgRP neurons via binding to the olfactory receptor Olfr734

		(PubMed:32337066). May also play a role in sperm motility in testis via interaction with Olfr734 receptor (PubMed:31798959). {ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682, ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959, ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
Versican core protein	3357	FUNCTION: May play a role in intercellular signaling and in connecting cells with the extracellular matrix. May take part in the regulation of cell motility, growth and differentiation. Binds hyaluronic acid.
All-trans-retinol 13,14-reductase	609	FUNCTION: Catalyzes the saturation of all-trans-retinol to all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779, PubMed:19139408). Does not exhibit any activity toward all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers (PubMed:15358783). May play a role in the metabolism of vitamin A (PubMed:15358783, PubMed:17253779). Independently of retinol conversion, may regulate liver metabolism upstream of MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This effect seems not to mimic the in vivo situation in which animals show increased adiposity in the absence of RETSAT (PubMed:19940255). {ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779, ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
Calcium-transporting ATPase type 2C member 1	918	FUNCTION: ATP-driven pump that supplies the Golgi apparatus with Ca(2+) and Mn(2+) ions, both essential cofactors for processing and trafficking of newly synthesized proteins in the secretory pathway (By similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on the cytoplasmic side of the membrane and delivers them to the lumenal side. The transfer of ions across the membrane is coupled to ATP hydrolysis and is associated with a transient phosphorylation that shifts the pump conformation from inward-facing to outward-facing state (By similarity). Plays a primary role in the maintenance of Ca(2+) homeostasis in the trans-Golgi compartment with a functional impact on Golgi and post-Golgi protein sorting as well as a structural impact on cisternae morphology. Responsible for loading the Golgi stores with Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation and epidermis integrity (By similarity). Participates in Ca(2+) and Mn(2+) ions uptake into the Golgi store of hippocampal neurons and regulates protein trafficking required for neural polarity (PubMed:19793975). May also play a role in the maintenance of Ca(2+) and Mn(2+) homeostasis and signaling in the cytosol while preventing cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194, ECO:0000269 PubMed:19793975}.
Exopolyphosphatase PRUNE1	454	FUNCTION: Phosphodiesterase (PDE) that has higher activity toward cAMP than cGMP, as substrate. Plays a role in cell proliferation,

		migration and differentiation, and acts as a negative regulator of NME1.
		Plays a role in the regulation of neurogenesis. Involved in the regulation
A 1:		of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma	41.5	FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl
membrane-associated	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte
protein		differentiation. {ECO:0000250}.
		FUNCTION: Regulator of phosphate homeostasis (By similarity).
		Inhibits renal tubular phosphate transport by reducing SLC34A1 levels
Fibroblast growth factor		(By similarity). Acts directly on the parathyroid to decrease PTH
23	251	secretion (By similarity). Regulator of vitamin-D metabolism (By
		similarity). Negatively regulates osteoblasts differentiation and matrix
		mineralization (By similarity). Up-regulates EGR1 expression in the
		presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
		FUNCTION: Receptor for extracellularly released ATP acting as a
		ligand-gated ion channel that plays multiple role in immunity and central
		nervous system physiology (PubMed:26456657, PubMed:35119925).
		Plays a key role in initial steps of T-cell activation and Ca(2+)
		microdomain formation (PubMed:35119925). Participates also in basal
P2X purinoceptor 4	388	T-cell activity without TCR/CD3 stimulation (PubMed:35119925).
F2A purmoceptor 4	366	Promotes the differentiation and activation of Th17 cells via expression
		of retinoic acid-related orphan receptor C/RORC (By similarity). Upon
		activation, drives microglia motility via the PI3K/Akt pathway
		(PubMed:17299767). {ECO:0000250 UniProtKB:Q99571,
		ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:26456657,
		ECO:0000269 PubMed:35119925}.
		FUNCTION: Glycosyltransferase which regulates the biosynthesis of
		heparan sulfate (HS). Important for both skeletal development and
F		hematopoiesis, through the formation of HS proteoglycans (HSPGs).
Exostosin-like 3	918	Required for the function of REG3A in regulating keratinocyte
		proliferation and differentiation (By similarity).
		{ECO:0000250 UniProtKB:O43909}.
		FUNCTION: Component of the ESCRT-I complex, a regulator of
Vacuolar protein		vesicular trafficking process. Required for the sorting of endocytic
sorting-associated protein	285	ubiquitinated cargos into multivesicular bodies. May be involved in cell
37B		growth and differentiation (By similarity). {ECO:0000250}.
		FUNCTION: Has no ubiquitin ligase activity on its own. The
		UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical
Ubiquitin-conjugating	147	poly-ubiquitin chains that are linked through 'Lys-63'. This type of
		poly-ubiquitination activates IKK and does not seem to involve protein
		degradation by the proteasome. Plays a role in the activation of
enzyme E2 variant 1		NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates
		transcriptional activation of target genes. Plays a role in the control of
		progress through the cell cycle and differentiation (By similarity). Plays a
		role in the error-free DNA repair pathway and contributes to the survival

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		of cells after DNA damage. Promotes TRIM5 capsid-specific restriction
		activity and the UBE2V1-UBE2N heterodimer acts in concert with
		TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate
		the MAP3K7/TAK1 complex which in turn results in the induction and
		expression of NF-kappa-B and MAPK-responsive inflammatory genes
		(By similarity). Together with RNF135 and UBE2N, catalyzes the viral
		RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to
		activate the downstream signaling pathway that leads to interferon beta
		production (By similarity). UBE2V1-UBE2N together with TRAF3IP2
		E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6,
		a component of IL17A-mediated signaling pathway. {ECO:0000250,
		ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
		FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties
		conjugated to substrates and thus, functions to process newly synthesized
Ubiquitin		Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains
carboxyl-terminal	1055	and prevents proteasomal degradation of substrates. Hydrolyzes both
hydrolase 25		'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
		{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
		may have a role in the regulation of muscular differentiation and function.
		FUNCTION: Transcriptional regulator involved in different processes
		such as glucose metabolism, aerobic glycolysis, muscle cell
		differentiation and autophagy (PubMed:25402684, PubMed:29861159,
		PubMed:30700909). Recognizes and binds the forkhead DNA sequence
		motif (5'-GTAAACA-3') and can both act as a transcription activator or
		repressor, depending on the context (PubMed:25402684,
		PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
		key regulator of metabolic reprogramming towards aerobic glycolysis, a
		process in which glucose is converted to lactate in the presence of oxygen
		(PubMed:30700909). Acts by promoting expression of enzymes for
		glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
	-10	kinase (PKLR) and lactate dehydrogenase), while suppressing further
Forkhead box protein K1	719	oxidation of pyruvate in the mitochondria by up-regulating pyruvate
		dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
		plays a role in gluconeogenesis during overnight fasting, when lactate
		from white adipose tissue and muscle is the main substrate
		(PubMed:30700909). Involved in mTORC1-mediated metabolic
		reprogramming: in response to mTORC1 signaling, translocates into the
		nucleus and regulates the expression of genes associated with glycolysis
		and downstream anabolic pathways, such as HIF1A, thereby regulating
		glucose metabolism (PubMed:29861159). Together with FOXK2, acts as
		a negative regulator of autophagy in skeletal muscle: in response to
		starvation, enters the nucleus, binds the promoters of autophagy genes
		and represses their expression, preventing proteolysis of skeletal muscle
		proteins (PubMed:25402684). Acts as a transcriptional regulator of the
		·

		myogenic progenitor cell population in skeletal muscle
		(PubMed:8007964, PubMed:9271401, PubMed:12446708,
		PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
		of myoglobin (MB) gene, regulating the myogenic progenitor cell
		population (PubMed:8007964, PubMed:9271401). Promotes muscle
		progenitor cell proliferation by repressing the transcriptional activity of
		FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
		PubMed:22956541). Involved in remodeling processes of adult muscles
		that occur in response to physiological stimuli (PubMed:9271401,
		PubMed:22956541). Required to correct temporal orchestration of
		molecular and cellular events necessary for muscle repair
		(PubMed:10792059). Represses myogenic differentiation by inhibiting
		MEFC activity (PubMed:22956541). Positively regulates
		Wnt/beta-catenin signaling by translocating DVL into the nucleus (By
		similarity). Reduces virus replication, probably by binding the interferon
		stimulated response element (ISRE) to promote antiviral gene expression
		(By similarity). {ECO:0000250 UniProtKB:P85037,
		ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:12446708,
		ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:25402684,
		ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:30700909,
		ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.
		FUNCTION: Component of the cleavage and polyadenylation specificity
		factor (CPSF) complex that plays a key role in pre-mRNA 3'-end
		formation, recognizing the AAUAAA signal sequence and interacting
		with poly(A) polymerase and other factors to bring about cleavage and
		poly(A) addition. Has endonuclease activity, and functions as mRNA
		3'-end-processing endonuclease. Also involved in the histone 3'-end
		pre-mRNA processing. U7 snRNP-dependent protein that induces both
		the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a
		5' to 3' exonuclease for degrading the subsequent downstream cleavage
	684	product (DCP) of mature histone mRNAs. Cleavage occurs after the
Cleavage and		5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl
polyadenylation		group on the upstream fragment containing the stem loop (SL) and 5'
specificity factor subunit	001	phosphate on the downstream cleavage product (DCP) starting with CU
3		nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive
		and degrades the DCP RNA substrate even after complete removal of the
		U7-binding site. Binds to the downstream cleavage product (DCP) of
		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
		(miRNAs) during embryonic stem cell differentiation via its interaction
		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
		primary transcript except miR-92a (PubMed:26255770). Only required
		primary transcript except link-32a (Publicu:202331/0). Only required

		T
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
		pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
		ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
		FUNCTION: Serine/threonine kinase which acts as an essential
		component of the MAP kinase signal transduction pathway.
		MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an
		important role in the MAPK/ERK cascade. They participate also in a
		signaling cascade initiated by activated KIT and KITLG/SCF. Depending
		on the cellular context, the MAPK/ERK cascade mediates diverse
		biological functions such as cell growth, adhesion, survival and
		differentiation through the regulation of transcription, translation,
		cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role
		in initiation and regulation of meiosis, mitosis, and postmitotic functions
		in differentiated cells by phosphorylating a number of transcription
		factors. About 160 substrates have already been discovered for ERKs.
		Many of these substrates are localized in the nucleus, and seem to
		participate in the regulation of transcription upon stimulation. However,
		other substrates are found in the cytosol as well as in other cellular
		organelles, and those are responsible for processes such as translation,
		mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also
		involved in the regulation of the endosomal dynamics, including
		lysosome processing and endosome cycling through the perinuclear
Mitogen-activated protein	358	recycling compartment (PNRC); as well as in the fragmentation of the
kinase 1		Golgi apparatus during mitosis. The substrates include transcription
		factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1),
		cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT,
		PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD,
		BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of
		translation (such as EIF4EBP1) and a variety of other signaling-related
		molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases
		(such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3,
		RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2,
		RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and
		phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other
		substrates which enable the propagation the MAPK/ERK signal to
		additional cytosolic and nuclear targets, thereby extending the specificity of the cascade. Mediates phosphorylation of TPR in response to EGF
		stimulation. May play a role in the spindle assembly checkpoint.
		Phosphorylates PML and promotes its interaction with PIN1, leading to
		PML degradation. Phosphorylates CDK2AP2 (By similarity).
		{ECO:0000250 UniProtKB:P28482, ECO:0000250 UniProtKB:P63086,
		ECO:0000269 PubMed:10753946, ECO:0000269 PubMed:11702783,

	I	
		ECO:0000269 PubMed:12134156, ECO:0000303 PubMed:16393692,
		ECO:0000303 PubMed:19565474, ECO:0000303 PubMed:21779493}.;
		FUNCTION: Acts as a transcriptional repressor. Binds to a
		[GC]AAA[GC] consensus sequence. Repress the expression of interferon
		gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1,
		IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1.
		Transcriptional activity is independent of kinase activity.
		{ECO:0000250 UniProtKB:P28482}.
		FUNCTION: RNA-binding protein that acts as a key regulator of
		N6-methyladenosine (m6A) methylation of RNAs, thereby regulating
		different processes, such as hematopoietic cell homeostasis, alternative
		splicing of mRNAs and X chromosome inactivation mediated by Xist
		RNA (PubMed:29535189). Associated component of the WMM
		complex, a complex that mediates N6-methyladenosine (m6A)
		methylation of RNAs, a modification that plays a role in the efficiency of
		mRNA splicing and RNA processing (PubMed:29535189). Plays a key
		role in m6A methylation, possibly by binding target RNAs and recruiting
		the WMM complex (PubMed:29535189). Involved in random X
		inactivation mediated by Xist RNA: acts by binding Xist RNA and
		recruiting the WMM complex, which mediates m6A methylation, leading
		to target YTHDC1 reader on Xist RNA and promoting transcription
		repression activity of Xist (By similarity). Required for the development
		of multiple tissues, such as the maintenance of the homeostasis of
		long-term hematopoietic stem cells and for megakaryocyte (MK) and
		B-cell differentiation (PubMed:17283045, PubMed:17376872,
RNA-binding protein 15	962	PubMed:18981216, PubMed:25468569). Regulates megakaryocyte
		differentiation by regulating alternative splicing of genes important for
		megakaryocyte differentiation; probably regulates alternative splicing via
		m6A regulation (By similarity). Required for placental vascular
		branching morphogenesis and embryonic development of the heart and
		spleen (PubMed:18981216). Acts as a regulator of thrombopoietin
		response in hematopoietic stem cells by regulating alternative splicing of
		MPL (PubMed:25468569). May also function as an mRNA export factor,
		stimulating export and expression of RTE-containing mRNAs which are
		present in many retrotransposons that require to be exported prior to
		splicing (By similarity). High affinity binding of pre-mRNA to RBM15
		may allow targeting of the mRNP to the export helicase DBP5 in a
		manner that is independent of splicing-mediated NXF1 deposition,
		resulting in export prior to splicing (By similarity). May be implicated in
		HOX gene regulation (By similarity).
		{ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:17283045,
		ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18981216,
		ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29535189}.
Activating signal	581	FUNCTION: Transcription coactivator which associates with nuclear
	1	1

cointegrator 1		receptors, transcriptional coactivators including EP300, CREBBP and NCOA1, and basal transcription factors like TBP and TFIIA to facilitate nuclear receptors-mediated transcription. May thereby play an important role in establishing distinct coactivator complexes under different cellular conditions. Plays a role in thyroid hormone receptor and estrogen receptor transactivation (By similarity). Also involved in androgen receptor transactivation (PubMed:12077347). Plays a pivotal role in the transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of transrepression between nuclear receptor and either AP1 or NF-kappa-B. May play a role in the development of neuromuscular junction (By similarity). May play a role in late myogenic differentiation (PubMed:27008887). Also functions as part of the RQC trigger (RQT) complex that activates the ribosome quality control (RQC) pathway, a pathway that degrades nascent peptide chains during problematic translation (By similarity). {ECO:0000250 UniProtKB:Q15650, ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
Histone-lysine N-methyltransferase SETD2	2537	ECO:0000269 PubMed:27008887}.  FUNCTION: Histone methyltransferase that specifically trimethylates 'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36' (H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By similarity). Represents the main enzyme generating H3K36me3, a specific tag for epigenetic transcriptional activation (PubMed:18157086, PubMed:20133625). Plays a role in chromatin structure modulation during elongation by coordinating recruitment of the FACT complex and by interacting with hyperphosphorylated POLR2A (By similarity). Acts as a key regulator of DNA mismatch repair in G1 and early S phase by generating H3K36me3, a mark required to recruit MSH6 subunit of the MutS alpha complex: early recruitment of the MutS alpha complex to chromatin to be replicated allows a quick identification of mismatch DNA to initiate the mismatch repair reaction (By similarity). Required for DNA double-strand break repair in response to DNA damage: acts by mediating formation of H3K36me3, promoting recruitment of RAD51 and DNA repair via homologous recombination (HR) (By similarity). Acts as a tumor suppressor (By similarity). H3K36me3 also plays an essential role in the maintenance of a heterochromatic state, by recruiting DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also enhanced in intron-containing genes, suggesting that SETD2 recruitment is enhanced by splicing and that splicing is coupled to recruitment of elongating RNA polymerase (By similarity). Required during angiogenesis (PubMed:20133625). Required for endoderm development by promoting embryonic stem cell differentiation toward endoderm: acts by mediating formation of H3K36me3 in distal promoter regions of FGFR3, leading to regulate transcription initiation of FGFR3

	1	(D.134.105040000) T. 1122. (112.11.11.11.11.11.11.11.11.11.11.11.11.
		(PubMed:25242323). In addition to histones, also mediates methylation
		of other proteins, such as tubulins and STAT1 (PubMed:27518565).
		Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B
		(alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis
		and cytokinesis and may be a specific tag in cytoskeletal remodeling
		(PubMed:27518565). Involved in interferon-alpha-induced antiviral
		defense by mediating both monomethylation of STAT1 at 'Lys-525' and
		catalyzing H3K36me3 on promoters of some interferon-stimulated genes
		(ISGs) to activate gene transcription (By similarity).
		{ECO:0000250 UniProtKB:Q9BYW2,
		ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625,
		ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.
		FUNCTION: RNA-binding protein that plays a central role in
		myelinization (PubMed:10864952, PubMed:11917126). Also required for
		visceral endoderm function and blood vessel development
		(PubMed:11892011, PubMed:16470614). Binds to the
		5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence
		(PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA
		export, mRNA stability and protein translation, as well as cellular
		processes including apoptosis, cell cycle, glial cell fate and development
	341	(PubMed:10535969, PubMed:12467586, PubMed:11297509,
		PubMed:11917126, PubMed:15568022). Required to protect and promote
		stability of mRNAs such as MBP and CDKN1B which promotes
		oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022).
		Participates in mRNA transport by regulating the nuclear export of MBP
Protein quaking		mRNA (PubMed:12467586). May also play a role in smooth muscle
		development (PubMed:14706070). {ECO:0000269 PubMed:10535969,
		ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509,
		ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126,
		ECO:0000269 PubMed:12467586, ECO:0000269 PubMed:14706070,
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388,
		ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved
		in regulation of mRNA splicing of MAG pre-mRNA by acting as a
		negative regulator of MAG exon 12 alternative splicing.
		{ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can induce
		apoptosis, while heterodimerization with other isoforms results in nuclear
		translocation of isoform 3 and suppression of apoptosis.
		{ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a
		translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.
		FUNCTION: May act as a GTPase-activating protein for Rab family
	1255	protein(s). May play a role in the cell cycle and differentiation of various
TBC1 domain family member 1		tissues. Involved in the trafficking and translocation of
		GLUT4-containing vesicles and insulin-stimulated glucose uptake into
		cells. {ECO:0000269 PubMed:19740738}.
		Cons. (1200.000020)   uoivied.17/70/30 (.

Mesenteric		FUNCTION: Involved in processes that promote adipocyte
estrogen-dependent	303	differentiation, lipid accumulation, and glucose uptake in mature
adipogenesis protein		adipocytes. {ECO:0000269 PubMed:22510272}.
SWI/SNF complex subunit SMARCC2	1213	FUNCTION: Involved in transcriptional activation and repression of select genes by chromatin remodeling (alteration of DNA-nucleosome topology). Component of SWI/SNF chromatin remodeling complexes that carry out key enzymatic activities, changing chromatin structure by altering DNA-histone contacts within a nucleosome in an ATP-dependent manner. Can stimulate the ATPase activity of the catalytic subunit of these complexes. May be required for CoREST dependent repression of neuronal specific gene promoters in non-neuronal cells. Belongs to the neural progenitors-specific chromatin remodeling complex (npBAF complex) and the neuron-specific chromatin remodeling complex (npBAF complex). During neural development a switch from a stem/progenitor to a postmitotic chromatin remodeling mechanism occurs as neurons exit the cell cycle and become committed to their adult state. The transition from proliferating neural stem/progenitor cells to postmitotic neurons requires a switch in subunit composition of the npBAF and nBAF complexes. As neural progenitors exit mitosis and differentiate into neurons, npBAF complexes which contain ACTL6A/BAF53A and PHF10/BAF45A, are exchanged for homologous alternative ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in neuron-specific complexes (nBAF). The npBAF complex is essential for the self-renewal/proliferative capacity of the multipotent neural stem cells. The nBAF complex along with CREST plays a role regulating the activity of genes essential for dendrite growth (PubMed:17640523). Critical regulator of myeloid differentiation, controlling granulocytopoiesis and the expression of genes involved in neutrophil granule formation (PubMed:28369036). [ECO:0000269 PubMed:31216030, ECO:00000303 PubMed:22952240, ECO:0000303 PubMed:26601204}.
Protein prune homolog 2	3084	FUNCTION: May play an important role in regulating differentiation, survival and aggressiveness of the tumor cells. {ECO:0000250}.
Ninjurin-1	152	FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion molecule involved in various processes such as inflammation, cell death, axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008, PubMed:24347169, PubMed:24917672, PubMed:31526566, PubMed:33472215). Promotes cell adhesion by mediating homophilic interactions via its extracellular N-terminal adhesion motif (N-NAM) (PubMed:24917672, PubMed:30510259). Involved in the progression of the inflammatory stress by promoting cell-to-cell interactions between immune cells and endothelial cells (PubMed:24917672, PubMed:30510259). Involved in leukocyte migration during

inflammation by promoting transendothelial migration of macrophages via homotypic binding (PubMed:24917672). Promotes the migration of monocytes across the brain endothelium to central nervous system inflammatory lesions (By similarity). Acts as a regulator of Toll-like receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during systemic inflammation; directly binds LPS (PubMed:25860173). Acts as a mediator of both programmed and necrotic cell death (PubMed:19557008, PubMed:33472215). Plays a key role in the induction of plasma membrane rupture during programmed and necrotic cell death: oligomerizes in response to death stimuli to mediate plasma membrane rupture (cytolysis), leading to release intracellular molecules named damage-associated molecular patterns (DAMPs) that propagate the inflammatory response (PubMed:33472215). Plays a role in nerve regeneration by promoting maturation of Schwann cells (PubMed:31526566). Acts as a regulator of angiogenesis (PubMed:25766274, PubMed:30354207). Promotes the formation of new vessels by mediating the interaction between capillary pericyte cells and endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates vascular functions in penile tissue as well as vascular formation (PubMed:24979788). Promotes osteoclasts development by enhancing the survival of prefusion osteoclasts (PubMed:30700695). Also involved in striated muscle growth and differentiation (PubMed:31091274). Also involved in cell senescence in a p53/TP53 manner, possibly by acting as an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620, PubMed:29073078). {ECO:0000250|UniProtKB:Q92982, ECO:0000269|PubMed:19557008, ECO:0000269|PubMed:23690620, ECO:0000269|PubMed:24347169, ECO:0000269|PubMed:24917672, ECO:0000269|PubMed:24979788, ECO:0000269|PubMed:25766274, ECO:0000269|PubMed:25860173, ECO:0000269|PubMed:29073078, ECO:0000269|PubMed:30354207, ECO:0000269|PubMed:30510259, ECO:0000269|PubMed:30700695, ECO:0000269|PubMed:31091274, ECO:0000269|PubMed:31526566, ECO:0000269|PubMed:33472215}.; FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage, which has chemotactic activity (PubMed:23142597). Acts as an anti-inflammatory mediator by promoting monocyte recruitment, thereby ameliorating atherosclerosis (PubMed:32883094). {ECO:0000269|PubMed:23142597, ECO:0000269|PubMed:32883094}. FUNCTION: Phosphorylates a large number of substrates in the cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B, cAMP-dependent protein ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9 kinase catalytic subunit 351 and VASP (PubMed:10805756, PubMed:19223768). Regulates the alpha abundance of compartmentalized pools of its regulatory subunits through phosphorylation of PJA2 which binds and ubiquitinates these subunits, leading to their subsequent proteolysis (By similarity). RORA is activated

		by phosphorylation. Required for glucose-mediated adipogenic
		differentiation increase and osteogenic differentiation inhibition from
		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
		circulating platelets in a resting state by phosphorylating proteins in
		numerous platelet inhibitory pathways when in complex with
		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
		thrombin and collagen disrupt these complexes and free active PRKACA
		stimulates platelets and leads to platelet aggregation by phosphorylating
		VASP. RYR2 channel activity is potentiated by phosphorylation in
		presence of luminal Ca(2+), leading to reduced amplitude and increased
		frequency of store overload-induced Ca(2+) release (SOICR)
		characterized by an increased rate of Ca(2+) release and propagation
		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
		ECO:0000250 Chin TottkB:177012, ECO:0000250 Chin TottkB:127751,
		FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm
		flagellum to promote spermatozoa capacitation.
		{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.
		FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples
		to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in
Interleukin-4 receptor	810	promoting Th2 differentiation. The IL4/IL13 responses are involved in
subunit alpha		regulating IgE production and, chemokine and mucus production at sites
		of allergic inflammation. In certain cell types, can signal through
		activation of insulin receptor substrates, IRS1/IRS2.
		FUNCTION: Required for mitosis progression. Promotes the nucleation
Protein NEDD1	660	of microtubules from the spindle (By similarity). May play an important
		role during the embryonic development and differentiation of the central
		nervous system (PubMed:1378265).

FUNCTION: Calcium-dependent, calmodulin-stimulated protein phosphatase which plays an essential role in the transduction of intracellular Ca(2+)-mediated signals (PubMed:7791792, PubMed:26794871). Many of the substrates contain a PxIxIT motif and/or a LxVP motif (By similarity). In response to increased Ca(2+) levels, dephosphorylates and activates phosphatase SSH1 which results in cofilin dephosphorylation (By similarity). In response to increased Ca(2+) levels following mitochondrial depolarization, dephosphorylates DNM1L inducing DNM1L translocation to the mitochondrion (By similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+) release probability at hippocampal neuronal soma and synaptic terminals (By similarity). Dephosphorylates heat shock protein HSPB1 (By similarity). Dephosphorylates and activates transcription factor NFATC1 (By similarity). Dephosphorylates and inactivates transcription factor ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation from 14-3-3 proteins (By similarity). Required for postnatal development of the nephrogenic zone and superficial glomeruli in the kidneys, cell cycle homeostasis in the nephrogenic zone, and ultimately normal kidney function (PubMed:15509543). Plays a role in intracellular AQP2 processing and localization to the apical membrane in the kidney, may thereby be required for efficient kidney filtration (PubMed:16735444). Protein phosphatase 3 521 catalytic subunit alpha Required for secretion of salivary enzymes amylase, peroxidase, lysozyme and sialic acid via formation of secretory vesicles in the submandibular glands (PubMed:21435446). Required for calcineurin activity and homosynaptic depotentiation in the hippocampus (PubMed:10200317). Required for normal differentiation and survival of keratinocytes and therefore required for epidermis superstructure formation (PubMed:19626032). Positively regulates osteoblastic bone formation, via promotion of osteoblast differentiation (PubMed:16286645). Positively regulates osteoclast differentiation, potentially via NFATC1 signaling (PubMed:16968888). May play a role in skeletal muscle fiber type specification, potentially via NFATC1 signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK signaling via inhibition of nuclear translocation of the transcription factors RELA and RELB (PubMed:26029823). Required for antigen-specific T-cell proliferation response (PubMed:8627154). {ECO:0000250|UniProtKB:P48452, ECO:0000250|UniProtKB:P63329, ECO:0000250|UniProtKB:Q08209, ECO:0000269|PubMed:10200317, ECO:0000269|PubMed:12773574, ECO:0000269|PubMed:15509543, ECO:0000269|PubMed:16286645, ECO:0000269|PubMed:16735444, ECO:0000269|PubMed:16968888, ECO:0000269|PubMed:19626032, ECO:0000269|PubMed:21435446, ECO:0000269|PubMed:26029823,

ECO:0000269|PubMed:26794871, ECO:0000269|PubMed:7791792,

		ECO:0000269 PubMed:8627154}.
SLAM family member 5	329	FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell:B-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling; independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretion; involving ITSM 2 (PubMed:20628063). Positively regulates macroautophagy in primary dendritic cells via stabilization of IRF8; inhibits TRIM21-mediated proteasomal degradation of IRF8 (By similarity). {ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20153220, ECO:0000269 PubMed:20628063, ECO:00000369 PubMed:20628063, ECO:00000369 PubMed:20628063, ECO:0000369 PubMed:20628063, ECO:0000369 Pu
Transmembrane anterior posterior transformation protein 1	564	FUNCTION: Plays a role in primary cilia formation (By similarity). May act as a downstream effector of HOXC8 possibly by transducing or transmitting extracellular information required for axial skeletal patterning during development (By similarity). May be involved in cartilage and bone development (By similarity). May play a role in the differentiation of cranial neural crest cells (By similarity). {ECO:0000250 UniProtKB:A2BIE7, ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
Fibrillin-1	2873	FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm diameter microfibrils of the extracellular matrix, which conveys both structural and regulatory properties to load-bearing connective tissues. Fibrillin-1-containing microfibrils provide long-term force bearing structural support. In tissues such as the lung, blood vessels and skin, microfibrils form the periphery of the elastic fiber, acting as a scaffold for

the deposition of elastin. In addition, microfibrils can occur as elastin-independent networks in tissues such as the ciliary zonule, tendon, cornea and glomerulus where they provide tensile strength and have anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis through specific interactions with growth factors, such as the bone morphogenetic proteins (BMPs), growth and differentiation factors (GDFs) and latent transforming growth factor-beta-binding proteins (LTBPs), cell-surface integrins and other extracellular matrix protein and proteoglycan components (By similarity). Regulates osteoblast maturation by controlling TGF-beta bioavailability and calibrating TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively regulates osteoclastogenesis by binding and sequestering an osteoclast differentiation and activation factor TNFSF11. This leads to disruption of TNFSF11-induced Ca(2+) signaling and impairment of TNFSF11-mediated nuclear translocation and activation of transcription factor NFATC1 which regulates genes important for osteoclast differentiation and function (PubMed:24039232). Mediates cell adhesion via its binding to cell surface receptors integrins ITGAV:ITGB3 and ITGA5:ITGB1. Binds heparin and this interaction plays an important role in the assembly of microfibrils (By similarity). {ECO:0000250|UniProtKB:P35555, ECO:0000269|PubMed:20855508, ECO:0000269|PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine secreted by white adipose tissue that plays an important regulatory role in the glucose metabolism of liver, muscle and pancreas (PubMed:31230984, PubMed:30997682). Hormone that targets the liver in response to fasting to increase plasma glucose levels (PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface of hepatocytes and promotes hepatocyte glucose release by activating the protein kinase A activity in the liver, resulting in rapid glucose release into the circulation (PubMed:31230984). May act as a regulator of adaptive thermogenesis by inhibiting browning and energy consumption, while increasing lipid deposition in white adipose tissue (PubMed:33705351). Also acts as an orexigenic hormone that increases appetite: crosses the blood brain barrier and exerts effects on the hypothalamus (PubMed:29106398). In the arcuate nucleus of the hypothalamus, asprosin directly activates orexigenic AgRP neurons and indirectly inhibits anorexigenic POMC neurons, resulting in appetite stimulation (PubMed:29106398, PubMed:32337066). Activates orexigenic AgRP neurons via binding to the olfactory receptor Olfr734 (PubMed:32337066). May also play a role in sperm motility in testis via interaction with Olfr734 receptor (PubMed:31798959). {ECO:0000269|PubMed:29106398, ECO:0000269|PubMed:30997682, ECO:0000269|PubMed:31230984, ECO:0000269|PubMed:31798959, ECO:0000269|PubMed:32337066, ECO:0000269|PubMed:33705351}.

Versican core protein	3357	FUNCTION: May play a role in intercellular signaling and in connecting cells with the extracellular matrix. May take part in the regulation of cell motility, growth and differentiation. Binds hyaluronic acid.
All-trans-retinol 13,14-reductase	609	FUNCTION: Catalyzes the saturation of all-trans-retinol to all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779, PubMed:19139408). Does not exhibit any activity toward all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers (PubMed:15358783). May play a role in the metabolism of vitamin A (PubMed:15358783, PubMed:17253779). Independently of retinol conversion, may regulate liver metabolism upstream of MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This effect seems not to mimic the in vivo situation in which animals show increased adiposity in the absence of RETSAT (PubMed:19940255). {ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:1913940255, ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
Calcium-transporting ATPase type 2C member 1	918	FUNCTION: ATP-driven pump that supplies the Golgi apparatus with Ca(2+) and Mn(2+) ions, both essential cofactors for processing and trafficking of newly synthesized proteins in the secretory pathway (By similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on the cytoplasmic side of the membrane and delivers them to the lumenal side. The transfer of ions across the membrane is coupled to ATP hydrolysis and is associated with a transient phosphorylation that shifts the pump conformation from inward-facing to outward-facing state (By similarity). Plays a primary role in the maintenance of Ca(2+) homeostasis in the trans-Golgi compartment with a functional impact on Golgi and post-Golgi protein sorting as well as a structural impact on cisternae morphology. Responsible for loading the Golgi stores with Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation and epidermis integrity (By similarity). Participates in Ca(2+) and Mn(2+) ions uptake into the Golgi store of hippocampal neurons and regulates protein trafficking required for neural polarity (PubMed:19793975). May also play a role in the maintenance of Ca(2+) and Mn(2+) homeostasis and signaling in the cytosol while preventing cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194, ECO:0000269 PubMed:19793975}.
Exopolyphosphatase PRUNE1	454	FUNCTION: Phosphodiesterase (PDE) that has higher activity toward cAMP than cGMP, as substrate. Plays a role in cell proliferation, migration and differentiation, and acts as a negative regulator of NME1. Plays a role in the regulation of neurogenesis. Involved in the regulation of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma membrane-associated	415	FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl acetate and phenyl acetate (By similarity). May play a role in adipocyte

protein		differentiation. {ECO:0000250}.
		FUNCTION: Regulator of phosphate homeostasis (By similarity).
		Inhibits renal tubular phosphate transport by reducing SLC34A1 levels
		(By similarity). Acts directly on the parathyroid to decrease PTH
Fibroblast growth factor	251	secretion (By similarity). Regulator of vitamin-D metabolism (By
23		similarity). Negatively regulates osteoblasts differentiation and matrix
		mineralization (By similarity). Up-regulates EGR1 expression in the
		presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
		FUNCTION: Receptor for extracellularly released ATP acting as a
		ligand-gated ion channel that plays multiple role in immunity and central
		nervous system physiology (PubMed:26456657, PubMed:35119925).
		Plays a key role in initial steps of T-cell activation and Ca(2+)
		microdomain formation (PubMed:35119925). Participates also in basal
		T-cell activity without TCR/CD3 stimulation (PubMed:35119925).
P2X purinoceptor 4	388	Promotes the differentiation and activation of Th17 cells via expression
		of retinoic acid-related orphan receptor C/RORC (By similarity). Upon
		activation, drives microglia motility via the PI3K/Akt pathway
		(PubMed:17299767). {ECO:0000250 UniProtKB:Q99571,
		ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:26456657,
		ECO:0000269 PubMed:35119925}.
		FUNCTION: Glycosyltransferase which regulates the biosynthesis of
	918	heparan sulfate (HS). Important for both skeletal development and
		hematopoiesis, through the formation of HS proteoglycans (HSPGs).
Exostosin-like 3		Required for the function of REG3A in regulating keratinocyte
		proliferation and differentiation (By similarity).
		{ECO:0000250 UniProtKB:O43909}.
		FUNCTION: Component of the ESCRT-I complex, a regulator of
Vacuolar protein		vesicular trafficking process. Required for the sorting of endocytic
sorting-associated protein	285	ubiquitinated cargos into multivesicular bodies. May be involved in cell
37B		growth and differentiation (By similarity). {ECO:0000250}.
		FUNCTION: Has no ubiquitin ligase activity on its own. The
		UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical
		poly-ubiquitin chains that are linked through 'Lys-63'. This type of
		poly-ubiquitination activates IKK and does not seem to involve protein
		degradation by the proteasome. Plays a role in the activation of
Ubiquitin-conjugating enzyme E2 variant 1		NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates
	147	transcriptional activation of target genes. Plays a role in the control of
		progress through the cell cycle and differentiation (By similarity). Plays a
		role in the error-free DNA repair pathway and contributes to the survival of cells after DNA damage. Promotes TRIM5 capsid-specific restriction
		activity and the UBE2V1-UBE2N heterodimer acts in concert with
		TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate
		the MAP3K7/TAK1 complex which in turn results in the induction and
		expression of NF-kappa-B and MAPK-responsive inflammatory genes

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		(By similarity). Together with RNF135 and UBE2N, catalyzes the viral
		RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to
		activate the downstream signaling pathway that leads to interferon beta
		production (By similarity). UBE2V1-UBE2N together with TRAF3IP2
		E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6,
		a component of IL17A-mediated signaling pathway. {ECO:0000250,
		ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
		FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties
		conjugated to substrates and thus, functions to process newly synthesized
Ubiquitin		Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains
carboxyl-terminal	1055	and prevents proteasomal degradation of substrates. Hydrolyzes both
hydrolase 25		'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
		{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
		may have a role in the regulation of muscular differentiation and function.
		FUNCTION: Transcriptional regulator involved in different processes
		such as glucose metabolism, aerobic glycolysis, muscle cell
		differentiation and autophagy (PubMed:25402684, PubMed:29861159,
		PubMed:30700909). Recognizes and binds the forkhead DNA sequence
		motif (5'-GTAAACA-3') and can both act as a transcription activator or
		repressor, depending on the context (PubMed:25402684,
		PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
	719	key regulator of metabolic reprogramming towards aerobic glycolysis, a
		process in which glucose is converted to lactate in the presence of oxygen
		(PubMed:30700909). Acts by promoting expression of enzymes for
		glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
		kinase (PKLR) and lactate dehydrogenase), while suppressing further
		oxidation of pyruvate in the mitochondria by up-regulating pyruvate
		dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
Forkhead box protein K1		plays a role in gluconeogenesis during overnight fasting, when lactate
		from white adipose tissue and muscle is the main substrate
		(PubMed:30700909). Involved in mTORC1-mediated metabolic
		reprogramming: in response to mTORC1 signaling, translocates into the
		nucleus and regulates the expression of genes associated with glycolysis
		and downstream anabolic pathways, such as HIF1A, thereby regulating
		glucose metabolism (PubMed:29861159). Together with FOXK2, acts as
		a negative regulator of autophagy in skeletal muscle: in response to
		starvation, enters the nucleus, binds the promoters of autophagy genes
		and represses their expression, preventing proteolysis of skeletal muscle
		proteins (PubMed:25402684). Acts as a transcriptional regulator of the
		myogenic progenitor cell population in skeletal muscle
		(PubMed:8007964, PubMed:9271401, PubMed:12446708,
		PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
		of myoglobin (MB) gene, regulating the myogenic progenitor cell
		population (PubMed:8007964, PubMed:9271401). Promotes muscle
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		progenitor cell proliferation by repressing the transcriptional activity of
		FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
		PubMed:22956541). Involved in remodeling processes of adult muscles
		that occur in response to physiological stimuli (PubMed:9271401,
		PubMed:22956541). Required to correct temporal orchestration of
		molecular and cellular events necessary for muscle repair
		(PubMed:10792059). Represses myogenic differentiation by inhibiting
		MEFC activity (PubMed:22956541). Positively regulates
		Wnt/beta-catenin signaling by translocating DVL into the nucleus (By
		similarity). Reduces virus replication, probably by binding the interferon
		stimulated response element (ISRE) to promote antiviral gene expression
		(By similarity). {ECO:0000250 UniProtKB:P85037,
		ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:12446708,
		ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:25402684,
		ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:30700909,
		ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.
		FUNCTION: Component of the cleavage and polyadenylation specificity
		factor (CPSF) complex that plays a key role in pre-mRNA 3'-end
		formation, recognizing the AAUAAA signal sequence and interacting
		with poly(A) polymerase and other factors to bring about cleavage and
		poly(A) addition. Has endonuclease activity, and functions as mRNA
		3'-end-processing endonuclease. Also involved in the histone 3'-end
		pre-mRNA processing. U7 snRNP-dependent protein that induces both
		the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a
		5' to 3' exonuclease for degrading the subsequent downstream cleavage
		product (DCP) of mature histone mRNAs. Cleavage occurs after the
		5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl
		group on the upstream fragment containing the stem loop (SL) and 5'
Cleavage and		phosphate on the downstream cleavage product (DCP) starting with CU
polyadenylation		nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive
specificity factor subunit	684	and degrades the DCP RNA substrate even after complete removal of the
3		U7-binding site. Binds to the downstream cleavage product (DCP) of
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		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
		(miRNAs) during embryonic stem cell differentiation via its interaction
		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
		primary transcript except miR-92a (PubMed:26255770). Only required
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
		pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
		ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
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Mitogen-activated protein kinase 1

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FUNCTION: Serine/threonine kinase which acts as an essential component of the MAP kinase signal transduction pathway. MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an important role in the MAPK/ERK cascade. They participate also in a signaling cascade initiated by activated KIT and KITLG/SCF. Depending on the cellular context, the MAPK/ERK cascade mediates diverse biological functions such as cell growth, adhesion, survival and differentiation through the regulation of transcription, translation, cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role in initiation and regulation of meiosis, mitosis, and postmitotic functions in differentiated cells by phosphorylating a number of transcription factors. About 160 substrates have already been discovered for ERKs. Many of these substrates are localized in the nucleus, and seem to participate in the regulation of transcription upon stimulation. However, other substrates are found in the cytosol as well as in other cellular organelles, and those are responsible for processes such as translation, mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also involved in the regulation of the endosomal dynamics, including lysosome processing and endosome cycling through the perinuclear recycling compartment (PNRC); as well as in the fragmentation of the Golgi apparatus during mitosis. The substrates include transcription factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1), cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT, PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD, BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of translation (such as EIF4EBP1) and a variety of other signaling-related molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases (such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3, RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2, RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other substrates which enable the propagation the MAPK/ERK signal to additional cytosolic and nuclear targets, thereby extending the specificity of the cascade. Mediates phosphorylation of TPR in response to EGF stimulation. May play a role in the spindle assembly checkpoint. Phosphorylates PML and promotes its interaction with PIN1, leading to PML degradation. Phosphorylates CDK2AP2 (By similarity). {ECO:0000250|UniProtKB:P28482, ECO:0000250|UniProtKB:P63086, ECO:0000269|PubMed:10753946, ECO:0000269|PubMed:11702783, ECO:0000269|PubMed:12134156, ECO:0000303|PubMed:16393692, ECO:0000303|PubMed:19565474, ECO:0000303|PubMed:21779493}.; FUNCTION: Acts as a transcriptional repressor. Binds to a [GC]AAA[GC] consensus sequence. Repress the expression of interferon gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1,

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		IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1.
		Transcriptional activity is independent of kinase activity.
		{ECO:0000250 UniProtKB:P28482}.
		FUNCTION: RNA-binding protein that acts as a key regulator of
		N6-methyladenosine (m6A) methylation of RNAs, thereby regulating
		different processes, such as hematopoietic cell homeostasis, alternative
		splicing of mRNAs and X chromosome inactivation mediated by Xist
		RNA (PubMed:29535189). Associated component of the WMM
		complex, a complex that mediates N6-methyladenosine (m6A)
		methylation of RNAs, a modification that plays a role in the efficiency of
		mRNA splicing and RNA processing (PubMed:29535189). Plays a key
		role in m6A methylation, possibly by binding target RNAs and recruiting
		the WMM complex (PubMed:29535189). Involved in random X
		inactivation mediated by Xist RNA: acts by binding Xist RNA and
		recruiting the WMM complex, which mediates m6A methylation, leading
		to target YTHDC1 reader on Xist RNA and promoting transcription
		repression activity of Xist (By similarity). Required for the development
		of multiple tissues, such as the maintenance of the homeostasis of
		long-term hematopoietic stem cells and for megakaryocyte (MK) and
		B-cell differentiation (PubMed:17283045, PubMed:17376872,
RNA-binding protein 15	962	PubMed:18981216, PubMed:25468569). Regulates megakaryocyte
		differentiation by regulating alternative splicing of genes important for
		megakaryocyte differentiation; probably regulates alternative splicing via
		m6A regulation (By similarity). Required for placental vascular
		branching morphogenesis and embryonic development of the heart and
		spleen (PubMed:18981216). Acts as a regulator of thrombopoietin
		response in hematopoietic stem cells by regulating alternative splicing of
		MPL (PubMed:25468569). May also function as an mRNA export factor,
		stimulating export and expression of RTE-containing mRNAs which are
		present in many retrotransposons that require to be exported prior to
		splicing (By similarity). High affinity binding of pre-mRNA to RBM15
		may allow targeting of the mRNP to the export helicase DBP5 in a
		manner that is independent of splicing-mediated NXF1 deposition,
		resulting in export prior to splicing (By similarity). May be implicated in
		HOX gene regulation (By similarity).
		{ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:17283045,
		ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18981216,
		ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29535189}.
		FUNCTION: Transcription coactivator which associates with nuclear
Activating signal	501	receptors, transcriptional coactivators including EP300, CREBBP and
		NCOA1, and basal transcription factors like TBP and TFIIA to facilitate
cointegrator 1	581	nuclear receptors-mediated transcription. May thereby play an important
		role in establishing distinct coactivator complexes under different cellular
		conditions. Plays a role in thyroid hormone receptor and estrogen
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		receptor transactivation (By similarity). Also involved in androgen receptor transactivation (PubMed:12077347). Plays a pivotal role in the transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of
		transrepression between nuclear receptor and either AP1 or NF-kappa-B.
		May play a role in the development of neuromuscular junction (By
		similarity). May play a role in late myogenic differentiation
		(PubMed:27008887). Also functions as part of the RQC trigger (RQT)
		complex that activates the ribosome quality control (RQC) pathway, a
		pathway that degrades nascent peptide chains during problematic
		translation (By similarity). {ECO:0000250 UniProtKB:Q15650,
		ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
		ECO:0000269 PubMed:27008887}.
		FUNCTION: Histone methyltransferase that specifically trimethylates
		'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36'
		(H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is
		capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
		similarity). Represents the main enzyme generating H3K36me3, a
		specific tag for epigenetic transcriptional activation (PubMed:18157086,
		PubMed:20133625). Plays a role in chromatin structure modulation
		during elongation by coordinating recruitment of the FACT complex and
		by interacting with hyperphosphorylated POLR2A (By similarity). Acts
		as a key regulator of DNA mismatch repair in G1 and early S phase by
		generating H3K36me3, a mark required to recruit MSH6 subunit of the
		MutS alpha complex: early recruitment of the MutS alpha complex to
		chromatin to be replicated allows a quick identification of mismatch
		DNA to initiate the mismatch repair reaction (By similarity). Required for
TT's to a section of		DNA double-strand break repair in response to DNA damage: acts by
Histone-lysine	2537	mediating formation of H3K36me3, promoting recruitment of RAD51
N-methyltransferase SETD2	2337	and DNA repair via homologous recombination (HR) (By similarity).
SEIDZ		Acts as a tumor suppressor (By similarity). H3K36me3 also plays an
		essential role in the maintenance of a heterochromatic state, by recruiting
		DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also
		enhanced in intron-containing genes, suggesting that SETD2 recruitment
		is enhanced by splicing and that splicing is coupled to recruitment of
		elongating RNA polymerase (By similarity). Required during
		angiogenesis (PubMed:20133625). Required for endoderm development
		by promoting embryonic stem cell differentiation toward endoderm: acts
		by mediating formation of H3K36me3 in distal promoter regions of
		FGFR3, leading to regulate transcription initiation of FGFR3
		(PubMed:25242323). In addition to histones, also mediates methylation
		of other proteins, such as tubulins and STAT1 (PubMed:27518565).
		Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B
		(alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis
		and cytokinesis and may be a specific tag in cytoskeletal remodeling

(PubMed:27518565). Involved in interferor-alpha-induced antiviral defense by mediating both monomethylation of STAT1 at 'Lys-525' and catalyzing H3K36ms3 on promoters of some interferon-stimulated genes (ISGs) to activate gene transcription (By similarity). [ECO:0000250](LiniProttB:29BYW2, ECO:00002269]PubMed:20133625, ECO:0000269]PubMed:25518565}.  EUNCTION: RNA-binding protein that plays a central role in myelinization (PubMed:1857086, ECO:0000269]PubMed:27518565}.  FUNCTION: RNA-binding protein that plays a central role in myelinization (PubMed:10864952, PubMed:11917126). Also required for visceral endoderm function and blood vessel development (PubMed:1892011, PubMed:16470614). Binds to the 5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence (PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA export, mRNA stability and protein translation, as well as cellular processes including apoptosis, cell cycle, glial cell fate and development (PubMed:160435896), PubMed:15580022). Required to protect and promote stability of mRNAs such as MBP and CDKN1B which promotes oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022). Participates in mRNA transport by regulating the nuclear export of MBP mRNA (PubMed:14768670). (ECO:0000269]PubMed:1568022). Percoipate in mRNA transport by regulating the nuclear export of MBP mRNA (PubMed:14766070). (ECO:0000269]PubMed:11971709. ECO:0000269]PubMed:11971709. EVENCTION: Isoform 1 as involved in regulation of mRNA splicing of MAG pre-mRNA by acting as a neg			(D-1M-1275105(5) L1 11 1
catalyzing H3K36me3 on promoters of some interferon-stimulated genes (ISGs) to activate gene transcription (By similarity).  {ECO:0000250 UniProtKB:Q9BYW2, ECO:0000259 PubMed:20133625, ECO:0000269 PubMed:25187086, ECO:0000269 PubMed:20133625, ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.  FUNCTION: RNA-binding protein that plays a central role in myelinization (PubMed:10864952, PubMed:11917126). Also required for visceral endoderm function and blood vessel development (PubMed:11892011, PubMed:16470614). Binds to the 5'-NACUAAY-N(1,20)-UAAY-3'RNA core sequence (PubMed:16401388). Acts by regulating pre-mRNA splicing, mRNA export, mRNA stability and protein translation, as well as cellular processes including apoptosis, cell cycle, glial cell fate and development (PubMed:103535969, PubMed:15568022). Required to protect and promote stability of mRNAs such as MBP and CDKN1B which promotes oligodendrocyte differentiation (PubMed:10353969, PubMed:15568022). Participates in mRNA transport by regulating the nuclear export of MBP mRNA (PubMed:12467586). May also play a role in smooth muscle development (PubMed:14706070). [ECO:0000269]PubMed:15568022). ECO:0000269]PubMed:1897509, ECO:0000269]PubMed:18064952, ECO:0000269]PubMed:1197716, ECO:0000269]PubMed:1197166, ECO:0000269]PubMed:1197166, ECO:0000269]PubMed:1197166, ECO:0000269]PubMed:16470614; FUNCTION: Isoform 1 is involved in regulation of mRNA splicing of MAG pre-mRNA by acting as a negative regulator of mRNA splicing of MAG pre-mRNA by acting as a negative regulator of mRNA splicing of MAG pre-mRNA by acting as a negative regulator of isoform 3 and suppression of apoptosis. (ECO:0000269]PubMed:1197726;; FUNCTION: Isoform 4 acts as a translational repressor for GLII. (ECO:0000269]PubMed:16198329}.  FUNCTION: May act as a GTPase-activating protein for Rab family protein(s). May play a role in the cell cycle and differentiation of various tissues. Involved in the trafficking and translocation of various tissues. Involved in the trafficking and translocati			1 · · · · · · · · · · · · · · · · · · ·
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1 1/15 1	SWI/SNF complex	1212	FUNCTION: Involved in transcriptional activation and repression of
subunit SMARCC2 select genes by chromatin remodeling (alteration of DNA-nucleosome	subunit SMARCC2	1213	select genes by chromatin remodeling (alteration of DNA-nucleosome

		topology). Component of SWI/SNF chromatin remodeling complexes that carry out key enzymatic activities, changing chromatin structure by altering DNA-histone contacts within a nucleosome in an ATP-dependent manner. Can stimulate the ATPase activity of the catalytic subunit of these complexes. May be required for CoREST dependent repression of neuronal specific gene promoters in non-neuronal cells. Belongs to the neural progenitors-specific chromatin remodeling complex (npBAF complex) and the neuron-specific chromatin remodeling complex (nBAF complex). During neural development a switch from a stem/progenitor to a postmitotic chromatin remodeling mechanism occurs as neurons exit the cell cycle and become committed to their adult state. The transition from proliferating neural stem/progenitor cells to postmitotic neurons requires a switch in subunit composition of the npBAF and nBAF complexes. As neural progenitors exit mitosis and differentiate into neurons, npBAF complexes which contain ACTL6A/BAF53A and PHF10/BAF45A, are exchanged for homologous alternative ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in neuron-specific complexes (nBAF). The npBAF complex is essential for the self-renewal/proliferative capacity of the multipotent neural stem cells. The nBAF complex along with CREST plays a role regulating the activity of genes essential for dendrite growth (PubMed:17640523). Critical regulator of myeloid differentiation, controlling granulocytopoiesis and the expression of genes involved in neutrophil granule formation (PubMed:28369036). [ECO:0000269 PubMed:31216030, ECO:0000269 PubMed:28369036, ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240, ECO:0000303 PubMed:26601204}.
Protein prune homolog 2	3084	FUNCTION: May play an important role in regulating differentiation, survival and aggressiveness of the tumor cells. {ECO:0000250}.
Ninjurin-1	152	FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion molecule involved in various processes such as inflammation, cell death, axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008, PubMed:24347169, PubMed:24917672, PubMed:31526566, PubMed:33472215). Promotes cell adhesion by mediating homophilic interactions via its extracellular N-terminal adhesion motif (N-NAM) (PubMed:24917672, PubMed:30510259). Involved in the progression of the inflammatory stress by promoting cell-to-cell interactions between immune cells and endothelial cells (PubMed:24917672, PubMed:30510259). Involved in leukocyte migration during inflammation by promoting transendothelial migration of macrophages via homotypic binding (PubMed:24917672). Promotes the migration of monocytes across the brain endothelium to central nervous system inflammatory lesions (By similarity). Acts as a regulator of Toll-like receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during

systemic inflammation; directly binds LPS (PubMed:25860173). Acts as a mediator of both programmed and necrotic cell death (PubMed:19557008, PubMed:33472215). Plays a key role in the induction of plasma membrane rupture during programmed and necrotic cell death: oligomerizes in response to death stimuli to mediate plasma membrane rupture (cytolysis), leading to release intracellular molecules named damage-associated molecular patterns (DAMPs) that propagate the inflammatory response (PubMed:33472215). Plays a role in nerve regeneration by promoting maturation of Schwann cells (PubMed:31526566). Acts as a regulator of angiogenesis (PubMed:25766274, PubMed:30354207). Promotes the formation of new vessels by mediating the interaction between capillary pericyte cells and endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates vascular functions in penile tissue as well as vascular formation (PubMed:24979788). Promotes osteoclasts development by enhancing the survival of prefusion osteoclasts (PubMed:30700695). Also involved in striated muscle growth and differentiation (PubMed:31091274). Also involved in cell senescence in a p53/TP53 manner, possibly by acting as an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620, PubMed:29073078). {ECO:0000250|UniProtKB:Q92982, ECO:0000269|PubMed:19557008, ECO:0000269|PubMed:23690620, ECO:0000269|PubMed:24347169, ECO:0000269|PubMed:24917672, ECO:0000269|PubMed:24979788, ECO:0000269|PubMed:25766274, ECO:0000269|PubMed:25860173, ECO:0000269|PubMed:29073078, ECO:0000269|PubMed:30354207, ECO:0000269|PubMed:30510259, ECO:0000269|PubMed:30700695, ECO:0000269|PubMed:31091274, ECO:0000269|PubMed:31526566, ECO:0000269|PubMed:33472215}.; FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage, which has chemotactic activity (PubMed:23142597). Acts as an anti-inflammatory mediator by promoting monocyte recruitment, thereby ameliorating atherosclerosis (PubMed:32883094). {ECO:0000269|PubMed:23142597, ECO:0000269|PubMed:32883094}. FUNCTION: Phosphorylates a large number of substrates in the cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B, ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9 and VASP (PubMed:10805756, PubMed:19223768). Regulates the abundance of compartmentalized pools of its regulatory subunits through cAMP-dependent protein phosphorylation of PJA2 which binds and ubiquitinates these subunits, kinase catalytic subunit 351 leading to their subsequent proteolysis (By similarity). RORA is activated alpha by phosphorylation. Required for glucose-mediated adipogenic differentiation increase and osteogenic differentiation inhibition from osteoblasts (By similarity). Involved in chondrogenesis by mediating phosphorylation of SOX9 (PubMed:10805756). Involved in the regulation of platelets in response to thrombin and collagen; maintains

		circulating platelets in a resting state by phosphorylating proteins in numerous platelet inhibitory pathways when in complex with NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but thrombin and collagen disrupt these complexes and free active PRKACA stimulates platelets and leads to platelet aggregation by phosphorylating VASP. RYR2 channel activity is potentiated by phosphorylation in presence of luminal Ca(2+), leading to reduced amplitude and increased frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propagation velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude and resting cytosolic Ca(2+). PSMC5/RPT6 activation by phosphorylation stimulates proteasome. Negatively regulates tight junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation. NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding. Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and morphogenesis (By similarity). Prevents meiosis resumption in prophase-arrested oocytes via CDC25B inactivation by phosphorylation (PubMed:19223768). May also regulate rapid eye movement (REM) sleep in the pedunculopontine tegmental (PPT) (By similarity). Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this phosphorylation promotes HSF1 nuclear localization and transcriptional activity upon heat shock (By similarity). {ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791, ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.; FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm flagellum to promote spermatozoa capacitation. {ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.
Interleukin-4 receptor subunit alpha	810	FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in promoting Th2 differentiation. The IL4/IL13 responses are involved in regulating IgE production and, chemokine and mucus production at sites of allergic inflammation. In certain cell types, can signal through activation of insulin receptor substrates, IRS1/IRS2.
Protein NEDD1	660	FUNCTION: Required for mitosis progression. Promotes the nucleation of microtubules from the spindle (By similarity). May play an important role during the embryonic development and differentiation of the central nervous system (PubMed:1378265).  {ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
Protein phosphatase 3 catalytic subunit alpha	521	FUNCTION: Calcium-dependent, calmodulin-stimulated protein phosphatase which plays an essential role in the transduction of intracellular Ca(2+)-mediated signals (PubMed:7791792, PubMed:26794871). Many of the substrates contain a PxIxIT motif and/or a LxVP motif (By similarity). In response to increased Ca(2+)

levels, dephosphorylates and activates phosphatase SSH1 which results in cofilin dephosphorylation (By similarity). In response to increased Ca(2+) levels following mitochondrial depolarization, dephosphorylates DNM1L inducing DNM1L translocation to the mitochondrion (By similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+) release probability at hippocampal neuronal soma and synaptic terminals (By similarity). Dephosphorylates heat shock protein HSPB1 (By similarity). Dephosphorylates and activates transcription factor NFATC1 (By similarity). Dephosphorylates and inactivates transcription factor ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation from 14-3-3 proteins (By similarity). Required for postnatal development of the nephrogenic zone and superficial glomeruli in the kidneys, cell cycle homeostasis in the nephrogenic zone, and ultimately normal kidney function (PubMed:15509543). Plays a role in intracellular AQP2 processing and localization to the apical membrane in the kidney, may thereby be required for efficient kidney filtration (PubMed:16735444). Required for secretion of salivary enzymes amylase, peroxidase, lysozyme and sialic acid via formation of secretory vesicles in the submandibular glands (PubMed:21435446). Required for calcineurin activity and homosynaptic depotentiation in the hippocampus (PubMed:10200317). Required for normal differentiation and survival of keratinocytes and therefore required for epidermis superstructure formation (PubMed:19626032). Positively regulates osteoblastic bone formation, via promotion of osteoblast differentiation (PubMed:16286645). Positively regulates osteoclast differentiation, potentially via NFATC1 signaling (PubMed:16968888). May play a role in skeletal muscle fiber type specification, potentially via NFATC1 signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK signaling via inhibition of nuclear translocation of the transcription factors RELA and RELB (PubMed:26029823). Required for antigen-specific T-cell proliferation response (PubMed:8627154). {ECO:0000250|UniProtKB:P48452, ECO:0000250|UniProtKB:P63329, ECO:0000250|UniProtKB:Q08209, ECO:0000269|PubMed:10200317, ECO:0000269|PubMed:12773574, ECO:0000269|PubMed:15509543, ECO:0000269|PubMed:16286645, ECO:0000269|PubMed:16735444, ECO:0000269|PubMed:16968888, ECO:0000269|PubMed:19626032, ECO:0000269|PubMed:21435446, ECO:0000269|PubMed:26029823, ECO:0000269|PubMed:26794871, ECO:0000269|PubMed:7791792, ECO:0000269|PubMed:8627154}. FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in

SLAM family member 5

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		the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell:B-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling; independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretion; involving ITSM 2 (PubMed:20628063). Positively regulates macroautophagy in primary dendritic cells via stabilization of IRF8; inhibits TRIM21-mediated proteasomal degradation of IRF8 (By similarity). {ECO:0000250 UniProtKB:Q9UIB8, ECO:0000269 PubMed:16037392, ECO:0000269 PubMed:20153220, ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259, ECO:0000269 PubMed:25801429, ECO:0000305}.
Transmembrane anterior posterior transformation protein 1	564	FUNCTION: Plays a role in primary cilia formation (By similarity). May act as a downstream effector of HOXC8 possibly by transducing or transmitting extracellular information required for axial skeletal patterning during development (By similarity). May be involved in cartilage and bone development (By similarity). May play a role in the differentiation of cranial neural crest cells (By similarity). {ECO:0000250 UniProtKB:A2BIE7, ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
Fibrillin-1	2873	FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm diameter microfibrils of the extracellular matrix, which conveys both structural and regulatory properties to load-bearing connective tissues. Fibrillin-1-containing microfibrils provide long-term force bearing structural support. In tissues such as the lung, blood vessels and skin, microfibrils form the periphery of the elastic fiber, acting as a scaffold for the deposition of elastin. In addition, microfibrils can occur as elastin-independent networks in tissues such as the ciliary zonule, tendon, cornea and glomerulus where they provide tensile strength and have anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis through specific interactions with growth factors, such as the bone

		morphogenetic proteins (BMPs), growth and differentiation factors
		(GDFs) and latent transforming growth factor-beta-binding proteins
		(LTBPs), cell-surface integrins and other extracellular matrix protein and
		proteoglycan components (By similarity). Regulates osteoblast
		maturation by controlling TGF-beta bioavailability and calibrating
		TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively
		regulates osteoclastogenesis by binding and sequestering an osteoclast
		differentiation and activation factor TNFSF11. This leads to disruption of
		TNFSF11-induced Ca(2+) signaling and impairment of
		TNFSF11-mediated nuclear translocation and activation of transcription
		factor NFATC1 which regulates genes important for osteoclast
		differentiation and function (PubMed:24039232). Mediates cell adhesion
		via its binding to cell surface receptors integrins ITGAV:ITGB3 and
		ITGA5:ITGB1. Binds heparin and this interaction plays an important rol
		in the assembly of microfibrils (By similarity).
		{ECO:0000250 UniProtKB:P35555, ECO:0000269 PubMed:20855508,
		ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokir
		secreted by white adipose tissue that plays an important regulatory role
		the glucose metabolism of liver, muscle and pancreas
		(PubMed:31230984, PubMed:30997682). Hormone that targets the liver
		in response to fasting to increase plasma glucose levels
		(PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface
		of hepatocytes and promotes hepatocyte glucose release by activating th
		protein kinase A activity in the liver, resulting in rapid glucose release
		into the circulation (PubMed:31230984). May act as a regulator of
		adaptive thermogenesis by inhibiting browning and energy consumption
		while increasing lipid deposition in white adipose tissue
		(PubMed:33705351). Also acts as an orexigenic hormone that increases
		appetite: crosses the blood brain barrier and exerts effects on the
		hypothalamus (PubMed:29106398). In the arcuate nucleus of the
		hypothalamus, asprosin directly activates orexigenic AgRP neurons and
		indirectly inhibits anorexigenic POMC neurons, resulting in appetite
		stimulation (PubMed:29106398, PubMed:32337066). Activates
		orexigenic AgRP neurons via binding to the olfactory receptor Olfr734
		(PubMed:32337066). May also play a role in sperm motility in testis via
		interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682,
		ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959,
		ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
		FUNCTION: May play a role in intercellular signaling and in connectin
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cel
1		motility, growth and differentiation. Binds hyaluronic acid.
All-trans-retinol		FUNCTION: Catalyzes the saturation of all-trans-retinol to
13,14-reductase	609	all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779,

P2X purinoceptor 4	388	similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.  FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central nervous system physiology (PubMed:26456657, PubMed:35119925).  Plays a key role in initial steps of T-cell activation and Ca(2+) microdomain formation (PubMed:35119925). Participates also in basal T-cell activity without TCR/CD3 stimulation (PubMed:35119925).  Promotes the differentiation and activation of Th17 cells via expression of retinoic acid-related orphan receptor C/RORC (By similarity). Upon activation, drives microglia motility via the PI3K/Akt pathway (PubMed:17299767). {ECO:0000250 UniProtKB:Q99571, ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:35119925}.
Exostosin-like 3	918	FUNCTION: Glycosyltransferase which regulates the biosynthesis of heparan sulfate (HS). Important for both skeletal development and hematopoiesis, through the formation of HS proteoglycans (HSPGs).  Required for the function of REG3A in regulating keratinocyte proliferation and differentiation (By similarity).  {ECO:0000250 UniProtKB:O43909}.
Vacuolar protein sorting-associated protein 37B	285	FUNCTION: Component of the ESCRT-I complex, a regulator of vesicular trafficking process. Required for the sorting of endocytic ubiquitinated cargos into multivesicular bodies. May be involved in cell growth and differentiation (By similarity). {ECO:0000250}.
Ubiquitin-conjugating enzyme E2 variant 1	147	FUNCTION: Has no ubiquitin ligase activity on its own. The UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical poly-ubiquitin chains that are linked through 'Lys-63'. This type of poly-ubiquitination activates IKK and does not seem to involve protein degradation by the proteasome. Plays a role in the activation of NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates transcriptional activation of target genes. Plays a role in the control of progress through the cell cycle and differentiation (By similarity). Plays a role in the error-free DNA repair pathway and contributes to the survival of cells after DNA damage. Promotes TRIM5 capsid-specific restriction activity and the UBE2V1-UBE2N heterodimer acts in concert with TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate the MAP3K7/TAK1 complex which in turn results in the induction and expression of NF-kappa-B and MAPK-responsive inflammatory genes (By similarity). Together with RNF135 and UBE2N, catalyzes the viral RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to activate the downstream signaling pathway that leads to interferon beta production (By similarity). UBE2V1-UBE2N together with TRAF3IP2 E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6,

		CCO 0000250
		a component of IL17A-mediated signaling pathway. {ECO:0000250,
		ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
		FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties
		conjugated to substrates and thus, functions to process newly synthesized
Ubiquitin		Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains
carboxyl-terminal	1055	and prevents proteasomal degradation of substrates. Hydrolyzes both
hydrolase 25		'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
		{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
		may have a role in the regulation of muscular differentiation and function.
		FUNCTION: Transcriptional regulator involved in different processes
		such as glucose metabolism, aerobic glycolysis, muscle cell
		differentiation and autophagy (PubMed:25402684, PubMed:29861159,
		PubMed:30700909). Recognizes and binds the forkhead DNA sequence
		motif (5'-GTAAACA-3') and can both act as a transcription activator or
		repressor, depending on the context (PubMed:25402684,
		PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
		key regulator of metabolic reprogramming towards aerobic glycolysis, a
		process in which glucose is converted to lactate in the presence of oxygen
		(PubMed:30700909). Acts by promoting expression of enzymes for
		glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
		kinase (PKLR) and lactate dehydrogenase), while suppressing further
		oxidation of pyruvate in the mitochondria by up-regulating pyruvate
		dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
		plays a role in gluconeogenesis during overnight fasting, when lactate
		from white adipose tissue and muscle is the main substrate
		(PubMed:30700909). Involved in mTORC1-mediated metabolic
Forkhead box protein K1	719	reprogramming: in response to mTORC1 signaling, translocates into the
		nucleus and regulates the expression of genes associated with glycolysis
		and downstream anabolic pathways, such as HIF1A, thereby regulating
		glucose metabolism (PubMed:29861159). Together with FOXK2, acts as
		a negative regulator of autophagy in skeletal muscle: in response to
		starvation, enters the nucleus, binds the promoters of autophagy genes
		and represses their expression, preventing proteolysis of skeletal muscle
		proteins (PubMed:25402684). Acts as a transcriptional regulator of the
		myogenic progenitor cell population in skeletal muscle
		(PubMed:8007964, PubMed:9271401, PubMed:12446708,
		PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
		of myoglobin (MB) gene, regulating the myogenic progenitor cell
		population (PubMed:8007964, PubMed:9271401). Promotes muscle
		progenitor cell proliferation by repressing the transcriptional activity of
		FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
		PubMed:22956541). Involved in remodeling processes of adult muscles
		that occur in response to physiological stimuli (PubMed:9271401,
		PubMed:22956541). Required to correct temporal orchestration of
	l	, 1

		molecular and cellular events necessary for muscle repair
		(PubMed:10792059). Represses myogenic differentiation by inhibiting
		MEFC activity (PubMed:22956541). Positively regulates
		Wnt/beta-catenin signaling by translocating DVL into the nucleus (By
		similarity). Reduces virus replication, probably by binding the interferon
		stimulated response element (ISRE) to promote antiviral gene expression
		(By similarity). {ECO:0000250 UniProtKB:P85037,
		ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:12446708,
		ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:25402684,
		ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:30700909,
		ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.
		FUNCTION: Component of the cleavage and polyadenylation specificity
		factor (CPSF) complex that plays a key role in pre-mRNA 3'-end
		formation, recognizing the AAUAAA signal sequence and interacting
		with poly(A) polymerase and other factors to bring about cleavage and
		poly(A) addition. Has endonuclease activity, and functions as mRNA
		3'-end-processing endonuclease. Also involved in the histone 3'-end
		pre-mRNA processing. U7 snRNP-dependent protein that induces both
		the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a
		5' to 3' exonuclease for degrading the subsequent downstream cleavage
		product (DCP) of mature histone mRNAs. Cleavage occurs after the
	684	5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl
		group on the upstream fragment containing the stem loop (SL) and 5'
Cleavage and		phosphate on the downstream cleavage product (DCP) starting with CU
_		nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive
polyadenylation		
specificity factor subunit		and degrades the DCP RNA substrate even after complete removal of the
3		U7-binding site. Binds to the downstream cleavage product (DCP) of
		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
		(miRNAs) during embryonic stem cell differentiation via its interaction
		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
		primary transcript except miR-92a (PubMed:26255770). Only required
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
	358	pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
		ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
		FUNCTION: Serine/threonine kinase which acts as an essential
Mitagen activated protein		component of the MAP kinase signal transduction pathway.
Mitogen-activated protein kinase 1		MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an
		important role in the MAPK/ERK cascade. They participate also in a
		signaling cascade initiated by activated KIT and KITLG/SCF. Depending
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on the cellular context, the MAPK/ERK cascade mediates diverse biological functions such as cell growth, adhesion, survival and differentiation through the regulation of transcription, translation, cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role in initiation and regulation of meiosis, mitosis, and postmitotic functions in differentiated cells by phosphorylating a number of transcription factors. About 160 substrates have already been discovered for ERKs. Many of these substrates are localized in the nucleus, and seem to participate in the regulation of transcription upon stimulation. However, other substrates are found in the cytosol as well as in other cellular organelles, and those are responsible for processes such as translation, mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also involved in the regulation of the endosomal dynamics, including lysosome processing and endosome cycling through the perinuclear recycling compartment (PNRC); as well as in the fragmentation of the Golgi apparatus during mitosis. The substrates include transcription factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1), cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT, PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD, BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of translation (such as EIF4EBP1) and a variety of other signaling-related molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases (such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3, RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2, RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other substrates which enable the propagation the MAPK/ERK signal to additional cytosolic and nuclear targets, thereby extending the specificity of the cascade. Mediates phosphorylation of TPR in response to EGF stimulation. May play a role in the spindle assembly checkpoint. Phosphorylates PML and promotes its interaction with PIN1, leading to PML degradation. Phosphorylates CDK2AP2 (By similarity). {ECO:0000250|UniProtKB:P28482, ECO:0000250|UniProtKB:P63086, ECO:0000269|PubMed:10753946, ECO:0000269|PubMed:11702783, ECO:0000269|PubMed:12134156, ECO:0000303|PubMed:16393692, ECO:0000303|PubMed:19565474, ECO:0000303|PubMed:21779493}.; FUNCTION: Acts as a transcriptional repressor. Binds to a [GC]AAA[GC] consensus sequence. Repress the expression of interferon gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1, IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1. Transcriptional activity is independent of kinase activity. {ECO:0000250|UniProtKB:P28482}.

RNA-binding protein 15

FUNCTION: RNA-binding protein that acts as a key regulator of N6-methyladenosine (m6A) methylation of RNAs, thereby regulating

different processes, such as hematopoietic cell homeostasis, alternative splicing of mRNAs and X chromosome inactivation mediated by Xist RNA (PubMed:29535189). Associated component of the WMM complex, a complex that mediates N6-methyladenosine (m6A) methylation of RNAs, a modification that plays a role in the efficiency of mRNA splicing and RNA processing (PubMed:29535189). Plays a key role in m6A methylation, possibly by binding target RNAs and recruiting the WMM complex (PubMed:29535189). Involved in random X inactivation mediated by Xist RNA: acts by binding Xist RNA and recruiting the WMM complex, which mediates m6A methylation, leading to target YTHDC1 reader on Xist RNA and promoting transcription repression activity of Xist (By similarity). Required for the development of multiple tissues, such as the maintenance of the homeostasis of long-term hematopoietic stem cells and for megakaryocyte (MK) and B-cell differentiation (PubMed:17283045, PubMed:17376872, PubMed:18981216, PubMed:25468569). Regulates megakaryocyte differentiation by regulating alternative splicing of genes important for megakaryocyte differentiation; probably regulates alternative splicing via m6A regulation (By similarity). Required for placental vascular branching morphogenesis and embryonic development of the heart and spleen (PubMed:18981216). Acts as a regulator of thrombopoietin response in hematopoietic stem cells by regulating alternative splicing of MPL (PubMed:25468569). May also function as an mRNA export factor, stimulating export and expression of RTE-containing mRNAs which are present in many retrotransposons that require to be exported prior to splicing (By similarity). High affinity binding of pre-mRNA to RBM15 may allow targeting of the mRNP to the export helicase DBP5 in a manner that is independent of splicing-mediated NXF1 deposition, resulting in export prior to splicing (By similarity). May be implicated in HOX gene regulation (By similarity). {ECO:0000250|UniProtKB:Q96T37, ECO:0000269|PubMed:17283045, ECO:0000269|PubMed:17376872, ECO:0000269|PubMed:18981216, ECO:0000269|PubMed:25468569, ECO:0000269|PubMed:29535189}. FUNCTION: Transcription coactivator which associates with nuclear receptors, transcriptional coactivators including EP300, CREBBP and NCOA1, and basal transcription factors like TBP and TFIIA to facilitate nuclear receptors-mediated transcription. May thereby play an important role in establishing distinct coactivator complexes under different cellular Activating signal 581 conditions. Plays a role in thyroid hormone receptor and estrogen cointegrator 1 receptor transactivation (By similarity). Also involved in androgen receptor transactivation (PubMed:12077347). Plays a pivotal role in the transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of transrepression between nuclear receptor and either AP1 or NF-kappa-B. May play a role in the development of neuromuscular junction (By

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		similarity). May play a role in late myogenic differentiation
		(PubMed:27008887). Also functions as part of the RQC trigger (RQT)
		complex that activates the ribosome quality control (RQC) pathway, a
		pathway that degrades nascent peptide chains during problematic
		translation (By similarity). {ECO:0000250 UniProtKB:Q15650,
		ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
		ECO:0000269 PubMed:27008887}.
		FUNCTION: Histone methyltransferase that specifically trimethylates
		'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36'
		(H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is
		capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
		similarity). Represents the main enzyme generating H3K36me3, a
		specific tag for epigenetic transcriptional activation (PubMed:18157086,
		PubMed:20133625). Plays a role in chromatin structure modulation
		during elongation by coordinating recruitment of the FACT complex and
		by interacting with hyperphosphorylated POLR2A (By similarity). Acts
		as a key regulator of DNA mismatch repair in G1 and early S phase by
		generating H3K36me3, a mark required to recruit MSH6 subunit of the
		MutS alpha complex: early recruitment of the MutS alpha complex to
		chromatin to be replicated allows a quick identification of mismatch
		DNA to initiate the mismatch repair reaction (By similarity). Required for
		DNA double-strand break repair in response to DNA damage: acts by
		mediating formation of H3K36me3, promoting recruitment of RAD51
		and DNA repair via homologous recombination (HR) (By similarity).
Histone-lysine		Acts as a tumor suppressor (By similarity). H3K36me3 also plays an
N-methyltransferase	2537	essential role in the maintenance of a heterochromatic state, by recruiting
SETD2		DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also
		enhanced in intron-containing genes, suggesting that SETD2 recruitment
		is enhanced by splicing and that splicing is coupled to recruitment of
		elongating RNA polymerase (By similarity). Required during
		angiogenesis (PubMed:20133625). Required for endoderm development
		by promoting embryonic stem cell differentiation toward endoderm: acts
		by mediating formation of H3K36me3 in distal promoter regions of
		FGFR3, leading to regulate transcription initiation of FGFR3
		(PubMed:25242323). In addition to histones, also mediates methylation
		of other proteins, such as tubulins and STAT1 (PubMed:27518565).
		Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B
		(alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis
		and cytokinesis and may be a specific tag in cytoskeletal remodeling
		(PubMed:27518565). Involved in interferon-alpha-induced antiviral
		defense by mediating both monomethylation of STAT1 at 'Lys-525' and
		catalyzing H3K36me3 on promoters of some interferon-stimulated genes
		(ISGs) to activate gene transcription (By similarity).
		(ECO:0000250 UniProtKB:Q9BYW2,
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		ECO.0000260[D.:LM1.19157096 ECO.0000260[D.:LM1.20122625
		ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625,
	-	ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.
		FUNCTION: RNA-binding protein that plays a central role in
		myelinization (PubMed:10864952, PubMed:11917126). Also required for
		visceral endoderm function and blood vessel development
		(PubMed:11892011, PubMed:16470614). Binds to the
		5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence
		(PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA
		export, mRNA stability and protein translation, as well as cellular
		processes including apoptosis, cell cycle, glial cell fate and development
		(PubMed:10535969, PubMed:12467586, PubMed:11297509,
		PubMed:11917126, PubMed:15568022). Required to protect and promote
		stability of mRNAs such as MBP and CDKN1B which promotes
		oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022).
		Participates in mRNA transport by regulating the nuclear export of MBP
Protein quaking	341	mRNA (PubMed: 12467586). May also play a role in smooth muscle
1 8		development (PubMed:14706070). {ECO:0000269 PubMed:10535969,
		ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509,
		ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126,
		ECO:0000269 PubMed:12467586, ECO:0000269 PubMed:14706070,
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388,
		ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved
		in regulation of mRNA splicing of MAG pre-mRNA by acting as a
		negative regulator of MAG exon 12 alternative splicing.
		{ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can induce
		apoptosis, while heterodimerization with other isoforms results in nuclear
		translocation of isoform 3 and suppression of apoptosis.
		{ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a
	-	translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.
		FUNCTION: May act as a GTPase-activating protein for Rab family
TBC1 domain family		protein(s). May play a role in the cell cycle and differentiation of various
member 1	1255	tissues. Involved in the trafficking and translocation of
		GLUT4-containing vesicles and insulin-stimulated glucose uptake into
		cells. {ECO:0000269 PubMed:19740738}.
Mesenteric		FUNCTION: Involved in processes that promote adipocyte
estrogen-dependent	303	differentiation, lipid accumulation, and glucose uptake in mature
adipogenesis protein		adipocytes. {ECO:0000269 PubMed:22510272}.
SWI/SNF complex subunit SMARCC2	1213	FUNCTION: Involved in transcriptional activation and repression of
		select genes by chromatin remodeling (alteration of DNA-nucleosome
		topology). Component of SWI/SNF chromatin remodeling complexes
		that carry out key enzymatic activities, changing chromatin structure by
		altering DNA-histone contacts within a nucleosome in an ATP-dependent
		manner. Can stimulate the ATPase activity of the catalytic subunit of
		these complexes. May be required for CoREST dependent repression of
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		neuronal specific gene promoters in non-neuronal cells. Belongs to the
		neural progenitors-specific chromatin remodeling complex (npBAF
		complex) and the neuron-specific chromatin remodeling complex (nBAF
		complex). During neural development a switch from a stem/progenitor to
		a postmitotic chromatin remodeling mechanism occurs as neurons exit
		the cell cycle and become committed to their adult state. The transition
		from proliferating neural stem/progenitor cells to postmitotic neurons
		requires a switch in subunit composition of the npBAF and nBAF
		complexes. As neural progenitors exit mitosis and differentiate into
		neurons, npBAF complexes which contain ACTL6A/BAF53A and
		PHF10/BAF45A, are exchanged for homologous alternative
		ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in
		neuron-specific complexes (nBAF). The npBAF complex is essential for
		the self-renewal/proliferative capacity of the multipotent neural stem
		cells. The nBAF complex along with CREST plays a role regulating the
		activity of genes essential for dendrite growth (PubMed:17640523).
		Critical regulator of myeloid differentiation, controlling
		granulocytopoiesis and the expression of genes involved in neutrophil
		granule formation (PubMed:28369036).
		{ECO:0000269 PubMed:17640523, ECO:0000269 PubMed:28369036,
		ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240,
		ECO:0000303 PubMed:26601204}.
		FUNCTION: May play an important role in regulating differentiation,
Protein prune homolog 2	3084	survival and aggressiveness of the tumor cells. {ECO:0000250}.
		FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion
		molecule involved in various processes such as inflammation, cell death,
		axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008,
		PubMed:24347169, PubMed:24917672, PubMed:31526566,
		PubMed:33472215). Promotes cell adhesion by mediating homophilic
		interactions via its extracellular N-terminal adhesion motif (N-NAM)
		(PubMed:24917672, PubMed:30510259). Involved in the progression of
		the inflammatory stress by promoting cell-to-cell interactions between
		immune cells and endothelial cells (PubMed:24917672,
Ninjurin-1	152	PubMed:30510259). Involved in leukocyte migration during
1 mg want 1	102	inflammation by promoting transendothelial migration of macrophages
		via homotypic binding (PubMed:24917672). Promotes the migration of
		monocytes across the brain endothelium to central nervous system
		inflammatory lesions (By similarity). Acts as a regulator of Toll-like
		receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during
		systemic inflammation; directly binds LPS (PubMed:25860173). Acts as
		a mediator of both programmed and necrotic cell death
		(PubMed:19557008, PubMed:33472215). Plays a key role in the
		induction of plasma membrane rupture during programmed and necrotic
		cell death: oligomerizes in response to death stimuli to mediate plasma
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		membrane rupture (cytolysis), leading to release intracellular molecules
		named damage-associated molecular patterns (DAMPs) that propagate
		the inflammatory response (PubMed:33472215). Plays a role in nerve
		regeneration by promoting maturation of Schwann cells
		(PubMed:31526566). Acts as a regulator of angiogenesis
		(PubMed:25766274, PubMed:30354207). Promotes the formation of new
		vessels by mediating the interaction between capillary pericyte cells and
		endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates
		vascular functions in penile tissue as well as vascular formation
		(PubMed:24979788). Promotes osteoclasts development by enhancing
		the survival of prefusion osteoclasts (PubMed:30700695). Also involved
		in striated muscle growth and differentiation (PubMed:31091274). Also
		involved in cell senescence in a p53/TP53 manner, possibly by acting as
		an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620,
		PubMed:29073078). {ECO:0000250 UniProtKB:Q92982,
		ECO:0000269 PubMed:19557008, ECO:0000269 PubMed:23690620,
		ECO:0000269 PubMed:24347169, ECO:0000269 PubMed:24917672,
		ECO:0000269 PubMed:24979788, ECO:0000269 PubMed:25766274,
		ECO:0000269 PubMed:25860173, ECO:0000269 PubMed:29073078,
		ECO:0000269 PubMed:30354207, ECO:0000269 PubMed:30510259,
		ECO:0000269 PubMed:30700695, ECO:0000269 PubMed:31091274,
		ECO:0000269 PubMed:31526566, ECO:0000269 PubMed:33472215}.;
		FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage,
		which has chemotactic activity (PubMed:23142597). Acts as an
		anti-inflammatory mediator by promoting monocyte recruitment, thereby
		ameliorating atherosclerosis (PubMed:32883094).
		{ECO:0000269 PubMed:23142597, ECO:0000269 PubMed:32883094}.
		FUNCTION: Phosphorylates a large number of substrates in the
		cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B,
		ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9
		and VASP (PubMed:10805756, PubMed:19223768). Regulates the
		abundance of compartmentalized pools of its regulatory subunits through
		phosphorylation of PJA2 which binds and ubiquitinates these subunits,
		leading to their subsequent proteolysis (By similarity). RORA is activated
cAMP-dependent protein		by phosphorylation. Required for glucose-mediated adipogenic
	351	differentiation increase and osteogenic differentiation inhibition from
alpha		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
		circulating platelets in a resting state by phosphorylating proteins in
		numerous platelet inhibitory pathways when in complex with
		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
		thrombin and collagen disrupt these complexes and free active PRKACA
		stimulates platelets and leads to platelet aggregation by phosphorylating

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		VASP. RYR2 channel activity is potentiated by phosphorylation in
		presence of luminal Ca(2+), leading to reduced amplitude and increased
		frequency of store overload-induced Ca(2+) release (SOICR)
		characterized by an increased rate of Ca(2+) release and propagation
		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
		ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.;
		FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm
		flagellum to promote spermatozoa capacitation.
		{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.
		FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples
	810	to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in
Interleukin-4 receptor		promoting Th2 differentiation. The IL4/IL13 responses are involved in
subunit alpha		regulating IgE production and, chemokine and mucus production at sites
		of allergic inflammation. In certain cell types, can signal through
		activation of insulin receptor substrates, IRS1/IRS2.
		FUNCTION: Required for mitosis progression. Promotes the nucleation
	660	of microtubules from the spindle (By similarity). May play an important
Protein NEDD1		role during the embryonic development and differentiation of the central
		nervous system (PubMed:1378265).
		{ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
		FUNCTION: Calcium-dependent, calmodulin-stimulated protein
		phosphatase which plays an essential role in the transduction of
		intracellular Ca(2+)-mediated signals (PubMed:7791792,
Protein phosphatase 3		PubMed:26794871). Many of the substrates contain a PxIxIT motif
	521	and/or a LxVP motif (By similarity). In response to increased Ca(2+)
catalytic subunit alpha		levels, dephosphorylates and activates phosphatase SSH1 which results in
catarytic sabanit aipna		cofilin dephosphorylation (By similarity). In response to increased
		Ca(2+) levels following mitochondrial depolarization, dephosphorylates
		DNM1L inducing DNM1L translocation to the mitochondrion (By
		similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+)

release probability at hippocampal neuronal soma and synaptic terminals (By similarity). Dephosphorylates heat shock protein HSPB1 (By similarity). Dephosphorylates and activates transcription factor NFATC1 (By similarity). Dephosphorylates and inactivates transcription factor ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation from 14-3-3 proteins (By similarity). Required for postnatal development of the nephrogenic zone and superficial glomeruli in the kidneys, cell cycle homeostasis in the nephrogenic zone, and ultimately normal kidney function (PubMed:15509543). Plays a role in intracellular AQP2 processing and localization to the apical membrane in the kidney, may thereby be required for efficient kidney filtration (PubMed:16735444). Required for secretion of salivary enzymes amylase, peroxidase, lysozyme and sialic acid via formation of secretory vesicles in the submandibular glands (PubMed:21435446). Required for calcineurin activity and homosynaptic depotentiation in the hippocampus (PubMed:10200317). Required for normal differentiation and survival of keratinocytes and therefore required for epidermis superstructure formation (PubMed:19626032). Positively regulates osteoblastic bone formation, via promotion of osteoblast differentiation (PubMed:16286645). Positively regulates osteoclast differentiation, potentially via NFATC1 signaling (PubMed:16968888). May play a role in skeletal muscle fiber type specification, potentially via NFATC1 signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK signaling via inhibition of nuclear translocation of the transcription factors RELA and RELB (PubMed:26029823). Required for antigen-specific T-cell proliferation response (PubMed:8627154). {ECO:0000250|UniProtKB:P48452, ECO:0000250|UniProtKB:P63329, ECO:0000250|UniProtKB:Q08209, ECO:0000269|PubMed:10200317, ECO:0000269|PubMed:12773574, ECO:0000269|PubMed:15509543, ECO:0000269|PubMed:16286645, ECO:0000269|PubMed:16735444, ECO:0000269|PubMed:16968888, ECO:0000269|PubMed:19626032, ECO:0000269|PubMed:21435446, ECO:0000269|PubMed:26029823, ECO:0000269|PubMed:26794871, ECO:0000269|PubMed:7791792, ECO:0000269|PubMed:8627154}. FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in SLAM family member 5 329 the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases

		proliferative responses of activated T-cells and SH2D1A/SAP does not
		seen be required for this process. Homophilic interactions enhance
		interferon gamma/IFNG secretion in lymphocytes and induce platelet
		stimulation via a SH2D1A/SAP-dependent pathway. May serve as a
		marker for hematopoietic progenitor cells (By similarity). Required for a
		prolonged T-cell:B-cell contact, optimal T follicular helper function, and
		germinal center formation (PubMed:20153220). In germinal centers
		involved in maintaining B cell tolerance and in preventing autoimmunity
		(PubMed:25801429). In mast cells negatively regulates high affinity
		immunoglobulin epsilon receptor signaling; independent of SH2D1A and
		SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In
		macrophages enhances LPS-induced MAPK phosphorylation and
		NF-kappaB activation and modulates LPS-induced cytokine secretion;
		involving ITSM 2 (PubMed:20628063). Positively regulates
		macroautophagy in primary dendritic cells via stabilization of IRF8;
		inhibits TRIM21-mediated proteasomal degradation of IRF8 (By
		similarity). {ECO:0000250 UniProtKB:Q9UIB8,
		ECO:0000269 PubMed:16037392, ECO:0000269 PubMed:20153220,
		ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259,
		ECO:0000269 PubMed:25801429, ECO:0000305}.
		FUNCTION: Plays a role in primary cilia formation (By similarity). May
		act as a downstream effector of HOXC8 possibly by transducing or
Transmembrane anterior		transmitting extracellular information required for axial skeletal
posterior transformation	564	patterning during development (By similarity). May be involved in
protein 1	304	cartilage and bone development (By similarity). May play a role in the
protein i		differentiation of cranial neural crest cells (By similarity).
		{ECO:0000250 UniProtKB:A2BIE7,
		ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
		FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm
		diameter microfibrils of the extracellular matrix, which conveys both
		structural and regulatory properties to load-bearing connective tissues.
		Fibrillin-1-containing microfibrils provide long-term force bearing
		structural support. In tissues such as the lung, blood vessels and skin,
		microfibrils form the periphery of the elastic fiber, acting as a scaffold for
		the deposition of elastin. In addition, microfibrils can occur as
E.1 .11: 1	2072	elastin-independent networks in tissues such as the ciliary zonule, tendon,
Fibrillin-1	2873	cornea and glomerulus where they provide tensile strength and have
		anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis
		through specific interactions with growth factors, such as the bone
		morphogenetic proteins (BMPs), growth and differentiation factors
		(GDFs) and latent transforming growth factor-beta-binding proteins
		(LTBPs), cell-surface integrins and other extracellular matrix protein and
		proteoglycan components (By similarity). Regulates osteoblast
		maturation by controlling TGF-beta bioavailability and calibrating
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		TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively
		regulates osteoclastogenesis by binding and sequestering an osteoclast
		differentiation and activation factor TNFSF11. This leads to disruption of
		TNFSF11-induced Ca(2+) signaling and impairment of
		TNFSF11-mediated nuclear translocation and activation of transcription
		factor NFATC1 which regulates genes important for osteoclast
		differentiation and function (PubMed:24039232). Mediates cell adhesion
		via its binding to cell surface receptors integrins ITGAV:ITGB3 and
		ITGA5:ITGB1. Binds heparin and this interaction plays an important role
		in the assembly of microfibrils (By similarity).
		{ECO:0000250 UniProtKB:P35555, ECO:0000269 PubMed:20855508,
		ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipoking
		secreted by white adipose tissue that plays an important regulatory role in
		the glucose metabolism of liver, muscle and pancreas
		(PubMed:31230984, PubMed:30997682). Hormone that targets the liver
		in response to fasting to increase plasma glucose levels
		(PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface
		of hepatocytes and promotes hepatocyte glucose release by activating the
		protein kinase A activity in the liver, resulting in rapid glucose release
		into the circulation (PubMed:31230984). May act as a regulator of
		adaptive thermogenesis by inhibiting browning and energy consumption,
		while increasing lipid deposition in white adipose tissue
		(PubMed:33705351). Also acts as an orexigenic hormone that increases
		appetite: crosses the blood brain barrier and exerts effects on the
		hypothalamus (PubMed:29106398). In the arcuate nucleus of the
		hypothalamus, asprosin directly activates orexigenic AgRP neurons and
		indirectly inhibits anorexigenic POMC neurons, resulting in appetite
		stimulation (PubMed:29106398, PubMed:32337066). Activates
		orexigenic AgRP neurons via binding to the olfactory receptor Olfr734
		(PubMed:32337066). May also play a role in sperm motility in testis via
		interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682,
		ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959,
		ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
		FUNCTION: May play a role in intercellular signaling and in connecting
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cell
versicali core protein	3337	motility, growth and differentiation. Binds hyaluronic acid.
		FUNCTION: Catalyzes the saturation of all-trans-retinol to
		all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779,
All-trans-retinol		PubMed:19139408). Does not exhibit any activity toward
13,14-reductase	609	all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers
		(PubMed:15358783). May play a role in the metabolism of vitamin A
		(PubMed:15358783, PubMed:17253779). Independently of retinol
		conversion, may regulate liver metabolism upstream of

		MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This effect seems not to mimic the in vivo situation in which animals show increased adiposity in the absence of RETSAT (PubMed:19940255). {ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779, ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255, ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}. FUNCTION: ATP-driven pump that supplies the Golgi apparatus with Ca(2+) and Mn(2+) ions, both essential cofactors for processing and trafficking of newly synthesized proteins in the secretory pathway (By similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on the cytoplasmic side of the membrane and delivers them to the lumenal side. The transfer of ions across the membrane is coupled to ATP hydrolysis and is associated with a transient phosphorylation that shifts the pump conformation from inward-facing to outward-facing state (By
Calcium-transporting ATPase type 2C member 1	918	similarity). Plays a primary role in the maintenance of Ca(2+) homeostasis in the trans-Golgi compartment with a functional impact on Golgi and post-Golgi protein sorting as well as a structural impact on cisternae morphology. Responsible for loading the Golgi stores with Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation and epidermis integrity (By similarity). Participates in Ca(2+) and Mn(2+) ions uptake into the Golgi store of hippocampal neurons and regulates protein trafficking required for neural polarity (PubMed:19793975). May also play a role in the maintenance of Ca(2+) and Mn(2+) homeostasis and signaling in the cytosol while preventing cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194, ECO:0000269 PubMed:19793975}.
Exopolyphosphatase PRUNE1	454	FUNCTION: Phosphodiesterase (PDE) that has higher activity toward cAMP than cGMP, as substrate. Plays a role in cell proliferation, migration and differentiation, and acts as a negative regulator of NME1. Plays a role in the regulation of neurogenesis. Involved in the regulation of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma membrane-associated protein	415	FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.
Fibroblast growth factor 23	251	FUNCTION: Regulator of phosphate homeostasis (By similarity). Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
P2X purinoceptor 4	388	FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central

		nervous system physiology (PubMed:26456657, PubMed:35119925).
		Plays a key role in initial steps of T-cell activation and Ca(2+)
		microdomain formation (PubMed:35119925). Participates also in basal
		T-cell activity without TCR/CD3 stimulation (PubMed:35119925).
		Promotes the differentiation and activation of Th17 cells via expression
		of retinoic acid-related orphan receptor C/RORC (By similarity). Upon
		activation, drives microglia motility via the PI3K/Akt pathway
		(PubMed:17299767). {ECO:0000250 UniProtKB:Q99571,
		ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:26456657,
		ECO:0000269 PubMed:35119925}.
		FUNCTION: Glycosyltransferase which regulates the biosynthesis of
		heparan sulfate (HS). Important for both skeletal development and
		hematopoiesis, through the formation of HS proteoglycans (HSPGs).
Exostosin-like 3	918	Required for the function of REG3A in regulating keratinocyte
		proliferation and differentiation (By similarity).
		{ECO:0000250 UniProtKB:O43909}.
		FUNCTION: Component of the ESCRT-I complex, a regulator of
Vacuolar protein		vesicular trafficking process. Required for the sorting of endocytic
sorting-associated protein	285	
37B		ubiquitinated cargos into multivesicular bodies. May be involved in cell
		growth and differentiation (By similarity). {ECO:0000250}.
		FUNCTION: Has no ubiquitin ligase activity on its own. The
	147	UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical
		poly-ubiquitin chains that are linked through 'Lys-63'. This type of
Ubiquitin-conjugating enzyme E2 variant 1		poly-ubiquitination activates IKK and does not seem to involve protein
		degradation by the proteasome. Plays a role in the activation of
		NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates
		transcriptional activation of target genes. Plays a role in the control of
		progress through the cell cycle and differentiation (By similarity). Plays a
		role in the error-free DNA repair pathway and contributes to the survival
		of cells after DNA damage. Promotes TRIM5 capsid-specific restriction
		activity and the UBE2V1-UBE2N heterodimer acts in concert with
		TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate
		the MAP3K7/TAK1 complex which in turn results in the induction and
		expression of NF-kappa-B and MAPK-responsive inflammatory genes
		(By similarity). Together with RNF135 and UBE2N, catalyzes the viral
		RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to
		activate the downstream signaling pathway that leads to interferon beta
		production (By similarity). UBE2V1-UBE2N together with TRAF3IP2
		E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6,
		a component of IL17A-mediated signaling pathway. {ECO:0000250,
		ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
Ubiquitin		FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties
carboxyl-terminal	1055	conjugated to substrates and thus, functions to process newly synthesized
hydrolase 25		Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains
11,0101030 23	<u> </u>	Conquirin, to recycle dorquirin inforcedies of to east porydorquirin chains

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	and prevents proteasomal degradation of substrates. Hydrolyzes both 'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
	{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
	may have a role in the regulation of muscular differentiation and function.
	FUNCTION: Transcriptional regulator involved in different processes
	such as glucose metabolism, aerobic glycolysis, muscle cell
	differentiation and autophagy (PubMed:25402684, PubMed:29861159,
	PubMed:30700909). Recognizes and binds the forkhead DNA sequence
	motif (5'-GTAAACA-3') and can both act as a transcription activator or
	repressor, depending on the context (PubMed:25402684,
	PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
	key regulator of metabolic reprogramming towards aerobic glycolysis, a
	process in which glucose is converted to lactate in the presence of oxygen
	(PubMed:30700909). Acts by promoting expression of enzymes for
	glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
	kinase (PKLR) and lactate dehydrogenase), while suppressing further
	oxidation of pyruvate in the mitochondria by up-regulating pyruvate
	dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
	plays a role in gluconeogenesis during overnight fasting, when lactate
	from white adipose tissue and muscle is the main substrate
	(PubMed:30700909). Involved in mTORC1-mediated metabolic
	reprogramming: in response to mTORC1 signaling, translocates into the
	nucleus and regulates the expression of genes associated with glycolysis
Forkhead box protein K1 719	and downstream anabolic pathways, such as HIF1A, thereby regulating
, , , ,	glucose metabolism (PubMed:29861159). Together with FOXK2, acts as
	a negative regulator of autophagy in skeletal muscle: in response to
	starvation, enters the nucleus, binds the promoters of autophagy genes
	and represses their expression, preventing proteolysis of skeletal muscle
	proteins (PubMed:25402684). Acts as a transcriptional regulator of the
	myogenic progenitor cell population in skeletal muscle
	(PubMed:8007964, PubMed:9271401, PubMed:12446708,
	PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
	of myoglobin (MB) gene, regulating the myogenic progenitor cell
	population (PubMed:8007964, PubMed:9271401). Promotes muscle
	progenitor cell proliferation by repressing the transcriptional activity of
	FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
	PubMed:22956541). Involved in remodeling processes of adult muscles
	that occur in response to physiological stimuli (PubMed:9271401,
	PubMed:22956541). Required to correct temporal orchestration of
	molecular and cellular events necessary for muscle repair
	(PubMed:10792059). Represses myogenic differentiation by inhibiting
	MEFC activity (PubMed:22956541). Positively regulates
	Wnt/beta-catenin signaling by translocating DVL into the nucleus (By
	similarity). Reduces virus replication, probably by binding the interferon

		stimulated response element (ISRE) to promote antiviral gene expression (By similarity). {ECO:0000250 UniProtKB:P85037, ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:12446708, ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:25402684, ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:30700909, ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.  FUNCTION: Component of the cleavage and polyadenylation specificity factor (CPSF) complex that plays a key role in pre-mRNA 3'-end formation, recognizing the AAUAAA signal sequence and interacting with poly(A) polymerase and other factors to bring about cleavage and poly(A) addition. Has endonuclease activity, and functions as mRNA 3'-end-processing endonuclease. Also involved in the histone 3'-end pre-mRNA processing. U7 snRNP-dependent protein that induces both
Cleavage and polyadenylation specificity factor subunit 3	684	the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a 5' to 3' exonuclease for degrading the subsequent downstream cleavage product (DCP) of mature histone mRNAs. Cleavage occurs after the 5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl group on the upstream fragment containing the stem loop (SL) and 5' phosphate on the downstream cleavage product (DCP) starting with CU nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive and degrades the DCP RNA substrate even after complete removal of the U7-binding site. Binds to the downstream cleavage product (DCP) of histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP dependent manner. Required for the selective processing of microRNAs (miRNAs) during embryonic stem cell differentiation via its interaction with ISY1 (PubMed:26255770, PubMed:29804889). Required for entering/progressing through S-phase of the cell cycle (By similarity). Required for the biogenesis of all miRNAs from the pri-miR-17-92 primary transcript except miR-92a (PubMed:26255770). Only required for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and pri-miR-96-183 primary transcripts, respectively (PubMed:29804889). {ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:19470752, ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
Mitogen-activated protein kinase 1	358	FUNCTION: Serine/threonine kinase which acts as an essential component of the MAP kinase signal transduction pathway.  MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an important role in the MAPK/ERK cascade. They participate also in a signaling cascade initiated by activated KIT and KITLG/SCF. Depending on the cellular context, the MAPK/ERK cascade mediates diverse biological functions such as cell growth, adhesion, survival and differentiation through the regulation of transcription, translation, cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role in initiation and regulation of meiosis, mitosis, and postmitotic functions

in differentiated cells by phosphorylating a number of transcription factors. About 160 substrates have already been discovered for ERKs. Many of these substrates are localized in the nucleus, and seem to participate in the regulation of transcription upon stimulation. However, other substrates are found in the cytosol as well as in other cellular organelles, and those are responsible for processes such as translation, mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also involved in the regulation of the endosomal dynamics, including lysosome processing and endosome cycling through the perinuclear recycling compartment (PNRC); as well as in the fragmentation of the Golgi apparatus during mitosis. The substrates include transcription factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1), cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT, PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD, BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of translation (such as EIF4EBP1) and a variety of other signaling-related molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases (such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3, RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2, RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other substrates which enable the propagation the MAPK/ERK signal to additional cytosolic and nuclear targets, thereby extending the specificity of the cascade. Mediates phosphorylation of TPR in response to EGF stimulation. May play a role in the spindle assembly checkpoint. Phosphorylates PML and promotes its interaction with PIN1, leading to PML degradation. Phosphorylates CDK2AP2 (By similarity). {ECO:0000250|UniProtKB:P28482, ECO:0000250|UniProtKB:P63086, ECO:0000269|PubMed:10753946, ECO:0000269|PubMed:11702783, ECO:0000269|PubMed:12134156, ECO:0000303|PubMed:16393692, ECO:0000303|PubMed:19565474, ECO:0000303|PubMed:21779493}.; FUNCTION: Acts as a transcriptional repressor. Binds to a [GC]AAA[GC] consensus sequence. Repress the expression of interferon gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1, IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1. Transcriptional activity is independent of kinase activity. {ECO:0000250|UniProtKB:P28482}. FUNCTION: RNA-binding protein that acts as a key regulator of N6-methyladenosine (m6A) methylation of RNAs, thereby regulating different processes, such as hematopoietic cell homeostasis, alternative RNA-binding protein 15 962 splicing of mRNAs and X chromosome inactivation mediated by Xist RNA (PubMed:29535189). Associated component of the WMM complex, a complex that mediates N6-methyladenosine (m6A) methylation of RNAs, a modification that plays a role in the efficiency of

mRNA splicing and RNA processing (PubMed:29535189). Plays a key role in m6A methylation, possibly by binding target RNAs and recruiting the WMM complex (PubMed:29535189). Involved in random X inactivation mediated by Xist RNA: acts by binding Xist RNA and recruiting the WMM complex, which mediates m6A methylation, leading to target YTHDC1 reader on Xist RNA and promoting transcription repression activity of Xist (By similarity). Required for the development of multiple tissues, such as the maintenance of the homeostasis of long-term hematopoietic stem cells and for megakaryocyte (MK) and B-cell differentiation (PubMed:17283045, PubMed:17376872, PubMed:18981216, PubMed:25468569). Regulates megakaryocyte differentiation by regulating alternative splicing of genes important for megakaryocyte differentiation; probably regulates alternative splicing via m6A regulation (By similarity). Required for placental vascular branching morphogenesis and embryonic development of the heart and spleen (PubMed:18981216). Acts as a regulator of thrombopoietin response in hematopoietic stem cells by regulating alternative splicing of MPL (PubMed:25468569). May also function as an mRNA export factor, stimulating export and expression of RTE-containing mRNAs which are present in many retrotransposons that require to be exported prior to splicing (By similarity). High affinity binding of pre-mRNA to RBM15 may allow targeting of the mRNP to the export helicase DBP5 in a manner that is independent of splicing-mediated NXF1 deposition, resulting in export prior to splicing (By similarity). May be implicated in HOX gene regulation (By similarity). {ECO:0000250|UniProtKB:Q96T37, ECO:0000269|PubMed:17283045, ECO:0000269|PubMed:17376872, ECO:0000269|PubMed:18981216, ECO:0000269|PubMed:25468569, ECO:0000269|PubMed:29535189}. FUNCTION: Transcription coactivator which associates with nuclear receptors, transcriptional coactivators including EP300, CREBBP and NCOA1, and basal transcription factors like TBP and TFIIA to facilitate nuclear receptors-mediated transcription. May thereby play an important role in establishing distinct coactivator complexes under different cellular conditions. Plays a role in thyroid hormone receptor and estrogen receptor transactivation (By similarity). Also involved in androgen receptor transactivation (PubMed:12077347). Plays a pivotal role in the Activating signal 581 cointegrator 1 transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of transrepression between nuclear receptor and either AP1 or NF-kappa-B. May play a role in the development of neuromuscular junction (By similarity). May play a role in late myogenic differentiation (PubMed:27008887). Also functions as part of the RQC trigger (RQT) complex that activates the ribosome quality control (RQC) pathway, a pathway that degrades nascent peptide chains during problematic translation (By similarity). {ECO:0000250|UniProtKB:Q15650,

		T
		ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
		ECO:0000269 PubMed:27008887}.
		FUNCTION: Histone methyltransferase that specifically trimethylates
		'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36'
		(H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is
		capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
		similarity). Represents the main enzyme generating H3K36me3, a
		specific tag for epigenetic transcriptional activation (PubMed:18157086,
		PubMed:20133625). Plays a role in chromatin structure modulation
		during elongation by coordinating recruitment of the FACT complex and
		by interacting with hyperphosphorylated POLR2A (By similarity). Acts
		as a key regulator of DNA mismatch repair in G1 and early S phase by
		generating H3K36me3, a mark required to recruit MSH6 subunit of the
		MutS alpha complex: early recruitment of the MutS alpha complex to
		chromatin to be replicated allows a quick identification of mismatch
		DNA to initiate the mismatch repair reaction (By similarity). Required for
		DNA double-strand break repair in response to DNA damage: acts by
		mediating formation of H3K36me3, promoting recruitment of RAD51
		and DNA repair via homologous recombination (HR) (By similarity).
		Acts as a tumor suppressor (By similarity). H3K36me3 also plays an
Histone-lysine		essential role in the maintenance of a heterochromatic state, by recruiting
N-methyltransferase	2537	DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also
SETD2		enhanced in intron-containing genes, suggesting that SETD2 recruitment
		is enhanced by splicing and that splicing is coupled to recruitment of
		elongating RNA polymerase (By similarity). Required during
		angiogenesis (PubMed:20133625). Required for endoderm development
		by promoting embryonic stem cell differentiation toward endoderm: acts
		by mediating formation of H3K36me3 in distal promoter regions of
		FGFR3, leading to regulate transcription initiation of FGFR3
		(PubMed:25242323). In addition to histones, also mediates methylation
		of other proteins, such as tubulins and STAT1 (PubMed:27518565).
		Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B
		(alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis
		and cytokinesis and may be a specific tag in cytoskeletal remodeling
		(PubMed:27518565). Involved in interferon-alpha-induced antiviral
		defense by mediating both monomethylation of STAT1 at 'Lys-525' and
		catalyzing H3K36me3 on promoters of some interferon-stimulated genes
		(ISGs) to activate gene transcription (By similarity).
		(ECO:0000250 UniProtKB:Q9BYW2,
		ECO:0000250 ChiriotkB.Q9B1 w2, ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625,
		ECO:0000269 PubMed:251242323, ECO:0000269 PubMed:27518565}.
Duotoin gualtina	2.41	FUNCTION: RNA-binding protein that plays a central role in
Protein quaking	341	myelinization (PubMed:10864952, PubMed:11917126). Also required for
		visceral endoderm function and blood vessel development

(PubMed: 11892011, PubMed: 16470614). Binds to the 5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence (PubMed: 16041388). Acts by regulating pre-mRNA splicing, mRNA export, mRNA stability and protein translation, as well as cellular processes including apoptosis, cell cycle, glial cell fate and development (PubMed: 10335969, PubMed: 12467586, PubMed: 11297509, PubMed: 11917126, PubMed: 15568022). Required to protect and promote stability of mRNAs such as MBP and CDKN1B which promotes oligodendrocyte differentiation (PubMed: 0535969, PubMed: 15568022). Participates in mRNA transport by regulating the nuclear export of MBP mRNA (PubMed: 12467586). May also play a role in smooth muscle development (PubMed: 14706070). {ECO:0000269}PubMed: 10353969, ECO:0000269}PubMed: 1892011, ECO:0000269}PubMed: 11297509, ECO:0000269}PubMed: 1892011, ECO:0000269}PubMed: 14706070, ECO:0000269}PubMed: 1892011, ECO:0000269}PubMed: 14706070, ECO:0000269}PubMed: 1892011, ECO:0000269}PubMed: 16041388, ECO:0000269}PubMed: 16470614); FUNCTION: Isoform 1 is involved in regulation of mRNA splicing of MAG pre-mRNA by acting as a negative regulator of MAG exon 12 alternative splicing. {ECO:0000269}PubMed: 197105}; FUNCTION: Isoform 3 can induce apoptosis, while heterodimerization with other isoforms results in nuclear translocation of isoform 3 and suppression of apoptosis. {ECO:0000269}PubMed: 11297509}; FUNCTION: Isoform 4 acts as a translational repressor for GL11. {ECO:0000269}PubMed: 16198329}.  FUNCTION: May act as a GTPase-activating protein for Rab family protein(s). May play a role in the cell cycle and differentiation of various tissues. Involved in the trafficking and translocation of GLUT4-containing vesicles and insulin-stimulated glucose uptake into cells. {ECO:0000269}PubMed: 19740738}.  FUNCTION: Involved in processes that promote adipocyte differentiation, lipid accumulation, and glucose uptake in mature adipogenesis protein  FUNCTION: Involved in transcriptional activation and repression of select genes by chromatin remodeling (al	S'-NACUAAY-N(1,20)-UAAY-3' RNA core se   (PubMed:16041388). Acts by regulating pre-mil   export, mRNA stability and protein translation,   processes including apoptosis, cell cycle, glial of   (PubMed:10535969, PubMed:12467586, PubM   PubMed:11917126, PubMed:15568022). Requil   stability of mRNAs such as MBP and CDKNIE   oligodendrocyte differentiation (PubMed:10535   Participates in mRNA transport by regulating th   mRNA (PubMed:12467586). May also play a re   development (PubMed:14706700). (ECO:00002   ECO:0000269]PubMed:10864952, ECO:00002   ECO:0000269]PubMed:11892011, ECO:00002   ECO:0000269]PubMed:11892011, ECO:00002   ECO:0000269]PubMed:15568022, ECO:00002   ECO:0000269]PubMed:15568022, ECO:00002   ECO:0000269]PubMed:197126}.; FUNCTIO   in regulation of mRNA splicing of MAG pre-minegative regulator of MAG exon 12 alternative.   (ECO:0000269]PubMed:11971726}.; FUNCTIO   in regulation of isoform 3 and suppression of appropriate of isoform 3 and suppression of appropria	. 1. 4. 41.
(PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA export, mRNA stability and protein translation, as well as cellular processes including apoptosis, cell cycle, glial cell fate and development (PubMed:1053596), PubMed:12467586, PubMed:1197709).  PubMed:1035969, PubMed:15568022). Required to protect and promote stability of mRNAs such as MBP and CDKNIB which promotes oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022). Participates in mRNA transport by regulating the nuclear export of MBP mRNA (PubMed:12467586). May also play a role in smooth muscle development (PubMed:14706070). {ECO:0000269 PubMed:10535969, ECO:0000269 PubMed:184706070}. {ECO:0000269 PubMed:14706070}. {ECO:0000269 PubMed:14670614}. {FUNCTION: Isoform 1 is involved in regulation of mRNA splicing of MAG pre-mRNA by acting as a negative regulator of MAG exon 12 alternative splicing. {ECO:0000269 PubMed:1670614}. {FUNCTION: Isoform 3 can induce apoptosis, while heterodimerization with other isoforms results in nuclear translocation of isoform 3 and suppression of apoptosis. {ECO:0000269 PubMed:11297509}. FUNCTION: Isoform 4 acts as a translational repressor for GLII. {ECO:0000269 PubMed:16198329}. FUNCTION: May act as a GTPase-activating protein for Rab family protein(s). May play a role in the cell cycle and differentiation of GILIT4-containing vesicles and insulin-stimulated glucose uptake into cells. {ECO:0000269 PubMed:19740738}. Mesenteric estrogen-dependent adipocytes. {ECO:0000269 PubMed:19740738}. FUNCTION: Involved in transcriptional activation and repression of select genes by chromatin remodeling (alteration of DNA-nucleosome topology). Component of SWI/SNF chromatin remodeling complexes that carry out key enzymatic activities, changing	(PubMed:16041388). Acts by regulating pre-mil export, mRNA stability and protein translation, processes including apoptosis, cell cycle, glial c (PubMed:10535969, PubMed:12467586, PubM PubMed:11917126, PubMed:15568022). Requistability of mRNAs such as MBP and CDKN1E oligodendrocyte differentiation (PubMed:10535 Participates in mRNA transport by regulating th mRNA (PubMed:12467586). May also play a redevelopment (PubMed:14706700). {ECO:00002} ECO:0000269]PubMed:10864952, ECO:00002 ECO:0000269]PubMed:18892011, ECO:00002 ECO:0000269]PubMed:1470614); FUNCTIO in regulation of mRNA splicing of MAG pre-minegative regulator of MAG exon 12 alternative (ECO:0000269]PubMed:11917126]; FUNCTIO in regulation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocation of isoform 3 and suppression of apoptosis, while heterodimerization with other it translocatio	
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altering DNA-histone contacts within a nucleosome in an ATP-dependent  SWI/SNF complex  1213  altering DNA-histone contacts within a nucleosome in an ATP-dependent manner. Can stimulate the ATPase activity of the catalytic subunit of	SWI/SNF complex subunit SMARCC2  altering DNA-histone contacts within a nucleose manner. Can stimulate the ATPase activity of the these complexes. May be required for CoREST neuronal specific gene promoters in non-neuron neural progenitors-specific chromatin remodeling	
SWI/SNF complex manner. Can stimulate the ATPase activity of the catalytic subunit of	SWI/SNF complex subunit SMARCC2 manner. Can stimulate the ATPase activity of the these complexes. May be required for CoREST neuronal specific gene promoters in non-neuron neural progenitors-specific chromatin remodeling	-
1 1213	subunit SMARCC2 these complexes. May be required for CoREST neuronal specific gene promoters in non-neuron neural progenitors-specific chromatin remodelir	=
subunit SMARCC2 these complexes. May be required for CoREST dependent repression of	subunit SMARCC2 these complexes. May be required for CoREST neuronal specific gene promoters in non-neuron neural progenitors-specific chromatin remodeling	•
	neural progenitors-specific chromatin remodelir	T dependent repression of
neuronal specific gene promoters in non-neuronal cells. Belongs to the		_
neural progenitors-specific chromatin remodeling complex (npBAF	complex) and the neuron-specific chromatin ren	eling complex (npBAF
complex) and the neuron-specific chromatin remodeling complex (nBAF		remodeling complex (nBAF
complex). During neural development a switch from a stem/progenitor to	complex). During neural development a switch	ch from a stem/progenitor to
	a postmitotic chromatin remodeling mechanism	sm occurs as neurons exit

		the cell cycle and become committed to their adult state. The transition
		from proliferating neural stem/progenitor cells to postmitotic neurons
		requires a switch in subunit composition of the npBAF and nBAF
		complexes. As neural progenitors exit mitosis and differentiate into
		neurons, npBAF complexes which contain ACTL6A/BAF53A and
		PHF10/BAF45A, are exchanged for homologous alternative
		ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in
		neuron-specific complexes (nBAF). The npBAF complex is essential for
		the self-renewal/proliferative capacity of the multipotent neural stem
		cells. The nBAF complex along with CREST plays a role regulating the
		activity of genes essential for dendrite growth (PubMed:17640523).
		Critical regulator of myeloid differentiation, controlling
		granulocytopoiesis and the expression of genes involved in neutrophil
		granule formation (PubMed:28369036).
		{ECO:0000269 PubMed:17640523, ECO:0000269 PubMed:28369036,
		ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240,
		ECO:0000269 PubMed:31210030, ECO:0000303 PubMed:22932240, ECO:0000303 PubMed:26601204}.
Protein prune homolog 2	3084	FUNCTION: May play an important role in regulating differentiation,
		survival and aggressiveness of the tumor cells. {ECO:0000250}.
		FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion
		molecule involved in various processes such as inflammation, cell death,
		axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008,
		PubMed:24347169, PubMed:24917672, PubMed:31526566,
		PubMed:33472215). Promotes cell adhesion by mediating homophilic
		interactions via its extracellular N-terminal adhesion motif (N-NAM)
		(PubMed:24917672, PubMed:30510259). Involved in the progression of
		the inflammatory stress by promoting cell-to-cell interactions between
		immune cells and endothelial cells (PubMed:24917672,
		PubMed:30510259). Involved in leukocyte migration during
		inflammation by promoting transendothelial migration of macrophages
		via homotypic binding (PubMed:24917672). Promotes the migration of
Ninjurin-1	152	monocytes across the brain endothelium to central nervous system
		inflammatory lesions (By similarity). Acts as a regulator of Toll-like
		receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during
		systemic inflammation; directly binds LPS (PubMed:25860173). Acts as
		a mediator of both programmed and necrotic cell death
		(PubMed:19557008, PubMed:33472215). Plays a key role in the
		induction of plasma membrane rupture during programmed and necrotic
		cell death: oligomerizes in response to death stimuli to mediate plasma
		membrane rupture (cytolysis), leading to release intracellular molecules
		named damage-associated molecular patterns (DAMPs) that propagate
		the inflammatory response (PubMed:33472215). Plays a role in nerve
		regeneration by promoting maturation of Schwann cells
		(PubMed:31526566). Acts as a regulator of angiogenesis

		(D.1) ( 1057((074 D.1) ( 1000(1007) D
		(PubMed:25766274, PubMed:30354207). Promotes the formation of new
		vessels by mediating the interaction between capillary pericyte cells and
		endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates
		vascular functions in penile tissue as well as vascular formation
		(PubMed:24979788). Promotes osteoclasts development by enhancing
		the survival of prefusion osteoclasts (PubMed:30700695). Also involved
		in striated muscle growth and differentiation (PubMed:31091274). Also
		involved in cell senescence in a p53/TP53 manner, possibly by acting as
		an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620,
		PubMed:29073078). {ECO:0000250 UniProtKB:Q92982,
		ECO:0000269 PubMed:19557008, ECO:0000269 PubMed:23690620,
		ECO:0000269 PubMed:24347169, ECO:0000269 PubMed:24917672,
		ECO:0000269 PubMed:24979788, ECO:0000269 PubMed:25766274,
		ECO:0000269 PubMed:25860173, ECO:0000269 PubMed:29073078,
		ECO:0000269 PubMed:30354207, ECO:0000269 PubMed:30510259,
		ECO:0000269 PubMed:30700695, ECO:0000269 PubMed:31091274,
		ECO:0000269 PubMed:31526566, ECO:0000269 PubMed:33472215}.;
		FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage,
		which has chemotactic activity (PubMed:23142597). Acts as an
		anti-inflammatory mediator by promoting monocyte recruitment, thereby
		ameliorating atherosclerosis (PubMed:32883094).
		{ECO:0000269 PubMed:23142597, ECO:0000269 PubMed:32883094}.
		FUNCTION: Phosphorylates a large number of substrates in the
		cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B,
	351	ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9
cAMP-dependent protein kinase catalytic subunit		and VASP (PubMed:10805756, PubMed:19223768). Regulates the
		abundance of compartmentalized pools of its regulatory subunits through
		phosphorylation of PJA2 which binds and ubiquitinates these subunits,
		leading to their subsequent proteolysis (By similarity). RORA is activated
		by phosphorylation. Required for glucose-mediated adipogenic
		differentiation increase and osteogenic differentiation inhibition from
		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
alpha		
		circulating platelets in a resting state by phosphorylating proteins in
		numerous platelet inhibitory pathways when in complex with
		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
		thrombin and collagen disrupt these complexes and free active PRKACA
		stimulates platelets and leads to platelet aggregation by phosphorylating
		VASP. RYR2 channel activity is potentiated by phosphorylation in
		presence of luminal Ca(2+), leading to reduced amplitude and increased
		frequency of store overload-induced Ca(2+) release (SOICR)
		characterized by an increased rate of Ca(2+) release and propagation
		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude

		Land Control Control Control
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
		ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.;
		FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm
		flagellum to promote spermatozoa capacitation.
		{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.
		FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples
		to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in
Interleukin-4 receptor	010	promoting Th2 differentiation. The IL4/IL13 responses are involved in
subunit alpha	810	regulating IgE production and, chemokine and mucus production at sites
		of allergic inflammation. In certain cell types, can signal through
		activation of insulin receptor substrates, IRS1/IRS2.
		FUNCTION: Required for mitosis progression. Promotes the nucleation
		of microtubules from the spindle (By similarity). May play an important
Protein NEDD1	660	role during the embryonic development and differentiation of the central
		nervous system (PubMed:1378265).
		{ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
		FUNCTION: Calcium-dependent, calmodulin-stimulated protein
		phosphatase which plays an essential role in the transduction of
		intracellular Ca(2+)-mediated signals (PubMed:7791792,
		PubMed:26794871). Many of the substrates contain a PxIxIT motif
		and/or a LxVP motif (By similarity). In response to increased Ca(2+)
		levels, dephosphorylates and activates phosphatase SSH1 which results in
		cofilin dephosphorylation (By similarity). In response to increased
Protein phosphatase 3	521	Ca(2+) levels following mitochondrial depolarization, dephosphorylates
catalytic subunit alpha	321	DNM1L inducing DNM1L translocation to the mitochondrion (By
		similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+)
		release probability at hippocampal neuronal soma and synaptic terminals
		(By similarity). Dephosphorylates heat shock protein HSPB1 (By
		similarity). Dephosphorylates and activates transcription factor NFATC1
		(By similarity). Dephosphorylates and inactivates transcription factor
		ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May

dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation from 14-3-3 proteins (By similarity). Required for postnatal development of the nephrogenic zone and superficial glomeruli in the kidneys, cell cycle homeostasis in the nephrogenic zone, and ultimately normal kidney function (PubMed:15509543). Plays a role in intracellular AQP2 processing and localization to the apical membrane in the kidney, may thereby be required for efficient kidney filtration (PubMed:16735444). Required for secretion of salivary enzymes amylase, peroxidase, lysozyme and sialic acid via formation of secretory vesicles in the submandibular glands (PubMed:21435446). Required for calcineurin activity and homosynaptic depotentiation in the hippocampus (PubMed:10200317). Required for normal differentiation and survival of keratinocytes and therefore required for epidermis superstructure formation (PubMed:19626032). Positively regulates osteoblastic bone formation, via promotion of osteoblast differentiation (PubMed:16286645). Positively regulates osteoclast differentiation, potentially via NFATC1 signaling (PubMed:16968888). May play a role in skeletal muscle fiber type specification, potentially via NFATC1 signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK signaling via inhibition of nuclear translocation of the transcription factors RELA and RELB (PubMed:26029823). Required for antigen-specific T-cell proliferation response (PubMed:8627154). {ECO:0000250|UniProtKB:P48452, ECO:0000250|UniProtKB:P63329, ECO:0000250|UniProtKB:Q08209, ECO:0000269|PubMed:10200317, ECO:0000269|PubMed:12773574, ECO:0000269|PubMed:15509543, ECO:0000269|PubMed:16286645, ECO:0000269|PubMed:16735444, ECO:0000269|PubMed:16968888, ECO:0000269|PubMed:19626032, ECO:0000269|PubMed:21435446, ECO:0000269|PubMed:26029823, ECO:0000269|PubMed:26794871, ECO:0000269|PubMed:7791792, ECO:0000269|PubMed:8627154}. FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 SLAM family member 5 329 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a

		prolonged T-cell:B-cell contact, optimal T follicular helper function, and
		germinal center formation (PubMed:20153220). In germinal centers
		involved in maintaining B cell tolerance and in preventing autoimmunity
		(PubMed:25801429). In mast cells negatively regulates high affinity
		immunoglobulin epsilon receptor signaling; independent of SH2D1A and
		SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In
		macrophages enhances LPS-induced MAPK phosphorylation and
		NF-kappaB activation and modulates LPS-induced cytokine secretion;
		involving ITSM 2 (PubMed:20628063). Positively regulates
		macroautophagy in primary dendritic cells via stabilization of IRF8;
		inhibits TRIM21-mediated proteasomal degradation of IRF8 (By
		similarity). {ECO:0000250 UniProtKB:Q9UIB8,
		ECO:0000269 PubMed:16037392, ECO:0000269 PubMed:20153220,
		ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259,
		ECO:0000269 PubMed:25801429, ECO:0000305}.
		FUNCTION: Plays a role in primary cilia formation (By similarity). May
		act as a downstream effector of HOXC8 possibly by transducing or
		transmitting extracellular information required for axial skeletal
Transmembrane anterior		patterning during development (By similarity). May be involved in
posterior transformation	564	cartilage and bone development (By similarity). May play a role in the
protein 1		differentiation of cranial neural crest cells (By similarity).
		{ECO:0000250 UniProtKB:A2BIE7,
		ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
		FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm
		diameter microfibrils of the extracellular matrix, which conveys both
		-
		structural and regulatory properties to load-bearing connective tissues.  Fibrillin-1-containing microfibrils provide long-term force bearing
	2072	structural support. In tissues such as the lung, blood vessels and skin,
		microfibrils form the periphery of the elastic fiber, acting as a scaffold for
		the deposition of elastin. In addition, microfibrils can occur as
		elastin-independent networks in tissues such as the ciliary zonule, tendon,
		cornea and glomerulus where they provide tensile strength and have
		anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis
Fibrillin-1	2873	through specific interactions with growth factors, such as the bone
		morphogenetic proteins (BMPs), growth and differentiation factors
		(GDFs) and latent transforming growth factor-beta-binding proteins
		(LTBPs), cell-surface integrins and other extracellular matrix protein and
		proteoglycan components (By similarity). Regulates osteoblast
		maturation by controlling TGF-beta bioavailability and calibrating
		TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively
		regulates osteoclastogenesis by binding and sequestering an osteoclast
		differentiation and activation factor TNFSF11. This leads to disruption of
		TNFSF11-induced Ca(2+) signaling and impairment of
		TNFSF11-mediated nuclear translocation and activation of transcription
	1	

		A NEW TOLEN AND A STATE OF THE
		factor NFATC1 which regulates genes important for osteoclast differentiation and function (PubMed:24039232). Mediates cell adhesion via its binding to cell surface receptors integrins ITGAV:ITGB3 and ITGA5:ITGB1. Binds heparin and this interaction plays an important role in the assembly of microfibrils (By similarity).
		{ECO:0000250 UniProtKB:P35555, ECO:0000269 PubMed:20855508, ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine
		secreted by white adipose tissue that plays an important regulatory role in the glucose metabolism of liver, muscle and pancreas
		(PubMed:31230984, PubMed:30997682). Hormone that targets the liver
		in response to fasting to increase plasma glucose levels
		(PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface
		of hepatocytes and promotes hepatocyte glucose release by activating the
		protein kinase A activity in the liver, resulting in rapid glucose release
		into the circulation (PubMed:31230984). May act as a regulator of
		adaptive thermogenesis by inhibiting browning and energy consumption,
		while increasing lipid deposition in white adipose tissue
		(PubMed:33705351). Also acts as an orexigenic hormone that increases
		appetite: crosses the blood brain barrier and exerts effects on the
		hypothalamus (PubMed:29106398). In the arcuate nucleus of the hypothalamus, asprosin directly activates orexigenic AgRP neurons and
		indirectly inhibits anorexigenic POMC neurons, resulting in appetite
		stimulation (PubMed:29106398, PubMed:32337066). Activates
		orexigenic AgRP neurons via binding to the olfactory receptor Olfr734
		(PubMed:32337066). May also play a role in sperm motility in testis via
		interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682,
		ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959,
		ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
		FUNCTION: May play a role in intercellular signaling and in connecting
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cell
		motility, growth and differentiation. Binds hyaluronic acid.
		FUNCTION: Catalyzes the saturation of all-trans-retinol to
		all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779,
		PubMed:19139408). Does not exhibit any activity toward
		all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers
A11 /		(PubMed: 15358783). May play a role in the metabolism of vitamin A
All-trans-retinol	609	(PubMed:15358783, PubMed:17253779). Independently of retinol
13,14-reductase		conversion, may regulate liver metabolism upstream of
		MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This
		effect seems not to mimic the in vivo situation in which animals show
		increased adiposity in the absence of RETSAT (PubMed:19940255).
		{ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779,
	l	

		ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255,
		ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
		FUNCTION: ATP-driven pump that supplies the Golgi apparatus with
		Ca(2+) and Mn(2+) ions, both essential cofactors for processing and
		trafficking of newly synthesized proteins in the secretory pathway (By
		similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on
		the cytoplasmic side of the membrane and delivers them to the lumenal
		side. The transfer of ions across the membrane is coupled to ATP
		hydrolysis and is associated with a transient phosphorylation that shifts
		the pump conformation from inward-facing to outward-facing state (By
Calcium-transporting		similarity). Plays a primary role in the maintenance of Ca(2+)
ATPase type 2C member	918	homeostasis in the trans-Golgi compartment with a functional impact on
1	)10	Golgi and post-Golgi protein sorting as well as a structural impact on
1		cisternae morphology. Responsible for loading the Golgi stores with
		Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation
		and epidermis integrity (By similarity). Participates in Ca(2+) and
		Mn(2+) ions uptake into the Golgi store of hippocampal neurons and
		regulates protein trafficking required for neural polarity
		(PubMed:19793975). May also play a role in the maintenance of Ca(2+)
		and Mn(2+) homeostasis and signaling in the cytosol while preventing
		cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194,
		ECO:0000269 PubMed:19793975}.
	454	FUNCTION: Phosphodiesterase (PDE) that has higher activity toward
		cAMP than cGMP, as substrate. Plays a role in cell proliferation,
Exopolyphosphatase		migration and differentiation, and acts as a negative regulator of NME1.
PRUNE1		Plays a role in the regulation of neurogenesis. Involved in the regulation
		of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma		FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl
membrane-associated	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte
protein		differentiation. {ECO:0000250}.
		FUNCTION: Regulator of phosphate homeostasis (By similarity).
	251	Inhibits renal tubular phosphate transport by reducing SLC34A1 levels
		(By similarity). Acts directly on the parathyroid to decrease PTH
Fibroblast growth factor		secretion (By similarity). Regulator of vitamin-D metabolism (By
23		similarity). Negatively regulates osteoblasts differentiation and matrix
		mineralization (By similarity). Up-regulates EGR1 expression in the
		presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
P2X purinoceptor 4	388	FUNCTION: Receptor for extracellularly released ATP acting as a
		ligand-gated ion channel that plays multiple role in immunity and central
		nervous system physiology (PubMed:26456657, PubMed:35119925).
		Plays a key role in initial steps of T-cell activation and Ca(2+)
		microdomain formation (PubMed:35119925). Participates also in basal
		T-cell activity without TCR/CD3 stimulation (PubMed:35119925).
		Promotes the differentiation and activation of Th17 cells via expression
		1 romotes the unrecentiation and activation of this / cens via expression

Exostosin-like 3	918	of retinoic acid-related orphan receptor C/RORC (By similarity). Upon activation, drives microglia motility via the PI3K/Akt pathway (PubMed:17299767). {ECO:0000250 UniProtKB:Q99571, ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:26456657, ECO:0000269 PubMed:35119925}.  FUNCTION: Glycosyltransferase which regulates the biosynthesis of heparan sulfate (HS). Important for both skeletal development and hematopoiesis, through the formation of HS proteoglycans (HSPGs). Required for the function of REG3A in regulating keratinocyte proliferation and differentiation (By similarity). {ECO:0000250 UniProtKB:O43909}.
Vacuolar protein sorting-associated protein 37B	285	FUNCTION: Component of the ESCRT-I complex, a regulator of vesicular trafficking process. Required for the sorting of endocytic ubiquitinated cargos into multivesicular bodies. May be involved in cell growth and differentiation (By similarity). {ECO:0000250}.
Ubiquitin-conjugating enzyme E2 variant 1	147	FUNCTION: Has no ubiquitin ligase activity on its own. The UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical poly-ubiquitin chains that are linked through 'Lys-63'. This type of poly-ubiquitination activates IKK and does not seem to involve protein degradation by the proteasome. Plays a role in the activation of NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates transcriptional activation of target genes. Plays a role in the control of progress through the cell cycle and differentiation (By similarity). Plays a role in the error-free DNA repair pathway and contributes to the survival of cells after DNA damage. Promotes TRIM5 capsid-specific restriction activity and the UBE2V1-UBE2N heterodimer acts in concert with TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate the MAP3K7/TAK1 complex which in turn results in the induction and expression of NF-kappa-B and MAPK-responsive inflammatory genes (By similarity). Together with RNF135 and UBE2N, catalyzes the viral RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to activate the downstream signaling pathway that leads to interferon beta production (By similarity). UBE2V1-UBE2N together with TRAF3IP2 E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6, a component of IL17A-mediated signaling pathway. {ECO:0000250, ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
Ubiquitin carboxyl-terminal hydrolase 25	1055	FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties conjugated to substrates and thus, functions to process newly synthesized Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains and prevents proteasomal degradation of substrates. Hydrolyzes both 'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity). {ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m) may have a role in the regulation of muscular differentiation and function.
Forkhead box protein K1	719	FUNCTION: Transcriptional regulator involved in different processes

such as glucose metabolism, aerobic glycolysis, muscle cell differentiation and autophagy (PubMed:25402684, PubMed:29861159, PubMed:30700909). Recognizes and binds the forkhead DNA sequence motif (5'-GTAAACA-3') and can both act as a transcription activator or repressor, depending on the context (PubMed:25402684, PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a key regulator of metabolic reprogramming towards aerobic glycolysis, a process in which glucose is converted to lactate in the presence of oxygen (PubMed:30700909). Acts by promoting expression of enzymes for glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate kinase (PKLR) and lactate dehydrogenase), while suppressing further oxidation of pyruvate in the mitochondria by up-regulating pyruvate dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably plays a role in gluconeogenesis during overnight fasting, when lactate from white adipose tissue and muscle is the main substrate (PubMed:30700909). Involved in mTORC1-mediated metabolic reprogramming: in response to mTORC1 signaling, translocates into the nucleus and regulates the expression of genes associated with glycolysis and downstream anabolic pathways, such as HIF1A, thereby regulating glucose metabolism (PubMed:29861159). Together with FOXK2, acts as a negative regulator of autophagy in skeletal muscle: in response to starvation, enters the nucleus, binds the promoters of autophagy genes and represses their expression, preventing proteolysis of skeletal muscle proteins (PubMed:25402684). Acts as a transcriptional regulator of the myogenic progenitor cell population in skeletal muscle (PubMed:8007964, PubMed:9271401, PubMed:12446708, PubMed:22956541). Binds to the upstream enhancer region (CCAC box) of myoglobin (MB) gene, regulating the myogenic progenitor cell population (PubMed:8007964, PubMed:9271401). Promotes muscle progenitor cell proliferation by repressing the transcriptional activity of FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708, PubMed:22956541). Involved in remodeling processes of adult muscles that occur in response to physiological stimuli (PubMed:9271401, PubMed:22956541). Required to correct temporal orchestration of molecular and cellular events necessary for muscle repair (PubMed:10792059). Represses myogenic differentiation by inhibiting MEFC activity (PubMed:22956541). Positively regulates Wnt/beta-catenin signaling by translocating DVL into the nucleus (By similarity). Reduces virus replication, probably by binding the interferon stimulated response element (ISRE) to promote antiviral gene expression (By similarity). {ECO:0000250|UniProtKB:P85037, ECO:0000269|PubMed:10792059, ECO:0000269|PubMed:12446708, ECO:0000269|PubMed:22956541, ECO:0000269|PubMed:25402684, ECO:0000269|PubMed:29861159, ECO:0000269|PubMed:30700909,

		ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:92714013
Cleavage and polyadenylation specificity factor subunit 3	684	ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.  FUNCTION: Component of the cleavage and polyadenylation specificity factor (CPSF) complex that plays a key role in pre-mRNA 3'-end formation, recognizing the AAUAAA signal sequence and interacting with poly(A) polymerase and other factors to bring about cleavage and poly(A) addition. Has endonuclease activity, and functions as mRNA 3'-end-processing endonuclease. Also involved in the histone 3'-end pre-mRNA processing. U7 snRNP-dependent protein that induces both the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a 5' to 3' exonuclease for degrading the subsequent downstream cleavage product (DCP) of mature histone mRNAs. Cleavage occurs after the
		5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl group on the upstream fragment containing the stem loop (SL) and 5' phosphate on the downstream cleavage product (DCP) starting with CU nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive and degrades the DCP RNA substrate even after complete removal of the U7-binding site. Binds to the downstream cleavage product (DCP) of histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP dependent manner. Required for the selective processing of microRNAs (miRNAs) during embryonic stem cell differentiation via its interaction with ISY1 (PubMed:26255770, PubMed:29804889). Required for entering/progressing through S-phase of the cell cycle (By similarity). Required for the biogenesis of all miRNAs from the pri-miR-17-92 primary transcript except miR-92a (PubMed:26255770). Only required for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and pri-miR-96-183 primary transcripts, respectively (PubMed:29804889). {ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211, ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752, ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
Mitogen-activated protein kinase 1	358	FUNCTION: Serine/threonine kinase which acts as an essential component of the MAP kinase signal transduction pathway.  MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an important role in the MAPK/ERK cascade. They participate also in a signaling cascade initiated by activated KIT and KITLG/SCF. Depending on the cellular context, the MAPK/ERK cascade mediates diverse biological functions such as cell growth, adhesion, survival and differentiation through the regulation of transcription, translation, cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role in initiation and regulation of meiosis, mitosis, and postmitotic functions in differentiated cells by phosphorylating a number of transcription factors. About 160 substrates have already been discovered for ERKs. Many of these substrates are localized in the nucleus, and seem to participate in the regulation of transcription upon stimulation. However, other substrates are found in the cytosol as well as in other cellular

organelles, and those are responsible for processes such as translation, mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also involved in the regulation of the endosomal dynamics, including lysosome processing and endosome cycling through the perinuclear recycling compartment (PNRC); as well as in the fragmentation of the Golgi apparatus during mitosis. The substrates include transcription factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1), cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT, PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD, BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of translation (such as EIF4EBP1) and a variety of other signaling-related molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases (such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3, RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2, RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other substrates which enable the propagation the MAPK/ERK signal to additional cytosolic and nuclear targets, thereby extending the specificity of the cascade. Mediates phosphorylation of TPR in response to EGF stimulation. May play a role in the spindle assembly checkpoint. Phosphorylates PML and promotes its interaction with PIN1, leading to PML degradation. Phosphorylates CDK2AP2 (By similarity). {ECO:0000250|UniProtKB:P28482, ECO:0000250|UniProtKB:P63086, ECO:0000269|PubMed:10753946, ECO:0000269|PubMed:11702783, ECO:0000269|PubMed:12134156, ECO:0000303|PubMed:16393692, ECO:0000303|PubMed:19565474, ECO:0000303|PubMed:21779493}.; FUNCTION: Acts as a transcriptional repressor. Binds to a [GC]AAA[GC] consensus sequence. Repress the expression of interferon gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1, IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1. Transcriptional activity is independent of kinase activity. {ECO:0000250|UniProtKB:P28482}. FUNCTION: RNA-binding protein that acts as a key regulator of N6-methyladenosine (m6A) methylation of RNAs, thereby regulating different processes, such as hematopoietic cell homeostasis, alternative splicing of mRNAs and X chromosome inactivation mediated by Xist RNA (PubMed:29535189). Associated component of the WMM complex, a complex that mediates N6-methyladenosine (m6A) RNA-binding protein 15 962 methylation of RNAs, a modification that plays a role in the efficiency of mRNA splicing and RNA processing (PubMed:29535189). Plays a key role in m6A methylation, possibly by binding target RNAs and recruiting the WMM complex (PubMed:29535189). Involved in random X inactivation mediated by Xist RNA: acts by binding Xist RNA and recruiting the WMM complex, which mediates m6A methylation, leading

to target YTHDC1 reader on Xist RNA and promoting transcer repression activity of Xist (By similarity). Required for the decomposition of multiple tissues, such as the maintenance of the homeostast long-term hematopoietic stem cells and for megakaryocyte (Normal Bercell differentiation (PubMed:17283045, PubMed:17376872). PubMed:18981216, PubMed:25468569). Regulates megakary differentiation by regulating alternative splicing of genes imposition megakaryocyte differentiation; probably regulates alternative m6A regulation (By similarity). Required for placental vascul branching morphogenesis and embryonic development of the spleen (PubMed:18981216). Acts as a regulator of thrombopor response in hematopoietic stem cells by regulating alternative MPL (PubMed:25468569). May also function as an mRNA estimulating export and expression of RTE-containing mRNAs	evelopment is of MK) and 2, vocyte ortant for splicing via ar heart and oietin
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PubMed:18981216, PubMed:25468569). Regulates megakary differentiation by regulating alternative splicing of genes imp megakaryocyte differentiation; probably regulates alternative m6A regulation (By similarity). Required for placental vascul branching morphogenesis and embryonic development of the spleen (PubMed:18981216). Acts as a regulator of thrombopor response in hematopoietic stem cells by regulating alternative MPL (PubMed:25468569). May also function as an mRNA expression of the spleen (PubMed:25468569).	vocyte ortant for splicing via ar heart and oietin
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branching morphogenesis and embryonic development of the spleen (PubMed:18981216). Acts as a regulator of thrombopor response in hematopoietic stem cells by regulating alternative MPL (PubMed:25468569). May also function as an mRNA example.	heart and bietin
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spleen (PubMed:18981216). Acts as a regulator of thrombopor response in hematopoietic stem cells by regulating alternative MPL (PubMed:25468569). May also function as an mRNA ex	oietin
response in hematopoietic stem cells by regulating alternative MPL (PubMed:25468569). May also function as an mRNA ex	
MPL (PubMed:25468569). May also function as an mRNA ex	splicing of
stillulating export and expression of KTE-containing inkivas	_
present in many retrotransposons that require to be exported p	
splicing (By similarity). High affinity binding of pre-mRNA t	
may allow targeting of the mRNP to the export helicase DBP:	
manner that is independent of splicing-mediated NXF1 depos	
resulting in export prior to splicing (By similarity). May be in	nplicated in
HOX gene regulation (By similarity).	
{ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:	
ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18	3981216,
ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29	9535189}.
FUNCTION: Transcription coactivator which associates with	nuclear
receptors, transcriptional coactivators including EP300, CREI	BBP and
NCOA1, and basal transcription factors like TBP and TFIIA t	to facilitate
nuclear receptors-mediated transcription. May thereby play ar	n important
role in establishing distinct coactivator complexes under diffe	rent cellular
conditions. Plays a role in thyroid hormone receptor and estro	gen
receptor transactivation (By similarity). Also involved in and	ogen
receptor transactivation (PubMed:12077347). Plays a pivotal	_
Activating signal transactivation of NF-kappa-B, SRF and AP1. Acts as a media	
cointegrator 1 transrepression between nuclear receptor and either AP1 or N	
May play a role in the development of neuromuscular junction	
similarity). May play a role in late myogenic differentiation	(2)
(PubMed:27008887). Also functions as part of the RQC trigg	or (DOT)
	, - /
complex that activates the ribosome quality control (RQC) pa	
pathway that degrades nascent peptide chains during problem	
translation (By similarity). {ECO:0000250 UniProtKB:Q1565	
ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12	2390891,
ECO:0000269 PubMed:27008887}.	
Histone-lysine FUNCTION: Histone methyltransferase that specifically trime	•
N-methyltransferase 2537 'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-	36'
SETD2 (H3K36me2) as substrate (PubMed:18157086, PubMed:2013	3625). It is

		capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
		similarity). Represents the main enzyme generating H3K36me3, a
		specific tag for epigenetic transcriptional activation (PubMed:18157086,
		PubMed:20133625). Plays a role in chromatin structure modulation
		during elongation by coordinating recruitment of the FACT complex and
		by interacting with hyperphosphorylated POLR2A (By similarity). Acts
		as a key regulator of DNA mismatch repair in G1 and early S phase by
		generating H3K36me3, a mark required to recruit MSH6 subunit of the
		MutS alpha complex: early recruitment of the MutS alpha complex to
		chromatin to be replicated allows a quick identification of mismatch
		DNA to initiate the mismatch repair reaction (By similarity). Required for
		DNA double-strand break repair in response to DNA damage: acts by
		mediating formation of H3K36me3, promoting recruitment of RAD51
		and DNA repair via homologous recombination (HR) (By similarity).
		Acts as a tumor suppressor (By similarity). H3K36me3 also plays an
		essential role in the maintenance of a heterochromatic state, by recruiting
		DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also
		enhanced in intron-containing genes, suggesting that SETD2 recruitment
		is enhanced by splicing and that splicing is coupled to recruitment of
		elongating RNA polymerase (By similarity). Required during
		angiogenesis (PubMed:20133625). Required for endoderm development
		by promoting embryonic stem cell differentiation toward endoderm: acts
		by mediating formation of H3K36me3 in distal promoter regions of
		FGFR3, leading to regulate transcription initiation of FGFR3
		(PubMed:25242323). In addition to histones, also mediates methylation
		of other proteins, such as tubulins and STAT1 (PubMed:27518565).
		Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B
		(alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis
		and cytokinesis and may be a specific tag in cytoskeletal remodeling
		(PubMed:27518565). Involved in interferon-alpha-induced antiviral
		defense by mediating both monomethylation of STAT1 at 'Lys-525' and
		catalyzing H3K36me3 on promoters of some interferon-stimulated genes
		(ISGs) to activate gene transcription (By similarity).
		{ECO:0000250 UniProtKB:Q9BYW2,
		ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625,
		ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.
		FUNCTION: RNA-binding protein that plays a central role in
		myelinization (PubMed:10864952, PubMed:11917126). Also required for
		visceral endoderm function and blood vessel development
		(PubMed:11892011, PubMed:16470614). Binds to the
Protein quaking	341	5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence
		(PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA
		export, mRNA stability and protein translation, as well as cellular
		processes including apoptosis, cell cycle, glial cell fate and development
		processes increasing apoptions, con office, giral con face and acverophient

	1	
		(PubMed:10535969, PubMed:12467586, PubMed:11297509,
		PubMed:11917126, PubMed:15568022). Required to protect and promote
		stability of mRNAs such as MBP and CDKN1B which promotes
		oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022).
		Participates in mRNA transport by regulating the nuclear export of MBP
		mRNA (PubMed:12467586). May also play a role in smooth muscle
		development (PubMed:14706070). {ECO:0000269 PubMed:10535969,
		ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509,
		ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126,
		ECO:0000269 PubMed:12467586, ECO:0000269 PubMed:14706070,
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388,
		ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved
		in regulation of mRNA splicing of MAG pre-mRNA by acting as a
		negative regulator of MAG exon 12 alternative splicing.
		{ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can induce
		apoptosis, while heterodimerization with other isoforms results in nuclear
		translocation of isoform 3 and suppression of apoptosis.
		{ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a
		translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.
	1255	FUNCTION: May act as a GTPase-activating protein for Rab family
TBC1 domain family		protein(s). May play a role in the cell cycle and differentiation of various
member 1		tissues. Involved in the trafficking and translocation of
		GLUT4-containing vesicles and insulin-stimulated glucose uptake into
		cells. {ECO:0000269 PubMed:19740738}.
Mesenteric		FUNCTION: Involved in processes that promote adipocyte
estrogen-dependent	303	differentiation, lipid accumulation, and glucose uptake in mature
adipogenesis protein		adipocytes. {ECO:0000269 PubMed:22510272}.
	1213	FUNCTION: Involved in transcriptional activation and repression of
		select genes by chromatin remodeling (alteration of DNA-nucleosome
		topology). Component of SWI/SNF chromatin remodeling complexes
		that carry out key enzymatic activities, changing chromatin structure by
		altering DNA-histone contacts within a nucleosome in an ATP-dependent
		manner. Can stimulate the ATPase activity of the catalytic subunit of
		these complexes. May be required for CoREST dependent repression of
		neuronal specific gene promoters in non-neuronal cells. Belongs to the
SWI/SNF complex subunit SMARCC2		neural progenitors-specific chromatin remodeling complex (npBAF
		complex) and the neuron-specific chromatin remodeling complex (nBAF
		complex). During neural development a switch from a stem/progenitor to
		a postmitotic chromatin remodeling mechanism occurs as neurons exit
		the cell cycle and become committed to their adult state. The transition
		from proliferating neural stem/progenitor cells to postmitotic neurons
		requires a switch in subunit composition of the npBAF and nBAF
		complexes. As neural progenitors exit mitosis and differentiate into
		neurons, npBAF complexes which contain ACTL6A/BAF53A and

		<del> </del>
		PHF10/BAF45A, are exchanged for homologous alternative
		ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in
		neuron-specific complexes (nBAF). The npBAF complex is essential for
		the self-renewal/proliferative capacity of the multipotent neural stem
		cells. The nBAF complex along with CREST plays a role regulating the
		activity of genes essential for dendrite growth (PubMed:17640523).
		Critical regulator of myeloid differentiation, controlling
		granulocytopoiesis and the expression of genes involved in neutrophil
		granule formation (PubMed:28369036).
		{ECO:0000269 PubMed:17640523, ECO:0000269 PubMed:28369036,
		ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240,
		ECO:0000303 PubMed:26601204}.
Protein prune homolog 2	3084	FUNCTION: May play an important role in regulating differentiation,
		survival and aggressiveness of the tumor cells. {ECO:0000250}.
		FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion
		molecule involved in various processes such as inflammation, cell death,
		axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008,
		PubMed:24347169, PubMed:24917672, PubMed:31526566,
		PubMed:33472215). Promotes cell adhesion by mediating homophilic
		interactions via its extracellular N-terminal adhesion motif (N-NAM)
		(PubMed:24917672, PubMed:30510259). Involved in the progression of
		the inflammatory stress by promoting cell-to-cell interactions between
		immune cells and endothelial cells (PubMed:24917672,
		PubMed:30510259). Involved in leukocyte migration during
		inflammation by promoting transendothelial migration of macrophages
		via homotypic binding (PubMed:24917672). Promotes the migration of
		monocytes across the brain endothelium to central nervous system
		inflammatory lesions (By similarity). Acts as a regulator of Toll-like
		receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during
Ninjurin-1	152	systemic inflammation; directly binds LPS (PubMed:25860173). Acts as
		a mediator of both programmed and necrotic cell death
		(PubMed:19557008, PubMed:33472215). Plays a key role in the
		induction of plasma membrane rupture during programmed and necrotic
		cell death: oligomerizes in response to death stimuli to mediate plasma
		membrane rupture (cytolysis), leading to release intracellular molecules
		named damage-associated molecular patterns (DAMPs) that propagate
		the inflammatory response (PubMed:33472215). Plays a role in nerve
		regeneration by promoting maturation of Schwann cells
		(PubMed:31526566). Acts as a regulator of angiogenesis
		(PubMed:25766274, PubMed:30354207). Promotes the formation of new
		vessels by mediating the interaction between capillary pericyte cells and
		endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates
		vascular functions in penile tissue as well as vascular formation
		(PubMed:24979788). Promotes osteoclasts development by enhancing

		the survival of prefusion osteoclasts (PubMed:30700695). Also involved
		in striated muscle growth and differentiation (PubMed:31091274). Also
		involved in cell senescence in a p53/TP53 manner, possibly by acting as
		an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620,
		PubMed:29073078). {ECO:0000250 UniProtKB:Q92982,
		ECO:0000269 PubMed:19557008, ECO:0000269 PubMed:23690620,
		ECO:0000269 PubMed:24347169, ECO:0000269 PubMed:24917672,
		ECO:0000269 PubMed:24979788, ECO:0000269 PubMed:25766274,
		ECO:0000269 PubMed:25860173, ECO:0000269 PubMed:29073078,
		ECO:0000269 PubMed:30354207, ECO:0000269 PubMed:30510259,
		ECO:0000269 PubMed:30700695, ECO:0000269 PubMed:31091274,
		ECO:0000269 PubMed:31526566, ECO:0000269 PubMed:33472215}.;
		FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage,
		which has chemotactic activity (PubMed:23142597). Acts as an
		anti-inflammatory mediator by promoting monocyte recruitment, thereby
		ameliorating atherosclerosis (PubMed:32883094).
		{ECO:0000269 PubMed:23142597, ECO:0000269 PubMed:32883094}.
		FUNCTION: Phosphorylates a large number of substrates in the
		cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B,
		ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9
		and VASP (PubMed:10805756, PubMed:19223768). Regulates the
		abundance of compartmentalized pools of its regulatory subunits through
		phosphorylation of PJA2 which binds and ubiquitinates these subunits,
		leading to their subsequent proteolysis (By similarity). RORA is activated
		by phosphorylation. Required for glucose-mediated adipogenic
		differentiation increase and osteogenic differentiation inhibition from
		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
cAMP-dependent protein		circulating platelets in a resting state by phosphorylating proteins in
kinase catalytic subunit	351	numerous platelet inhibitory pathways when in complex with
alpha		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
		thrombin and collagen disrupt these complexes and free active PRKACA
		stimulates platelets and leads to platelet aggregation by phosphorylating
		VASP. RYR2 channel activity is potentiated by phosphorylation in
		presence of luminal Ca(2+), leading to reduced amplitude and increased
		frequency of store overload-induced Ca(2+) release (SOICR)
		characterized by an increased rate of Ca(2+) release and propagation
		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog

		(Hh) signaling pathway that determines embryo pattern formation and morphogenesis (By similarity). Prevents meiosis resumption in prophase-arrested oocytes via CDC25B inactivation by phosphorylation (PubMed:19223768). May also regulate rapid eye movement (REM) sleep in the pedunculopontine tegmental (PPT) (By similarity). Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this phosphorylation promotes HSF1 nuclear localization and transcriptional activity upon heat shock (By similarity). {ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791, ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.; FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm flagellum to promote spermatozoa capacitation.
Interleukin-4 receptor subunit alpha	810	{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.  FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in promoting Th2 differentiation. The IL4/IL13 responses are involved in regulating IgE production and, chemokine and mucus production at sites of allergic inflammation. In certain cell types, can signal through activation of insulin receptor substrates, IRS1/IRS2.
Protein NEDD1	660	FUNCTION: Required for mitosis progression. Promotes the nucleation of microtubules from the spindle (By similarity). May play an important role during the embryonic development and differentiation of the central nervous system (PubMed:1378265).  {ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
Protein phosphatase 3 catalytic subunit alpha	521	FUNCTION: Calcium-dependent, calmodulin-stimulated protein phosphatase which plays an essential role in the transduction of intracellular Ca(2+)-mediated signals (PubMed:7791792, PubMed:26794871). Many of the substrates contain a PxIxIT motif and/or a LxVP motif (By similarity). In response to increased Ca(2+) levels, dephosphorylates and activates phosphatase SSH1 which results in cofilin dephosphorylation (By similarity). In response to increased Ca(2+) levels following mitochondrial depolarization, dephosphorylates DNM1L inducing DNM1L translocation to the mitochondrion (By similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+) release probability at hippocampal neuronal soma and synaptic terminals (By similarity). Dephosphorylates heat shock protein HSPB1 (By similarity). Dephosphorylates and activates transcription factor NFATC1 (By similarity). Dephosphorylates and inactivates transcription factor ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation from 14-3-3 proteins (By similarity). Required for postnatal development of the nephrogenic zone and superficial glomeruli in the kidneys, cell cycle homeostasis in the nephrogenic zone, and ultimately normal kidney function (PubMed:15509543). Plays a role in intracellular AQP2

thereby be required for efficient kidney filtration (PubMed:16735444). Required for secretion of salivary enzymes amylase, peroxidase, lysozyme and sialic acid via formation of secretory vesicles in the submandibular glands (PubMed:21435446). Required for calcineurin activity and homosynaptic depotentiation in the hippocampus (PubMed:10200317). Required for normal differentiation and survival of keratinocytes and therefore required for poidermis superstructure formation (PubMed:16966032). Positively regulates osteoblast differentiation (PubMed:1696645). Positively regulates osteoblast differentiation, potentially via nFATC1 signaling (PubMed:16968888). May play a role in skeletal muscle fiber type specification, potentially via NFATC1 signaling (PubMed:16968888). May play a role in skeletal muscle fiber type specification, potentially via NFATC1 signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK signaling via inhibition of nuclear translocation of the transcription factors RELA and RELB (PubMed:26029823). Required for antigen-specific T-cell proliferation response (PubMed:8627154). (ECC-0000250/UmiProtKB:48452, ECC-0000250/UmiProtKB:4852, ECC-0000250/UmiProtKB:4852, ECC-0000250/UmiProtKB:4852, ECC-0000250/UmiProtKB:4852, ECC-0000250/UmiProtKB:4852, ECC-0000250/UmiProtKB:4852, ECC-0000269/PubMed:16735444, ECC-0000269/PubMed:16735444, ECC-0000269/PubMed:16735444, ECC-0000269/PubMed:16735444, ECC-0000269/PubMed:16735444, ECC-0000269/PubMed:2609823, ECC-0000269/PubMed:2609823, ECC-0000269/PubMed:36271543.  FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by home-or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in mither regulation and interconnection of both innate and adaptive immune responses of activated T-cells and SHI2D1A/SAP and/or SHI2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/			
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involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity			prolonged T-cell:B-cell contact, optimal T follicular helper function, and
(PubMed:25801429). In mast cells negatively regulates high affinity			germinal center formation (PubMed:20153220). In germinal centers
			involved in maintaining B cell tolerance and in preventing autoimmunity
immunoglobulin epsilon receptor signaling; independent of SH2D1A and			(PubMed:25801429). In mast cells negatively regulates high affinity
			immunoglobulin epsilon receptor signaling; independent of SH2D1A and

		SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In
		macrophages enhances LPS-induced MAPK phosphorylation and
		NF-kappaB activation and modulates LPS-induced cytokine secretion;
		involving ITSM 2 (PubMed:20628063). Positively regulates
		macroautophagy in primary dendritic cells via stabilization of IRF8;
		inhibits TRIM21-mediated proteasomal degradation of IRF8 (By
		similarity). {ECO:0000250 UniProtKB:Q9UIB8,
		ECO:0000269 PubMed:16037392, ECO:0000269 PubMed:20153220,
		ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259,
		ECO:0000269 PubMed:25801429, ECO:0000305}.
		FUNCTION: Plays a role in primary cilia formation (By similarity). May
		act as a downstream effector of HOXC8 possibly by transducing or
		transmitting extracellular information required for axial skeletal
Transmembrane anterior		patterning during development (By similarity). May be involved in
posterior transformation	564	cartilage and bone development (By similarity). May play a role in the
protein 1		differentiation of cranial neural crest cells (By similarity).
		{ECO:0000250 UniProtKB:A2BIE7,
		ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
		FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm
		diameter microfibrils of the extracellular matrix, which conveys both
		structural and regulatory properties to load-bearing connective tissues.
		Fibrillin-1-containing microfibrils provide long-term force bearing
		structural support. In tissues such as the lung, blood vessels and skin,
		microfibrils form the periphery of the elastic fiber, acting as a scaffold for
		the deposition of elastin. In addition, microfibrils can occur as
		elastin-independent networks in tissues such as the ciliary zonule, tendon,
		cornea and glomerulus where they provide tensile strength and have
		anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis
		through specific interactions with growth factors, such as the bone
		morphogenetic proteins (BMPs), growth and differentiation factors
Fibrillin-1	2873	(GDFs) and latent transforming growth factor-beta-binding proteins
	2070	(LTBPs), cell-surface integrins and other extracellular matrix protein and
		proteoglycan components (By similarity). Regulates osteoblast
		maturation by controlling TGF-beta bioavailability and calibrating
		TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively
		regulates osteoclastogenesis by binding and sequestering an osteoclast
		differentiation and activation factor TNFSF11. This leads to disruption of
		TNFSF11-induced Ca(2+) signaling and impairment of
		TNFSF11-mediated nuclear translocation and activation of transcription
		factor NFATC1 which regulates genes important for osteoclast
		differentiation and function (PubMed:24039232). Mediates cell adhesion
		via its binding to cell surface receptors integrins ITGAV:ITGB3 and
		ITGA5:ITGB1. Binds heparin and this interaction plays an important role
		in the assembly of microfibrils (By similarity).
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		{ECO:0000250 UniProtKB:P35555, ECO:0000269 PubMed:20855508, ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine secreted by white adipose tissue that plays an important regulatory role in the glucose metabolism of liver, muscle and pancreas (PubMed:31230984, PubMed:30997682). Hormone that targets the liver in response to fasting to increase plasma glucose levels (PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface of hepatocytes and promotes hepatocyte glucose release by activating the protein kinase A activity in the liver, resulting in rapid glucose release into the circulation (PubMed:31230984). May act as a regulator of adaptive thermogenesis by inhibiting browning and energy consumption, while increasing lipid deposition in white adipose tissue (PubMed:33705351). Also acts as an orexigenic hormone that increases appetite: crosses the blood brain barrier and exerts effects on the hypothalamus (PubMed:29106398). In the arcuate nucleus of the hypothalamus, asprosin directly activates orexigenic AgRP neurons and indirectly inhibits anorexigenic POMC neurons, resulting in appetite
		of hepatocytes and promotes hepatocyte glucose release by activating the
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		stimulation (PubMed:29106398, PubMed:32337066). Activates
		orexigenic AgRP neurons via binding to the olfactory receptor Olfr734
		(PubMed:32337066). May also play a role in sperm motility in testis via
		interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682,
		ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959,
		ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
		FUNCTION: May play a role in intercellular signaling and in connecting
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cell
		motility, growth and differentiation. Binds hyaluronic acid.
		FUNCTION: Catalyzes the saturation of all-trans-retinol to
		all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779, PubMed:19139408). Does not exhibit any activity toward
		all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers
		(PubMed:15358783). May play a role in the metabolism of vitamin A
		(PubMed:15358783, PubMed:17253779). Independently of retinol
All-trans-retinol		conversion, may regulate liver metabolism upstream of
13,14-reductase	609	MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte
		differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This
		effect seems not to mimic the in vivo situation in which animals show
		increased adiposity in the absence of RETSAT (PubMed:19940255).
		{ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779,
		ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255,
Coloium torrar action		ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
Calcium-transporting ATPase type 2C member	918	FUNCTION: ATP-driven pump that supplies the Golgi apparatus with Ca(2+) and Mn(2+) ions, both essential cofactors for processing and
1	710	trafficking of newly synthesized proteins in the secretory pathway (By
1		marriering of newly synthesized proteins in the secretory pathway (By

		similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on
		the cytoplasmic side of the membrane and delivers them to the lumenal
		side. The transfer of ions across the membrane is coupled to ATP
		hydrolysis and is associated with a transient phosphorylation that shifts
		the pump conformation from inward-facing to outward-facing state (By
		similarity). Plays a primary role in the maintenance of Ca(2+)
		homeostasis in the trans-Golgi compartment with a functional impact on
		Golgi and post-Golgi protein sorting as well as a structural impact on
		cisternae morphology. Responsible for loading the Golgi stores with
		Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation
		and epidermis integrity (By similarity). Participates in Ca(2+) and
		Mn(2+) ions uptake into the Golgi store of hippocampal neurons and
		regulates protein trafficking required for neural polarity
		(PubMed:19793975). May also play a role in the maintenance of Ca(2+)
		and Mn(2+) homeostasis and signaling in the cytosol while preventing
		cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194,
		ECO:0000269 PubMed:19793975}.
		FUNCTION: Phosphodiesterase (PDE) that has higher activity toward
		cAMP than cGMP, as substrate. Plays a role in cell proliferation,
Exopolyphosphatase	454	migration and differentiation, and acts as a negative regulator of NME1.
PRUNE1		Plays a role in the regulation of neurogenesis. Involved in the regulation
		of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma		FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl
		1 2 21.2 121. Exhibits strong at presidence activity with octal hapitally.
membrane-associated	415	
membrane-associated	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte
membrane-associated protein	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.
	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity).
	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity).  Inhibits renal tubular phosphate transport by reducing SLC34A1 levels
		acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity).  Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH
protein	251	acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity).  Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By
Fibroblast growth factor		acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity).  Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix
Fibroblast growth factor		acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity).  Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the
Fibroblast growth factor		acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity).  Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
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Fibroblast growth factor		acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity).  Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.  FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central
Fibroblast growth factor		acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity). Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.  FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central nervous system physiology (PubMed:26456657, PubMed:35119925).
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Fibroblast growth factor 23	251	acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity). Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.  FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central nervous system physiology (PubMed:26456657, PubMed:35119925).  Plays a key role in initial steps of T-cell activation and Ca(2+) microdomain formation (PubMed:35119925). Participates also in basal T-cell activity without TCR/CD3 stimulation (PubMed:35119925).
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Fibroblast growth factor 23	251	acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity). Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.  FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central nervous system physiology (PubMed:26456657, PubMed:35119925).  Plays a key role in initial steps of T-cell activation and Ca(2+) microdomain formation (PubMed:35119925). Participates also in basal T-cell activity without TCR/CD3 stimulation (PubMed:35119925).
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Fibroblast growth factor 23	251	acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity). Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.  FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central nervous system physiology (PubMed:26456657, PubMed:35119925).  Plays a key role in initial steps of T-cell activation and Ca(2+) microdomain formation (PubMed:35119925). Participates also in basal T-cell activity without TCR/CD3 stimulation (PubMed:35119925).  Promotes the differentiation and activation of Th17 cells via expression of retinoic acid-related orphan receptor C/RORC (By similarity). Upon
Fibroblast growth factor 23	251	acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.  FUNCTION: Regulator of phosphate homeostasis (By similarity). Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.  FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central nervous system physiology (PubMed:26456657, PubMed:35119925). Plays a key role in initial steps of T-cell activation and Ca(2+) microdomain formation (PubMed:35119925). Participates also in basal T-cell activity without TCR/CD3 stimulation (PubMed:35119925). Promotes the differentiation and activation of Th17 cells via expression of retinoic acid-related orphan receptor C/RORC (By similarity). Upon activation, drives microglia motility via the PI3K/Akt pathway

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PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a key regulator of metabolic reprogramming towards aerobic glycolysis, a process in which glucose is converted to lactate in the presence of oxygen (PubMed:30700909). Acts by promoting expression of enzymes for glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate kinase (PKLR) and lactate dehydrogenase), while suppressing further oxidation of pyruvate in the mitochondria by up-regulating pyruvate dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably plays a role in gluconeogenesis during overnight fasting, when lactate from white adipose tissue and muscle is the main substrate (PubMed:30700909). Involved in mTORC1-mediated metabolic reprogramming: in response to mTORC1 signaling, translocates into the nucleus and regulates the expression of genes associated with glycolysis and downstream anabolic pathways, such as HIF1A, thereby regulating glucose metabolism (PubMed:29861159). Together with FOXK2, acts as a negative regulator of autophagy in skeletal muscle: in response to starvation, enters the nucleus, binds the promoters of autophagy genes and represses their expression, preventing proteolysis of skeletal muscle proteins (PubMed:25402684). Acts as a transcriptional regulator of the myogenic progenitor cell population in skeletal muscle (PubMed:8007964, PubMed:9271401, PubMed:12446708, PubMed:22956541). Binds to the upstream enhancer region (CCAC box) of myoglobin (MB) gene, regulating the myogenic progenitor cell population (PubMed:8007964, PubMed:9271401). Promotes muscle progenitor cell proliferation by repressing the transcriptional activity of FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708, PubMed:22956541). Involved in remodeling processes of adult muscles that occur in response to physiological stimuli (PubMed:9271401, PubMed:22956541). Required to correct temporal orchestration of molecular and cellular events necessary for muscle repair (PubMed:10792059). Represses myogenic differentiation by inhibiting MEFC activity (PubMed:22956541). Positively regulates Wnt/beta-catenin signaling by translocating DVL into the nucleus (By similarity). Reduces virus replication, probably by binding the interferon stimulated response element (ISRE) to promote antiviral gene expression (By similarity). {ECO:0000250|UniProtKB:P85037, ECO:0000269|PubMed:10792059, ECO:0000269|PubMed:12446708, ECO:0000269|PubMed:22956541, ECO:0000269|PubMed:25402684, ECO:0000269|PubMed:29861159, ECO:0000269|PubMed:30700909, ECO:0000269|PubMed:8007964, ECO:0000269|PubMed:9271401}. FUNCTION: Component of the cleavage and polyadenylation specificity factor (CPSF) complex that plays a key role in pre-mRNA 3'-end formation, recognizing the AAUAAA signal sequence and interacting with poly(A) polymerase and other factors to bring about cleavage and

Cleavage and polyadenylation specificity factor subunit 3

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		poly(A) addition. Has endonuclease activity, and functions as mRNA
		3'-end-processing endonuclease. Also involved in the histone 3'-end
		pre-mRNA processing. U7 snRNP-dependent protein that induces both
		the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a
		5' to 3' exonuclease for degrading the subsequent downstream cleavage
		product (DCP) of mature histone mRNAs. Cleavage occurs after the
		5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl
		group on the upstream fragment containing the stem loop (SL) and 5'
		phosphate on the downstream cleavage product (DCP) starting with CU
		nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive
		and degrades the DCP RNA substrate even after complete removal of the
		U7-binding site. Binds to the downstream cleavage product (DCP) of
		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
		(miRNAs) during embryonic stem cell differentiation via its interaction
		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
		primary transcript except miR-92a (PubMed:26255770). Only required
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
		pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
		ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
		FUNCTION: Serine/threonine kinase which acts as an essential
		component of the MAP kinase signal transduction pathway.
		MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an
		important role in the MAPK/ERK cascade. They participate also in a
		signaling cascade initiated by activated KIT and KITLG/SCF. Depending
		on the cellular context, the MAPK/ERK cascade mediates diverse
		biological functions such as cell growth, adhesion, survival and
		differentiation through the regulation of transcription, translation,
		cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role
Mitogen-activated protein	250	in initiation and regulation of meiosis, mitosis, and postmitotic functions
kinase 1	358	in differentiated cells by phosphorylating a number of transcription
		factors. About 160 substrates have already been discovered for ERKs.
		Many of these substrates are localized in the nucleus, and seem to
		participate in the regulation of transcription upon stimulation. However,
		other substrates are found in the cytosol as well as in other cellular
		organelles, and those are responsible for processes such as translation,
		mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also
		involved in the regulation of the endosomal dynamics, including
		lysosome processing and endosome cycling through the perinuclear
		recycling compartment (PNRC); as well as in the fragmentation of the

		<u> </u>
		Golgi apparatus during mitosis. The substrates include transcription factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1), cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT, PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD, BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of translation (such as EIF4EBP1) and a variety of other signaling-related molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases (such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3, RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2, RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other substrates which enable the propagation the MAPK/ERK signal to additional cytosolic and nuclear targets, thereby extending the specificity of the cascade. Mediates phosphorylation of TPR in response to EGF stimulation. May play a role in the spindle assembly checkpoint. Phosphorylates PML and promotes its interaction with PIN1, leading to PML degradation. Phosphorylates CDK2AP2 (By similarity). {ECO:0000250 UniProtKB:P28482, ECO:0000250 UniProtKB:P63086, ECO:0000269 PubMed:12134156, ECO:0000269 PubMed:1702783, ECO:0000269 PubMed:12134156, ECO:0000303 PubMed:21779493}.; FUNCTION: Acts as a transcriptional repressor. Binds to a [GC]AAA[GC] consensus sequence. Repress the expression of interferon gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1, IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1. Transcriptional activity is independent of kinase activity. {ECO:0000250 UniProtKB:P28482}.
RNA-binding protein 15	962	FUNCTION: RNA-binding protein that acts as a key regulator of N6-methyladenosine (m6A) methylation of RNAs, thereby regulating different processes, such as hematopoietic cell homeostasis, alternative splicing of mRNAs and X chromosome inactivation mediated by Xist RNA (PubMed:29535189). Associated component of the WMM complex, a complex that mediates N6-methyladenosine (m6A) methylation of RNAs, a modification that plays a role in the efficiency of mRNA splicing and RNA processing (PubMed:29535189). Plays a key role in m6A methylation, possibly by binding target RNAs and recruiting the WMM complex (PubMed:29535189). Involved in random X inactivation mediated by Xist RNA: acts by binding Xist RNA and recruiting the WMM complex, which mediates m6A methylation, leading to target YTHDC1 reader on Xist RNA and promoting transcription repression activity of Xist (By similarity). Required for the development of multiple tissues, such as the maintenance of the homeostasis of long-term hematopoietic stem cells and for megakaryocyte (MK) and B-cell differentiation (PubMed:17283045, PubMed:17376872,

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		PubMed:18981216, PubMed:25468569). Regulates megakaryocyte
		differentiation by regulating alternative splicing of genes important for
		megakaryocyte differentiation; probably regulates alternative splicing via
		m6A regulation (By similarity). Required for placental vascular
		branching morphogenesis and embryonic development of the heart and
		spleen (PubMed:18981216). Acts as a regulator of thrombopoietin
		response in hematopoietic stem cells by regulating alternative splicing of
		MPL (PubMed:25468569). May also function as an mRNA export factor,
		stimulating export and expression of RTE-containing mRNAs which are
		present in many retrotransposons that require to be exported prior to
		splicing (By similarity). High affinity binding of pre-mRNA to RBM15
		may allow targeting of the mRNP to the export helicase DBP5 in a
		manner that is independent of splicing-mediated NXF1 deposition,
		resulting in export prior to splicing (By similarity). May be implicated in
		HOX gene regulation (By similarity).
		{ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:17283045,
		ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18981216,
		ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29535189}.
		FUNCTION: Transcription coactivator which associates with nuclear
		receptors, transcriptional coactivators including EP300, CREBBP and
		NCOA1, and basal transcription factors like TBP and TFIIA to facilitate
	581	nuclear receptors-mediated transcription. May thereby play an important
		role in establishing distinct coactivator complexes under different cellular
		conditions. Plays a role in thyroid hormone receptor and estrogen
		receptor transactivation (By similarity). Also involved in androgen
		receptor transactivation (PubMed:12077347). Plays a pivotal role in the
Activating signal		transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of
cointegrator 1		transrepression between nuclear receptor and either AP1 or NF-kappa-B.
		May play a role in the development of neuromuscular junction (By
		similarity). May play a role in late myogenic differentiation
		(PubMed:27008887). Also functions as part of the RQC trigger (RQT)
		complex that activates the ribosome quality control (RQC) pathway, a
		pathway that degrades nascent peptide chains during problematic
		translation (By similarity). {ECO:0000250 UniProtKB:Q15650,
		ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
		ECO:0000269 PubMed:27008887}.
		FUNCTION: Histone methyltransferase that specifically trimethylates
		'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36'
		(H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is
Histone-lysine	2525	capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
N-methyltransferase	2537	similarity). Represents the main enzyme generating H3K36me3, a
SETD2		specific tag for epigenetic transcriptional activation (PubMed:18157086,
		PubMed:20133625). Plays a role in chromatin structure modulation
		during elongation by coordinating recruitment of the FACT complex and
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DNA double-strand break repair in response to DNA damage: acts by mediating formation of H3K36mc3, promoting recruitment of RAD51 and DNA repair via homologous recombination (HR) (By similarity). Acts as a tumor suppressor (By similarity). H3K36mc3 also plays an essential role in the maintenance of a heterochromatic state, by recruiting DNA methyltransferase DNMT3A (By similarity). H3K36mc3 is also enhanced in intron-containing genes, suggesting that SETD2 recruitment is enhanced by splicing and that splicing is coupled to recruitment of clongating RNA polymerase (By similarity). Required during angiogenesis (PubMed:20133625). Required for endoderm development by promoting embryonic stem cell differentiation toward endoderm: acts by mediating formation of H3K36mc3 in distal promoter regions of FGFR3 (PubMed:25242323). In addition to histones, also mediates methylation of other proteins, such as tubulins and STAT1 (PubMed:27518565). Trimethylates T.ys-40' of alpha-tubulins such as TUBA1B (alpha-TubK40mc3); alpha-TubK40mc3 is required for normal mitosis and cytokinesis and may be a specific tag in cytoskeletal remodeling (PubMed:27518565). Involved in interferon-alpha-induced antiviral defense by mediating both monomethylation of STAT1 at "Lys-S25' and catalyzing H3K36mc3 on promoters of some interferon-stimulated genes (ISGs) to activate gene transcription (By similarity). (ECO:0000250 UmiProtKB:Q9BYW2, ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.  FUNCTION: RNA-binding protein that plays a central role in myelinization (PubMed:10864952, PubMed:11917126). Also required fo visceral endoderm function and blood vessel development (PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA export, mRNA stability and protein translation, as well as cellular processes including apoptosis, cell cycle, glial cell fate and development (PubMed:1041388). Acts by byediating pre-mRNA splicing, mRNA export, mRNA stability and protein translation, as well as cellular processes including apoptosis, cell cycle, g			by interacting with hyperphosphorylated POLR2A (By similarity). Acts
MutS alpha complex: early recruitment of the MutS alpha complex to chromatin to be replicated allows a quick identification of mismatch DNA to initiate the mismatch repair reaction (By similarity). Required fo DNA double-strand break repair in response to DNA damage: acts by mediating formation of H3K36me3, promoting recruitment of RAD51 and DNA repair via homologous recombination (HR) (By similarity). Acts as a tumor suppressor (By similarity). H3K36me3 also plays an essential role in the maintenance of a heterochromatic state, by recruiting DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also enhanced in intron-containing genes, suggesting that SETD2 recruitment is enhanced by splicing and that splicing is coupled to recruitment of elongating RNA polymerase (By similarity). Required during angiogenesis (PubMed:20133625). Required for endoderm development by promoting embryonic stem cell differentiation toward endoderm: acts by mediating formation of H3K36me3 in distal promoter regions of FGFR3, leading to regulate transcription initiation of FGFR3 (PubMed:25242323). In addition to histones, also mediates methylation of other proteins, such as tubulins and STAT1 (PubMed:27518565). Trimethylates Tuys-40° of alpha-tubulins such as TUBA1B (alpha-TubK40me3), alpha-TubK40me3) is required for normal mitosis and eytokinesis and may be a specific tag in eytoskeletal remodeling (PubMed:27518565). Involved in interferon-alpha-induced antiviral defense by mediating both monomethylation of STAT1 at Tuys-52s and catalyzing H3K36me3 on promoters of some interferon-stimulated genes (ISGs) to activate gene transcription (By similarity). (ECO:0000250 UmiProtKB:QBYW2, ECO:0000250 UmiProtKB:QBYW2, ECO:0000250 UmiProtKB:QBYW2, ECO:0000250 PubMed:1187126, PubMed:1197126, Also required fo visceral endoderm function and blood vessel development (PubMed:10535969, PubMed:10535969, PubMed:1197509, PubMed:1197509, PubMed:11977160, PubMed:1967509, PubMed:115568022).			as a key regulator of DNA mismatch repair in G1 and early S phase by
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oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022).			PubMed:11917126, PubMed:15568022). Required to protect and promote
Participates in mRNA transport by regulating the nuclear export of MRP			oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022).
1 management of regulating the fraction expert of Fibr			Participates in mRNA transport by regulating the nuclear export of MBP

		mRNA (PubMed:12467586). May also play a role in smooth muscle
		development (PubMed:14706070). {ECO:0000269 PubMed:10535969, ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509,
		ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126,
		ECO:0000269 PubMed:12467586, ECO:0000269 PubMed:14706070,
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388,
		ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved
		in regulation of mRNA splicing of MAG pre-mRNA by acting as a
		negative regulator of MAG exon 12 alternative splicing.
		{ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can induce
		apoptosis, while heterodimerization with other isoforms results in nuclear
		translocation of isoform 3 and suppression of apoptosis.
		{ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a
		translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.
		FUNCTION: May act as a GTPase-activating protein for Rab family
		protein(s). May play a role in the cell cycle and differentiation of various
TBC1 domain family	1255	tissues. Involved in the trafficking and translocation of
member 1	1233	GLUT4-containing vesicles and insulin-stimulated glucose uptake into
		cells. {ECO:0000269 PubMed:19740738}.
Mesenteric		FUNCTION: Involved in processes that promote adipocyte
estrogen-dependent	303	differentiation, lipid accumulation, and glucose uptake in mature
adipogenesis protein	303	adipocytes. {ECO:0000269 PubMed:22510272}.
adipogenesis protein		FUNCTION: Involved in transcriptional activation and repression of
		select genes by chromatin remodeling (alteration of DNA-nucleosome
		topology). Component of SWI/SNF chromatin remodeling complexes
		that carry out key enzymatic activities, changing chromatin structure by
		altering DNA-histone contacts within a nucleosome in an ATP-dependent
		manner. Can stimulate the ATPase activity of the catalytic subunit of
		these complexes. May be required for CoREST dependent repression of
		neuronal specific gene promoters in non-neuronal cells. Belongs to the
		neural progenitors-specific chromatin remodeling complex (npBAF
		complex) and the neuron-specific chromatin remodeling complex (nBAF
SWI/SNF complex		complex) and the neuron-specific chromatin remodering complex (insAr- complex). During neural development a switch from a stem/progenitor to
subunit SMARCC2	1213	a postmitotic chromatin remodeling mechanism occurs as neurons exit
Subuliit SWARCC2		
		the cell cycle and become committed to their adult state. The transition
		from proliferating neural stem/progenitor cells to postmitotic neurons
		requires a switch in subunit composition of the npBAF and nBAF
		complexes. As neural progenitors exit mitosis and differentiate into
		neurons, npBAF complexes which contain ACTL6A/BAF53A and
		PHF10/BAF45A, are exchanged for homologous alternative
		ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in
		neuron-specific complexes (nBAF). The npBAF complex is essential for
		the self-renewal/proliferative capacity of the multipotent neural stem
		cells. The nBAF complex along with CREST plays a role regulating the

	1	T
		activity of genes essential for dendrite growth (PubMed:17640523).
		Critical regulator of myeloid differentiation, controlling
		granulocytopoiesis and the expression of genes involved in neutrophil
		granule formation (PubMed:28369036).
		{ECO:0000269 PubMed:17640523, ECO:0000269 PubMed:28369036,
		ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240,
		ECO:0000303 PubMed:26601204}.
Protein prune homolog 2	3084	FUNCTION: May play an important role in regulating differentiation,
1 Totelli prune nomolog 2	3004	survival and aggressiveness of the tumor cells. {ECO:0000250}.
		FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion
		molecule involved in various processes such as inflammation, cell death,
		axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008,
		PubMed:24347169, PubMed:24917672, PubMed:31526566,
		PubMed:33472215). Promotes cell adhesion by mediating homophilic
		interactions via its extracellular N-terminal adhesion motif (N-NAM)
		(PubMed:24917672, PubMed:30510259). Involved in the progression of
		the inflammatory stress by promoting cell-to-cell interactions between
		immune cells and endothelial cells (PubMed:24917672,
		PubMed:30510259). Involved in leukocyte migration during
		inflammation by promoting transendothelial migration of macrophages
		via homotypic binding (PubMed:24917672). Promotes the migration of
		monocytes across the brain endothelium to central nervous system
		inflammatory lesions (By similarity). Acts as a regulator of Toll-like
		receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during
		systemic inflammation; directly binds LPS (PubMed:25860173). Acts as
		a mediator of both programmed and necrotic cell death
Ninjurin-1	152	(PubMed:19557008, PubMed:33472215). Plays a key role in the
Willyurin-1	132	induction of plasma membrane rupture during programmed and necrotic
		cell death: oligomerizes in response to death stimuli to mediate plasma
		membrane rupture (cytolysis), leading to release intracellular molecules
		named damage-associated molecular patterns (DAMPs) that propagate
		the inflammatory response (PubMed:33472215). Plays a role in nerve
		regeneration by promoting maturation of Schwann cells
		(PubMed:31526566). Acts as a regulator of angiogenesis
		(PubMed:25766274, PubMed:30354207). Promotes the formation of new
		vessels by mediating the interaction between capillary pericyte cells and
		endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates
		vascular functions in penile tissue as well as vascular formation
		(PubMed:24979788). Promotes osteoclasts development by enhancing
		the survival of prefusion osteoclasts (PubMed:30700695). Also involved
		in striated muscle growth and differentiation (PubMed:31091274). Also
		involved in cell senescence in a p53/TP53 manner, possibly by acting as
		an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620,
		PubMed:29073078). {ECO:0000250 UniProtKB:Q92982,

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		ECO:0000269 PubMed:19557008, ECO:0000269 PubMed:23690620,
		ECO:0000269 PubMed:24347169, ECO:0000269 PubMed:24917672,
		ECO:0000269 PubMed:24979788, ECO:0000269 PubMed:25766274,
		ECO:0000269 PubMed:25860173, ECO:0000269 PubMed:29073078,
		ECO:0000269 PubMed:30354207, ECO:0000269 PubMed:30510259,
		ECO:0000269 PubMed:30700695, ECO:0000269 PubMed:31091274,
		ECO:0000269 PubMed:31526566, ECO:0000269 PubMed:33472215}.;
		FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage,
		which has chemotactic activity (PubMed:23142597). Acts as an
		anti-inflammatory mediator by promoting monocyte recruitment, thereby
		ameliorating atherosclerosis (PubMed:32883094).
		{ECO:0000269 PubMed:23142597, ECO:0000269 PubMed:32883094}.
		FUNCTION: Phosphorylates a large number of substrates in the
		cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B,
		ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9
		and VASP (PubMed:10805756, PubMed:19223768). Regulates the
		abundance of compartmentalized pools of its regulatory subunits through
		phosphorylation of PJA2 which binds and ubiquitinates these subunits,
		leading to their subsequent proteolysis (By similarity). RORA is activated
		by phosphorylation. Required for glucose-mediated adipogenic
		differentiation increase and osteogenic differentiation inhibition from
		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
		circulating platelets in a resting state by phosphorylating proteins in
		numerous platelet inhibitory pathways when in complex with
cAMP-dependent protein		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
kinase catalytic subunit	351	thrombin and collagen disrupt these complexes and free active PRKACA
alpha		stimulates platelets and leads to platelet aggregation by phosphorylating
		VASP. RYR2 channel activity is potentiated by phosphorylation in
		presence of luminal Ca(2+), leading to reduced amplitude and increased
		frequency of store overload-induced Ca(2+) release (SOICR)
		characterized by an increased rate of Ca(2+) release and propagation
		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		orecp in the pedanearopointine teginental (111) (by similarity).

		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
		ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.;
		FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm
		flagellum to promote spermatozoa capacitation.
		{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.
		FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples
		to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in
Interleukin-4 receptor	810	promoting Th2 differentiation. The IL4/IL13 responses are involved in
subunit alpha	810	regulating IgE production and, chemokine and mucus production at sites
		of allergic inflammation. In certain cell types, can signal through
		activation of insulin receptor substrates, IRS1/IRS2.
		FUNCTION: Required for mitosis progression. Promotes the nucleation
		of microtubules from the spindle (By similarity). May play an important
Protein NEDD1	660	role during the embryonic development and differentiation of the central
		nervous system (PubMed:1378265).
		{ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
		FUNCTION: Calcium-dependent, calmodulin-stimulated protein
		phosphatase which plays an essential role in the transduction of
		intracellular Ca(2+)-mediated signals (PubMed:7791792,
		PubMed:26794871). Many of the substrates contain a PxIxIT motif
		and/or a LxVP motif (By similarity). In response to increased Ca(2+)
		levels, dephosphorylates and activates phosphatase SSH1 which results in
		cofilin dephosphorylation (By similarity). In response to increased
		Ca(2+) levels following mitochondrial depolarization, dephosphorylates
		DNM1L inducing DNM1L translocation to the mitochondrion (By
		similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+)
		release probability at hippocampal neuronal soma and synaptic terminals
		(By similarity). Dephosphorylates heat shock protein HSPB1 (By
Protein phosphatase 3	521	
catalytic subunit alpha	521	similarity). Dephosphorylates and activates transcription factor NFATC1
		(By similarity). Dephosphorylates and inactivates transcription factor
		ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May
		dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation
		from 14-3-3 proteins (By similarity). Required for postnatal development
		of the nephrogenic zone and superficial glomeruli in the kidneys, cell
		cycle homeostasis in the nephrogenic zone, and ultimately normal kidney
		function (PubMed:15509543). Plays a role in intracellular AQP2
		processing and localization to the apical membrane in the kidney, may
		thereby be required for efficient kidney filtration (PubMed:16735444).
		Required for secretion of salivary enzymes amylase, peroxidase,
		lysozyme and sialic acid via formation of secretory vesicles in the
		submandibular glands (PubMed:21435446). Required for calcineurin
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		activity and homosynaptic depotentiation in the hippocampus
		(PubMed:10200317). Required for normal differentiation and survival of
		keratinocytes and therefore required for epidermis superstructure
		formation (PubMed:19626032). Positively regulates osteoblastic bone
		formation, via promotion of osteoblast differentiation
		(PubMed:16286645). Positively regulates osteoclast differentiation,
		potentially via NFATC1 signaling (PubMed:16968888). May play a role
		in skeletal muscle fiber type specification, potentially via NFATC1
		signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK
		signaling via inhibition of nuclear translocation of the transcription
		factors RELA and RELB (PubMed:26029823). Required for
		antigen-specific T-cell proliferation response (PubMed:8627154).
		{ECO:0000250 UniProtKB:P48452, ECO:0000250 UniProtKB:P63329,
		ECO:0000250 UniProtKB:Q08209, ECO:0000269 PubMed:10200317,
		ECO:0000269 PubMed:12773574, ECO:0000269 PubMed:15509543,
		ECO:0000269 PubMed:16286645, ECO:0000269 PubMed:16735444,
		ECO:0000269 PubMed:16968888, ECO:0000269 PubMed:19626032,
		ECO:0000269 PubMed:21435446, ECO:0000269 PubMed:26029823,
		ECO:0000269 PubMed:26794871, ECO:0000269 PubMed:7791792,
		ECO:0000269 PubMed:8627154}.
		FUNCTION: Self-ligand receptor of the signaling lymphocytic activation
		molecule (SLAM) family. SLAM receptors triggered by homo- or
		heterotypic cell-cell interactions are modulating the activation and
		differentiation of a wide variety of immune cells and thus are involved in
		the regulation and interconnection of both innate and adaptive immune
		response. Activities are controlled by presence or absence of small
		cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2
		(PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity
		dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases
		proliferative responses of activated T-cells and SH2D1A/SAP does not
		seen be required for this process. Homophilic interactions enhance
SLAM family member 5	329	interferon gamma/IFNG secretion in lymphocytes and induce platelet
		stimulation via a SH2D1A/SAP-dependent pathway. May serve as a
		marker for hematopoietic progenitor cells (By similarity). Required for a
		prolonged T-cell:B-cell contact, optimal T follicular helper function, and
		germinal center formation (PubMed:20153220). In germinal centers
		involved in maintaining B cell tolerance and in preventing autoimmunity
		(PubMed:25801429). In mast cells negatively regulates high affinity
		immunoglobulin epsilon receptor signaling; independent of SH2D1A and
		SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In
		macrophages enhances LPS-induced MAPK phosphorylation and
		NF-kappaB activation and modulates LPS-induced cytokine secretion;
		involving ITSM 2 (PubMed:20628063). Positively regulates
		macroautophagy in primary dendritic cells via stabilization of IRF8;
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		inhibits TRIM21-mediated proteasomal degradation of IRF8 (By
		similarity). {ECO:0000250 UniProtKB:Q9UIB8,
		ECO:0000269 PubMed:16037392, ECO:0000269 PubMed:20153220,
		ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259,
		ECO:0000269 PubMed:25801429, ECO:0000305}.
		FUNCTION: Plays a role in primary cilia formation (By similarity). May
		act as a downstream effector of HOXC8 possibly by transducing or
Transmembrane anterior		transmitting extracellular information required for axial skeletal
posterior transformation	564	patterning during development (By similarity). May be involved in
protein 1	304	cartilage and bone development (By similarity). May play a role in the
protein i		differentiation of cranial neural crest cells (By similarity).
		{ECO:0000250 UniProtKB:A2BIE7,
		ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
		FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm
		diameter microfibrils of the extracellular matrix, which conveys both
		structural and regulatory properties to load-bearing connective tissues.
		Fibrillin-1-containing microfibrils provide long-term force bearing
		structural support. In tissues such as the lung, blood vessels and skin,
		microfibrils form the periphery of the elastic fiber, acting as a scaffold for
	2873	the deposition of elastin. In addition, microfibrils can occur as
		elastin-independent networks in tissues such as the ciliary zonule, tendon,
		cornea and glomerulus where they provide tensile strength and have
		anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis
		through specific interactions with growth factors, such as the bone
		morphogenetic proteins (BMPs), growth and differentiation factors
		(GDFs) and latent transforming growth factor-beta-binding proteins
		(LTBPs), cell-surface integrins and other extracellular matrix protein and
		proteoglycan components (By similarity). Regulates osteoblast
Fibrillin-1		maturation by controlling TGF-beta bioavailability and calibrating
		TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively
		regulates osteoclastogenesis by binding and sequestering an osteoclast
		differentiation and activation factor TNFSF11. This leads to disruption of
		TNFSF11-induced Ca(2+) signaling and impairment of
		TNFSF11-mediated nuclear translocation and activation of transcription
		factor NFATC1 which regulates genes important for osteoclast
		differentiation and function (PubMed:24039232). Mediates cell adhesion
		via its binding to cell surface receptors integrins ITGAV:ITGB3 and
		ITGA5:ITGB1. Binds heparin and this interaction plays an important role
		in the assembly of microfibrils (By similarity).
		{ECO:0000250 UniProtKB:P35555, ECO:0000269 PubMed:20855508,
		ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine
		secreted by white adipose tissue that plays an important regulatory role in
		the glucose metabolism of liver, muscle and pancreas
		(PubMed:31230984, PubMed:30997682). Hormone that targets the liver
	1	(1 doisiod.31230704, 1 doisiod.30777002). Hormone that targets the fivel

		in managed to feating to increase along a firm of the second
		in response to fasting to increase plasma glucose levels
		(PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface
		of hepatocytes and promotes hepatocyte glucose release by activating the
		protein kinase A activity in the liver, resulting in rapid glucose release
		into the circulation (PubMed:31230984). May act as a regulator of
		adaptive thermogenesis by inhibiting browning and energy consumption,
		while increasing lipid deposition in white adipose tissue
		(PubMed:33705351). Also acts as an orexigenic hormone that increases
		appetite: crosses the blood brain barrier and exerts effects on the
		hypothalamus (PubMed:29106398). In the arcuate nucleus of the
		hypothalamus, asprosin directly activates orexigenic AgRP neurons and
		indirectly inhibits anorexigenic POMC neurons, resulting in appetite
		stimulation (PubMed:29106398, PubMed:32337066). Activates
		orexigenic AgRP neurons via binding to the olfactory receptor Olfr734
		(PubMed:32337066). May also play a role in sperm motility in testis via
		interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682,
		ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959,
		ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
		FUNCTION: May play a role in intercellular signaling and in connecting
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cell
		motility, growth and differentiation. Binds hyaluronic acid.
		FUNCTION: Catalyzes the saturation of all-trans-retinol to
		all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779,
		PubMed:19139408). Does not exhibit any activity toward
		all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers
		(PubMed:15358783). May play a role in the metabolism of vitamin A
		(PubMed:15358783, PubMed:17253779). Independently of retinol
All-trans-retinol	609	conversion, may regulate liver metabolism upstream of
13,14-reductase	009	MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte
		differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This
		effect seems not to mimic the in vivo situation in which animals show
		increased adiposity in the absence of RETSAT (PubMed:19940255).
		{ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779,
		ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255,
		ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
		FUNCTION: ATP-driven pump that supplies the Golgi apparatus with
		Ca(2+) and Mn(2+) ions, both essential cofactors for processing and
		trafficking of newly synthesized proteins in the secretory pathway (By
Calcium-transporting	010	similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on
ATPase type 2C member	918	the cytoplasmic side of the membrane and delivers them to the lumenal
1		side. The transfer of ions across the membrane is coupled to ATP
		hydrolysis and is associated with a transient phosphorylation that shifts
		the pump conformation from inward-facing to outward-facing state (By
	<u> </u>	5 - (-)

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		similarity). Plays a primary role in the maintenance of Ca(2+)
		homeostasis in the trans-Golgi compartment with a functional impact on
		Golgi and post-Golgi protein sorting as well as a structural impact on
		cisternae morphology. Responsible for loading the Golgi stores with
		Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation
		and epidermis integrity (By similarity). Participates in Ca(2+) and
		Mn(2+) ions uptake into the Golgi store of hippocampal neurons and
		regulates protein trafficking required for neural polarity
		(PubMed:19793975). May also play a role in the maintenance of Ca(2+)
		and Mn(2+) homeostasis and signaling in the cytosol while preventing
		cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194,
		ECO:0000269 PubMed:19793975}.
		FUNCTION: Phosphodiesterase (PDE) that has higher activity toward
		cAMP than cGMP, as substrate. Plays a role in cell proliferation,
Exopolyphosphatase	454	migration and differentiation, and acts as a negative regulator of NME1.
PRUNE1	7.7 <b>T</b>	Plays a role in the regulation of neurogenesis. Involved in the regulation
		of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
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Adipocyte plasma	415	FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl
membrane-associated	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte
protein		differentiation. {ECO:0000250}.
		FUNCTION: Regulator of phosphate homeostasis (By similarity).
	251	Inhibits renal tubular phosphate transport by reducing SLC34A1 levels
Fibroblast growth factor		(By similarity). Acts directly on the parathyroid to decrease PTH
23		secretion (By similarity). Regulator of vitamin-D metabolism (By
23		similarity). Negatively regulates osteoblasts differentiation and matrix
		mineralization (By similarity). Up-regulates EGR1 expression in the
		presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
		FUNCTION: Receptor for extracellularly released ATP acting as a
		ligand-gated ion channel that plays multiple role in immunity and central
		nervous system physiology (PubMed:26456657, PubMed:35119925).
		Plays a key role in initial steps of T-cell activation and Ca(2+)
		microdomain formation (PubMed:35119925). Participates also in basal
		T-cell activity without TCR/CD3 stimulation (PubMed:35119925).
P2X purinoceptor 4	388	Promotes the differentiation and activation of Th17 cells via expression
		of retinoic acid-related orphan receptor C/RORC (By similarity). Upon
		activation, drives microglia motility via the PI3K/Akt pathway
		(PubMed:17299767). {ECO:0000250 UniProtKB:Q99571,
		ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:26456657,
		ECO:0000269 PubMed:35119925}.
		FUNCTION: Glycosyltransferase which regulates the biosynthesis of
Exostosin-like 3	010	heparan sulfate (HS). Important for both skeletal development and
	918	hematopoiesis, through the formation of HS proteoglycans (HSPGs).
		Required for the function of REG3A in regulating keratinocyte
		proliferation and differentiation (By similarity).

		{ECO:0000250 UniProtKB:O43909}.
Vacuolar protein sorting-associated protein 37B	285	FUNCTION: Component of the ESCRT-I complex, a regulator of vesicular trafficking process. Required for the sorting of endocytic ubiquitinated cargos into multivesicular bodies. May be involved in cell growth and differentiation (By similarity). {ECO:0000250}.
Ubiquitin-conjugating enzyme E2 variant 1	147	FUNCTION: Has no ubiquitin ligase activity on its own. The UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical poly-ubiquitin chains that are linked through 'Lys-63'. This type of poly-ubiquitination activates IKK and does not seem to involve protein degradation by the proteasome. Plays a role in the activation of NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates transcriptional activation of target genes. Plays a role in the control of progress through the cell cycle and differentiation (By similarity). Plays a role in the error-free DNA repair pathway and contributes to the survival of cells after DNA damage. Promotes TRIM5 capsid-specific restriction activity and the UBE2V1-UBE2N heterodimer acts in concert with TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate the MAP3K7/TAK1 complex which in turn results in the induction and expression of NF-kappa-B and MAPK-responsive inflammatory genes (By similarity). Together with RNF135 and UBE2N, catalyzes the viral RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to activate the downstream signaling pathway that leads to interferon beta production (By similarity). UBE2V1-UBE2N together with TRAF3IP2 E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6, a component of IL17A-mediated signaling pathway. {ECO:0000250, ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
Ubiquitin carboxyl-terminal hydrolase 25	1055	FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties conjugated to substrates and thus, functions to process newly synthesized Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains and prevents proteasomal degradation of substrates. Hydrolyzes both 'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity). {ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m) may have a role in the regulation of muscular differentiation and function.
Forkhead box protein K1	719	FUNCTION: Transcriptional regulator involved in different processes such as glucose metabolism, aerobic glycolysis, muscle cell differentiation and autophagy (PubMed:25402684, PubMed:29861159, PubMed:30700909). Recognizes and binds the forkhead DNA sequence motif (5'-GTAAACA-3') and can both act as a transcription activator or repressor, depending on the context (PubMed:25402684, PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a key regulator of metabolic reprogramming towards aerobic glycolysis, a process in which glucose is converted to lactate in the presence of oxygen (PubMed:30700909). Acts by promoting expression of enzymes for glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate

kinase (PKLR) and lactate dehydrogenase), while suppressing further oxidation of pyruvate in the mitochondria by up-regulating pyruvate dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably plays a role in gluconeogenesis during overnight fasting, when lactate from white adipose tissue and muscle is the main substrate (PubMed:30700909). Involved in mTORC1-mediated metabolic reprogramming: in response to mTORC1 signaling, translocates into the nucleus and regulates the expression of genes associated with glycolysis and downstream anabolic pathways, such as HIF1A, thereby regulating glucose metabolism (PubMed:29861159). Together with FOXK2, acts as a negative regulator of autophagy in skeletal muscle: in response to starvation, enters the nucleus, binds the promoters of autophagy genes and represses their expression, preventing proteolysis of skeletal muscle proteins (PubMed:25402684). Acts as a transcriptional regulator of the myogenic progenitor cell population in skeletal muscle (PubMed:8007964, PubMed:9271401, PubMed:12446708, PubMed:22956541). Binds to the upstream enhancer region (CCAC box) of myoglobin (MB) gene, regulating the myogenic progenitor cell population (PubMed:8007964, PubMed:9271401). Promotes muscle progenitor cell proliferation by repressing the transcriptional activity of FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708, PubMed:22956541). Involved in remodeling processes of adult muscles that occur in response to physiological stimuli (PubMed:9271401, PubMed:22956541). Required to correct temporal orchestration of molecular and cellular events necessary for muscle repair (PubMed:10792059). Represses myogenic differentiation by inhibiting MEFC activity (PubMed:22956541). Positively regulates Wnt/beta-catenin signaling by translocating DVL into the nucleus (By similarity). Reduces virus replication, probably by binding the interferon stimulated response element (ISRE) to promote antiviral gene expression (By similarity). {ECO:0000250|UniProtKB:P85037, ECO:0000269|PubMed:10792059, ECO:0000269|PubMed:12446708, ECO:0000269|PubMed:22956541, ECO:0000269|PubMed:25402684, ECO:0000269|PubMed:29861159, ECO:0000269|PubMed:30700909, ECO:0000269|PubMed:8007964, ECO:0000269|PubMed:9271401}. FUNCTION: Component of the cleavage and polyadenylation specificity factor (CPSF) complex that plays a key role in pre-mRNA 3'-end formation, recognizing the AAUAAA signal sequence and interacting Cleavage and with poly(A) polymerase and other factors to bring about cleavage and polyadenylation 684 poly(A) addition. Has endonuclease activity, and functions as mRNA specificity factor subunit 3'-end-processing endonuclease. Also involved in the histone 3'-end 3 pre-mRNA processing. U7 snRNP-dependent protein that induces both the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a 5' to 3' exonuclease for degrading the subsequent downstream cleavage

		product (DCP) of mature histone mRNAs. Cleavage occurs after the
		5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl
		group on the upstream fragment containing the stem loop (SL) and 5'
		phosphate on the downstream cleavage product (DCP) starting with CU
		nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive
		and degrades the DCP RNA substrate even after complete removal of the
		U7-binding site. Binds to the downstream cleavage product (DCP) of
		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
		(miRNAs) during embryonic stem cell differentiation via its interaction
		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
		primary transcript except miR-92a (PubMed:26255770). Only required
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
		pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
		ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
		FUNCTION: Serine/threonine kinase which acts as an essential
		component of the MAP kinase signal transduction pathway.
		MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an
		important role in the MAPK/ERK cascade. They participate also in a
		signaling cascade initiated by activated KIT and KITLG/SCF. Depending
		on the cellular context, the MAPK/ERK cascade mediates diverse
		biological functions such as cell growth, adhesion, survival and
		differentiation through the regulation of transcription, translation,
		cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role
		in initiation and regulation of meiosis, mitosis, and postmitotic functions
		in differentiated cells by phosphorylating a number of transcription
		factors. About 160 substrates have already been discovered for ERKs.
Mitogen-activated protein	358	Many of these substrates are localized in the nucleus, and seem to
kinase 1		participate in the regulation of transcription upon stimulation. However,
		other substrates are found in the cytosol as well as in other cellular
		organelles, and those are responsible for processes such as translation,
		mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also
		involved in the regulation of the endosomal dynamics, including
		lysosome processing and endosome cycling through the perinuclear
		recycling compartment (PNRC); as well as in the fragmentation of the
		Golgi apparatus during mitosis. The substrates include transcription
		factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1),
		cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT,
		PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD,
		BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of
		2. 2., 2.151., 2.11.11., 12.13., 11.021 of 11.11.03., 10guiatois of

translation (such as EIF4EBP1) and a variety of other signaling-related molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases (such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3, RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2, RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other substrates which enable the propagation the MAPK/ERK signal to additional cytosolic and nuclear targets, thereby extending the specificity of the cascade. Mediates phosphorylation of TPR in response to EGF stimulation. May play a role in the spindle assembly checkpoint. Phosphorylates PML and promotes its interaction with PIN1, leading to PML degradation. Phosphorylates CDK2AP2 (By similarity). {ECO:0000250|UniProtKB:P28482, ECO:0000250|UniProtKB:P63086, ECO:0000269|PubMed:10753946, ECO:0000269|PubMed:11702783, ECO:0000269|PubMed:12134156, ECO:0000303|PubMed:16393692, ECO:0000303|PubMed:19565474, ECO:0000303|PubMed:21779493}.; FUNCTION: Acts as a transcriptional repressor. Binds to a [GC]AAA[GC] consensus sequence. Repress the expression of interferon gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1, IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1. Transcriptional activity is independent of kinase activity. {ECO:0000250|UniProtKB:P28482}. FUNCTION: RNA-binding protein that acts as a key regulator of N6-methyladenosine (m6A) methylation of RNAs, thereby regulating different processes, such as hematopoietic cell homeostasis, alternative splicing of mRNAs and X chromosome inactivation mediated by Xist RNA (PubMed:29535189). Associated component of the WMM complex, a complex that mediates N6-methyladenosine (m6A) methylation of RNAs, a modification that plays a role in the efficiency of mRNA splicing and RNA processing (PubMed:29535189). Plays a key role in m6A methylation, possibly by binding target RNAs and recruiting the WMM complex (PubMed:29535189). Involved in random X inactivation mediated by Xist RNA: acts by binding Xist RNA and RNA-binding protein 15 962 recruiting the WMM complex, which mediates m6A methylation, leading to target YTHDC1 reader on Xist RNA and promoting transcription repression activity of Xist (By similarity). Required for the development of multiple tissues, such as the maintenance of the homeostasis of long-term hematopoietic stem cells and for megakaryocyte (MK) and B-cell differentiation (PubMed:17283045, PubMed:17376872, PubMed:18981216, PubMed:25468569). Regulates megakaryocyte differentiation by regulating alternative splicing of genes important for megakaryocyte differentiation; probably regulates alternative splicing via m6A regulation (By similarity). Required for placental vascular branching morphogenesis and embryonic development of the heart and

		1 (D 116 110001016) :
		spleen (PubMed:18981216). Acts as a regulator of thrombopoietin
		response in hematopoietic stem cells by regulating alternative splicing of
		MPL (PubMed:25468569). May also function as an mRNA export factor,
		stimulating export and expression of RTE-containing mRNAs which are
		present in many retrotransposons that require to be exported prior to
		splicing (By similarity). High affinity binding of pre-mRNA to RBM15
		may allow targeting of the mRNP to the export helicase DBP5 in a
		manner that is independent of splicing-mediated NXF1 deposition,
		resulting in export prior to splicing (By similarity). May be implicated in
		HOX gene regulation (By similarity).
		{ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:17283045,
		ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18981216,
		ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29535189}.
		FUNCTION: Transcription coactivator which associates with nuclear
		receptors, transcriptional coactivators including EP300, CREBBP and
		NCOA1, and basal transcription factors like TBP and TFIIA to facilitate
		nuclear receptors-mediated transcription. May thereby play an important
		role in establishing distinct coactivator complexes under different cellular
		conditions. Plays a role in thyroid hormone receptor and estrogen
l		receptor transactivation (By similarity). Also involved in androgen
		receptor transactivation (PubMed:12077347). Plays a pivotal role in the
Activating signal		transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of
cointegrator 1	581	transrepression between nuclear receptor and either AP1 or NF-kappa-B.
Coming Guiter 1		May play a role in the development of neuromuscular junction (By
		similarity). May play a role in late myogenic differentiation
		(PubMed:27008887). Also functions as part of the RQC trigger (RQT)
		complex that activates the ribosome quality control (RQC) pathway, a
		pathway that degrades nascent peptide chains during problematic
		translation (By similarity). {ECO:0000250 UniProtKB:Q15650,
		ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
		ECO:0000269 PubMed:27008887}.
		FUNCTION: Histone methyltransferase that specifically trimethylates
		'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36'
		(H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is
		capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
		similarity). Represents the main enzyme generating H3K36me3, a
Histone-lysine		specific tag for epigenetic transcriptional activation (PubMed:18157086,
N-methyltransferase	2537	PubMed:20133625). Plays a role in chromatin structure modulation
SETD2		during elongation by coordinating recruitment of the FACT complex and
		by interacting with hyperphosphorylated POLR2A (By similarity). Acts
		as a key regulator of DNA mismatch repair in G1 and early S phase by
		generating H3K36me3, a mark required to recruit MSH6 subunit of the
		MutS alpha complex: early recruitment of the MutS alpha complex to
		chromatin to be replicated allows a quick identification of mismatch
1		i chromath to be reducated allows a duick identification of mismatch

		DNA to initiate the mismatch repair reaction (By similarity). Required for DNA double-strand break repair in response to DNA damage: acts by mediating formation of H3K36me3, promoting recruitment of RAD51 and DNA repair via homologous recombination (HR) (By similarity). Acts as a tumor suppressor (By similarity). H3K36me3 also plays an essential role in the maintenance of a heterochromatic state, by recruiting DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also enhanced in intron-containing genes, suggesting that SETD2 recruitment is enhanced by splicing and that splicing is coupled to recruitment of elongating RNA polymerase (By similarity). Required during angiogenesis (PubMed:20133625). Required for endoderm development by promoting embryonic stem cell differentiation toward endoderm: acts by mediating formation of H3K36me3 in distal promoter regions of FGFR3, leading to regulate transcription initiation of FGFR3 (PubMed:25242323). In addition to histones, also mediates methylation of other proteins, such as tubulins and STAT1 (PubMed:27518565). Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B (alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis and cytokinesis and may be a specific tag in cytoskeletal remodeling (PubMed:27518565). Involved in interferon-alpha-induced antiviral defense by mediating both monomethylation of STAT1 at 'Lys-525' and catalyzing H3K36me3 on promoters of some interferon-stimulated genes (ISGs) to activate gene transcription (By similarity). {ECO:0000250 UniProtKB:Q9BYW2, ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625,
Protein quaking	341	ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.  FUNCTION: RNA-binding protein that plays a central role in myelinization (PubMed:10864952, PubMed:11917126). Also required for visceral endoderm function and blood vessel development (PubMed:11892011, PubMed:16470614). Binds to the 5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence (PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA export, mRNA stability and protein translation, as well as cellular processes including apoptosis, cell cycle, glial cell fate and development (PubMed:10535969, PubMed:12467586, PubMed:11297509, PubMed:11917126, PubMed:15568022). Required to protect and promote stability of mRNAs such as MBP and CDKN1B which promotes oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022). Participates in mRNA transport by regulating the nuclear export of MBP mRNA (PubMed:12467586). May also play a role in smooth muscle development (PubMed:14706070). {ECO:0000269 PubMed:10535969, ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509, ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126, ECO:0000269 PubMed:12467586, ECO:0000269 PubMed:14706070,

ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388, ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involv in regulation of mRNA splicing of MAG pre-mRNA by acting as a negative regulator of MAG exon 12 alternative splicing. {ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can ind apoptosis, while heterodimerization with other isoforms results in nucl translocation of isoform 3 and suppression of apoptosis. {ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.  FUNCTION: May act as a GTPase-activating protein for Rab family protein(s). May play a role in the cell cycle and differentiation of variety	ed uce
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protein(s). May play a role in the cell cycle and differentiation of various	
protein(s). May play a role in the cell cycle and differentiation of various	
	ous
1BC1 domain family tissues. Involved in the trafficking and translocation of	
member 1  GLUT4-containing vesicles and insulin-stimulated glucose uptake into	)
cells. {ECO:0000269 PubMed:19740738}.	
Mesenteric FUNCTION: Involved in processes that promote adipocyte	
estrogen-dependent 303 differentiation, lipid accumulation, and glucose uptake in mature	
adipogenesis protein adipocytes. {ECO:0000269 PubMed:22510272}.	
FUNCTION: Involved in transcriptional activation and repression of	
select genes by chromatin remodeling (alteration of DNA-nucleosome	
topology). Component of SWI/SNF chromatin remodeling complexes	
that carry out key enzymatic activities, changing chromatin structure b	-
altering DNA-histone contacts within a nucleosome in an ATP-depend	lent
manner. Can stimulate the ATPase activity of the catalytic subunit of	
these complexes. May be required for CoREST dependent repression	of
neuronal specific gene promoters in non-neuronal cells. Belongs to the	•
neural progenitors-specific chromatin remodeling complex (npBAF	
complex) and the neuron-specific chromatin remodeling complex (nB.	AF
complex). During neural development a switch from a stem/progenitor	r to
a postmitotic chromatin remodeling mechanism occurs as neurons exit	t
the cell cycle and become committed to their adult state. The transition	1
SWI/SNF complex  1213 from proliferating neural stem/progenitor cells to postmitotic neurons	
subunit SMARCC2 requires a switch in subunit composition of the npBAF and nBAF	
complexes. As neural progenitors exit mitosis and differentiate into	
neurons, npBAF complexes which contain ACTL6A/BAF53A and	
PHF10/BAF45A, are exchanged for homologous alternative	
ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in	
neuron-specific complexes (nBAF). The npBAF complex is essential to	ıor
the self-renewal/proliferative capacity of the multipotent neural stem	
cells. The nBAF complex along with CREST plays a role regulating the	ne
activity of genes essential for dendrite growth (PubMed:17640523).	
Critical regulator of myeloid differentiation, controlling	
granulocytopoiesis and the expression of genes involved in neutrophil	
granule formation (PubMed:28369036).	
{ECO:0000269 PubMed:17640523, ECO:0000269 PubMed:28369036	Ď,

		ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240,
		ECO:0000303 PubMed:26601204}.
D ( 1 1 2	2004	FUNCTION: May play an important role in regulating differentiation,
Protein prune homolog 2	3084	survival and aggressiveness of the tumor cells. {ECO:0000250}.
		FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion
		molecule involved in various processes such as inflammation, cell death,
		axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008,
		PubMed:24347169, PubMed:24917672, PubMed:31526566,
		PubMed:33472215). Promotes cell adhesion by mediating homophilic
		interactions via its extracellular N-terminal adhesion motif (N-NAM)
		(PubMed:24917672, PubMed:30510259). Involved in the progression of
		the inflammatory stress by promoting cell-to-cell interactions between
		immune cells and endothelial cells (PubMed:24917672,
		PubMed:30510259). Involved in leukocyte migration during
		inflammation by promoting transendothelial migration of macrophages
		via homotypic binding (PubMed:24917672). Promotes the migration of
		monocytes across the brain endothelium to central nervous system
	152	inflammatory lesions (By similarity). Acts as a regulator of Toll-like
		receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during
		systemic inflammation; directly binds LPS (PubMed:25860173). Acts as
		a mediator of both programmed and necrotic cell death
		(PubMed:19557008, PubMed:33472215). Plays a key role in the
		induction of plasma membrane rupture during programmed and necrotic
		cell death: oligomerizes in response to death stimuli to mediate plasma
Ninjurin-1		membrane rupture (cytolysis), leading to release intracellular molecules
		named damage-associated molecular patterns (DAMPs) that propagate
		the inflammatory response (PubMed:33472215). Plays a role in nerve
		regeneration by promoting maturation of Schwann cells
		(PubMed:31526566). Acts as a regulator of angiogenesis
		(PubMed:25766274, PubMed:30354207). Promotes the formation of new
		vessels by mediating the interaction between capillary pericyte cells and
		endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates
		vascular functions in penile tissue as well as vascular formation
		(PubMed:24979788). Promotes osteoclasts development by enhancing
		the survival of prefusion osteoclasts (PubMed:30700695). Also involved
		in striated muscle growth and differentiation (PubMed:31091274). Also
		involved in cell senescence in a p53/TP53 manner, possibly by acting as
		an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620,
		PubMed:29073078). {ECO:0000250 UniProtKB:Q92982,
		ECO:0000269 PubMed:19557008, ECO:0000269 PubMed:23690620,
		ECO:0000269 PubMed:24347169, ECO:0000269 PubMed:24917672,
		ECO:0000269 PubMed:24979788, ECO:0000269 PubMed:25766274,
		ECO:0000269 PubMed:25860173, ECO:0000269 PubMed:29073078,
		ECO:0000269 PubMed:30354207, ECO:0000269 PubMed:30510259,

	ı	
		ECO:0000269 PubMed:30700695, ECO:0000269 PubMed:31091274,
		ECO:0000269 PubMed:31526566, ECO:0000269 PubMed:33472215}.;
		FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage,
		which has chemotactic activity (PubMed:23142597). Acts as an
		anti-inflammatory mediator by promoting monocyte recruitment, thereby
		ameliorating atherosclerosis (PubMed:32883094).
		{ECO:0000269 PubMed:23142597, ECO:0000269 PubMed:32883094}.
		FUNCTION: Phosphorylates a large number of substrates in the
		cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B,
		ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9
		and VASP (PubMed:10805756, PubMed:19223768). Regulates the
		abundance of compartmentalized pools of its regulatory subunits through
		phosphorylation of PJA2 which binds and ubiquitinates these subunits,
		leading to their subsequent proteolysis (By similarity). RORA is activated
		by phosphorylation. Required for glucose-mediated adipogenic
		differentiation increase and osteogenic differentiation inhibition from
		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
		circulating platelets in a resting state by phosphorylating proteins in
		numerous platelet inhibitory pathways when in complex with
		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
		thrombin and collagen disrupt these complexes and free active PRKACA
		stimulates platelets and leads to platelet aggregation by phosphorylating
cAMP-dependent protein		VASP. RYR2 channel activity is potentiated by phosphorylation in
kinase catalytic subunit	351	presence of luminal Ca(2+), leading to reduced amplitude and increased
alpha		frequency of store overload-induced Ca(2+) release (SOICR)
		characterized by an increased rate of Ca(2+) release and propagation
		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
		ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.;
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Interleukin-4 receptor subunit alpha	810	FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm flagellum to promote spermatozoa capacitation.  {ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.  FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in promoting Th2 differentiation. The IL4/IL13 responses are involved in regulating IgE production and, chemokine and mucus production at sites of allergic inflammation. In certain cell types, can signal through activation of insulin receptor substrates, IRS1/IRS2.  FUNCTION: Required for mitosis progression. Promotes the nucleation
Protein NEDD1	660	of microtubules from the spindle (By similarity). May play an important role during the embryonic development and differentiation of the central nervous system (PubMed:1378265).  {ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
Protein phosphatase 3 catalytic subunit alpha	521	FUNCTION: Calcium-dependent, calmodulin-stimulated protein phosphatase which plays an essential role in the transduction of intracellular Ca(2+)-mediated signals (PubMed:7791792, PubMed:26794871). Many of the substrates contain a PXIXIT motif and/or a LxVP motif (By similarity). In response to increased Ca(2+) levels, dephosphorylates and activates phosphatase SSH1 which results in cofilin dephosphorylation (By similarity). In response to increased Ca(2+) levels following mitochondrial depolarization, dephosphorylates DNM1L inducing DNM1L translocation to the mitochondrion (By similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+) release probability at hippocampal neuronal soma and synaptic terminals (By similarity). Dephosphorylates heat shock protein HSPB1 (By similarity). Dephosphorylates and activates transcription factor NFATC1 (By similarity). Dephosphorylates and inactivates transcription factor ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation from 14-3-3 proteins (By similarity). Required for postnatal development of the nephrogenic zone and superficial glomeruli in the kidneys, cell cycle homeostasis in the nephrogenic zone, and ultimately normal kidney function (PubMed:15509543). Plays a role in intracellular AQP2 processing and localization to the apical membrane in the kidney, may thereby be required for efficient kidney filtration (PubMed:16735444). Required for secretion of salivary enzymes amylase, peroxidase, lysozyme and sialic acid via formation of secretory vesicles in the submandibular glands (PubMed:21435446). Required for calcineurin activity and homosynaptic depotentiation in the hippocampus (PubMed:10200317). Required for normal differentiation and survival of keratinocytes and therefore required for epidermis superstructure formation (PubMed:19626032). Positively regulates osteoblastic bone formation, via promotion of osteoblast differentiation

(PubMed: 16286645,) Positively regulates osteoclast differentiation, potentially via NFATC1 signaling (PubMed:16068888), May play a role in skeletal muscle fiber type specification, potentially via NFATC1 signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK signaling via inhibition of nuclear translocation of the transcription factors RELA and RELB (PubMed:26028923), Required for antigen-specific T-cell proliferation response (PubMed:8627154). (ECO-0000250)UniProtKB:194852, ECO:0000269]PubMed:10200317, ECO-0000250]UniProtKB:208209, ECO-0000269]PubMed:10200317, ECO-0000269]PubMed:12773574, ECO-0000269]PubMed:16735444, ECO-0000269]PubMed:12773574, ECO-0000269]PubMed:16735444, ECO-0000269]PubMed:1286645, ECO-0000269]PubMed:16735444, ECO-0000269]PubMed:16286888, ECO-0000269]PubMed:16735444, ECO-0000269]PubMed:26794871, ECO-0000269]PubMed:167791792, ECO-0000269]PubMed:26794871, ECO-0000269]PubMed:26704871, ECO-0000269]PubMed:26704871, ECO-0000269]PubMed:26704871, ECO-0000269]PubMed:271791792, ECO-0000269]PubMed:26794871, ECO-0000269]PubMed:271791792, ECO-0000269]PubMed:26794871, ECO-0000269]PubMed:271791792, ECO-0000269]PubMed:26794871, ECO-0000269]PubMed:26794871, ECO-0000269]PubMed:271841, ECO-0000269]PubMed:27184141, ECO-0000269]PubMed:27184141, ECO-0000269]PubMe			
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ECO:0000269 PubMed:25801429, ECO:0000305}.			·
			ECO:0000269 PubMed:25801429, ECO:0000305}.

Transmembrane anterior posterior transformation protein 1	564	FUNCTION: Plays a role in primary cilia formation (By similarity). May act as a downstream effector of HOXC8 possibly by transducing or transmitting extracellular information required for axial skeletal patterning during development (By similarity). May be involved in cartilage and bone development (By similarity). May play a role in the differentiation of cranial neural crest cells (By similarity). {ECO:0000250 UniProtKB:A2BIE7, ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
Fibrillin-1	2873	FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm diameter microfibrils of the extracellular matrix, which conveys both structural and regulatory properties to load-bearing connective tissues. Fibrillin-1-containing microfibrils provide long-term force bearing structural support. In tissues such as the lung, blood vessels and skin, microfibrils form the periphery of the elastic fiber, acting as a scaffold for the deposition of elastin. In addition, microfibrils can occur as elastin-independent networks in tissues such as the ciliary zonule, tendon, cornea and glomerulus where they provide tensile strength and have anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis through specific interactions with growth factors, such as the bone morphogenetic proteins (BMPs), growth and differentiation factors (GDFs) and latent transforming growth factor-beta-binding proteins (LTBPs), cell-surface integrins and other extracellular matrix protein and proteoglycan components (By similarity). Regulates osteoblast maturation by controlling TGF-beta bioavailability and calibrating TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively regulates osteoclastogenesis by binding and sequestering an osteoclast differentiation and activation factor TNFSF11. This leads to disruption of TNFSF11-induced Ca(2+) signaling and impairment of TNFSF11-mediated nuclear translocation and activation of transcription factor NFATC1 which regulates genes important for osteoclast differentiation and function (PubMed:24039232). Mediates cell adhesion via its binding to cell surface receptors integrins ITGAV:ITGB3 and ITGA5:ITGB1. Binds heparin and this interaction plays an important role in the assembly of microfibrils (By similarity). {ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine secreted by white adipose tissue that plays an important regulatory role in the glucose metabolism of liver, muscle and pancreas (PubMed:31230984, PubMed:30997682). Hormone that targets the liver in response to fa

		adaptive thermogenesis by inhibiting browning and energy consumption,
		while increasing lipid deposition in white adipose tissue
		(PubMed:33705351). Also acts as an orexigenic hormone that increases
		appetite: crosses the blood brain barrier and exerts effects on the
		hypothalamus (PubMed:29106398). In the arcuate nucleus of the
		hypothalamus, asprosin directly activates orexigenic AgRP neurons and
		indirectly inhibits anorexigenic POMC neurons, resulting in appetite
		stimulation (PubMed:29106398, PubMed:32337066). Activates
		orexigenic AgRP neurons via binding to the olfactory receptor Olfr734
		(PubMed:32337066). May also play a role in sperm motility in testis via
		interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682,
		ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959,
		ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
		FUNCTION: May play a role in intercellular signaling and in connecting
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cell
7 Sistem core protein	3331	motility, growth and differentiation. Binds hyaluronic acid.
		FUNCTION: Catalyzes the saturation of all-trans-retinol to
		-
		all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779,
		PubMed:19139408). Does not exhibit any activity toward
	609	all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers
		(PubMed:15358783). May play a role in the metabolism of vitamin A
		(PubMed:15358783, PubMed:17253779). Independently of retinol
All-trans-retinol 13,14-reductase		conversion, may regulate liver metabolism upstream of
		MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte
		differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This
		effect seems not to mimic the in vivo situation in which animals show
		increased adiposity in the absence of RETSAT (PubMed:19940255).
		{ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779,
		ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255,
		ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
		FUNCTION: ATP-driven pump that supplies the Golgi apparatus with
		Ca(2+) and Mn(2+) ions, both essential cofactors for processing and
		trafficking of newly synthesized proteins in the secretory pathway (By
		similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on
		the cytoplasmic side of the membrane and delivers them to the lumenal
Calcium-transporting		side. The transfer of ions across the membrane is coupled to ATP
ATPase type 2C member	918	hydrolysis and is associated with a transient phosphorylation that shifts
1	710	the pump conformation from inward-facing to outward-facing state (By
•		similarity). Plays a primary role in the maintenance of Ca(2+)
		homeostasis in the trans-Golgi compartment with a functional impact on
		Golgi and post-Golgi protein sorting as well as a structural impact on
		cisternae morphology. Responsible for loading the Golgi stores with Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation

		and epidermis integrity (By similarity). Participates in Ca(2+) and Mn(2+) ions uptake into the Golgi store of hippocampal neurons and regulates protein trafficking required for neural polarity (PubMed:19793975). May also play a role in the maintenance of Ca(2+) and Mn(2+) homeostasis and signaling in the cytosol while preventing cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194, ECO:0000269 PubMed:19793975}.  FUNCTION: Phosphodiesterase (PDE) that has higher activity toward cAMP than cGMP, as substrate. Plays a role in cell proliferation,
Exopolyphosphatase PRUNE1	454	migration and differentiation, and acts as a negative regulator of NME1.  Plays a role in the regulation of neurogenesis. Involved in the regulation of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma membrane-associated protein	415	FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.
Fibroblast growth factor 23	251	FUNCTION: Regulator of phosphate homeostasis (By similarity). Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
P2X purinoceptor 4	388	FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central nervous system physiology (PubMed:26456657, PubMed:35119925). Plays a key role in initial steps of T-cell activation and Ca(2+) microdomain formation (PubMed:35119925). Participates also in basal T-cell activity without TCR/CD3 stimulation (PubMed:35119925). Promotes the differentiation and activation of Th17 cells via expression of retinoic acid-related orphan receptor C/RORC (By similarity). Upon activation, drives microglia motility via the PI3K/Akt pathway (PubMed:17299767). {ECO:0000250 UniProtKB:Q99571, ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:35119925}.
Exostosin-like 3	918	FUNCTION: Glycosyltransferase which regulates the biosynthesis of heparan sulfate (HS). Important for both skeletal development and hematopoiesis, through the formation of HS proteoglycans (HSPGs). Required for the function of REG3A in regulating keratinocyte proliferation and differentiation (By similarity). {ECO:0000250 UniProtKB:O43909}.
Vacuolar protein sorting-associated protein 37B	285	FUNCTION: Component of the ESCRT-I complex, a regulator of vesicular trafficking process. Required for the sorting of endocytic ubiquitinated cargos into multivesicular bodies. May be involved in cell growth and differentiation (By similarity). {ECO:0000250}.

		TYPICTYON II
		FUNCTION: Has no ubiquitin ligase activity on its own. The
		UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical
		poly-ubiquitin chains that are linked through 'Lys-63'. This type of
		poly-ubiquitination activates IKK and does not seem to involve protein
		degradation by the proteasome. Plays a role in the activation of
		NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates
		transcriptional activation of target genes. Plays a role in the control of
		progress through the cell cycle and differentiation (By similarity). Plays a
		role in the error-free DNA repair pathway and contributes to the survival
Ubiquitin-conjugating		of cells after DNA damage. Promotes TRIM5 capsid-specific restriction
enzyme E2 variant 1	147	activity and the UBE2V1-UBE2N heterodimer acts in concert with
chizyine Ez variant i		TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate
		the MAP3K7/TAK1 complex which in turn results in the induction and
		expression of NF-kappa-B and MAPK-responsive inflammatory genes
		(By similarity). Together with RNF135 and UBE2N, catalyzes the viral
		RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to
		activate the downstream signaling pathway that leads to interferon beta
		production (By similarity). UBE2V1-UBE2N together with TRAF3IP2
		E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6,
		a component of IL17A-mediated signaling pathway. {ECO:0000250,
		ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
		FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties
		conjugated to substrates and thus, functions to process newly synthesized
Ubiquitin		Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains
carboxyl-terminal	1055	and prevents proteasomal degradation of substrates. Hydrolyzes both
hydrolase 25		'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
		{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
		may have a role in the regulation of muscular differentiation and function.
		FUNCTION: Transcriptional regulator involved in different processes
	719	such as glucose metabolism, aerobic glycolysis, muscle cell
		differentiation and autophagy (PubMed:25402684, PubMed:29861159,
		PubMed:30700909). Recognizes and binds the forkhead DNA sequence
		motif (5'-GTAAACA-3') and can both act as a transcription activator or
		repressor, depending on the context (PubMed:25402684,
		PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
		key regulator of metabolic reprogramming towards aerobic glycolysis, a
Forkhead box protein K1		process in which glucose is converted to lactate in the presence of oxygen
		(PubMed:30700909). Acts by promoting expression of enzymes for
		glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
		kinase (PKLR) and lactate dehydrogenase), while suppressing further
		oxidation of pyruvate in the mitochondria by up-regulating pyruvate
		dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
		plays a role in gluconeogenesis during overnight fasting, when lactate
		from white adipose tissue and muscle is the main substrate
		Tom white despose closue and musele is the main substrate

(PubMed:30700909). Involved in mTORC1-mediated metabolic reprogramming: in response to mTORC1 signaling, translocates into the nucleus and regulates the expression of genes associated with glycolysis and downstream anabolic pathways, such as HIF1A, thereby regulating glucose metabolism (PubMed:29861159). Together with FOXK2, acts as a negative regulator of autophagy in skeletal muscle: in response to starvation, enters the nucleus, binds the promoters of autophagy genes and represses their expression, preventing proteolysis of skeletal muscle proteins (PubMed:25402684). Acts as a transcriptional regulator of the myogenic progenitor cell population in skeletal muscle (PubMed:8007964, PubMed:9271401, PubMed:12446708, PubMed:22956541). Binds to the upstream enhancer region (CCAC box) of myoglobin (MB) gene, regulating the myogenic progenitor cell population (PubMed:8007964, PubMed:9271401). Promotes muscle progenitor cell proliferation by repressing the transcriptional activity of FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708, PubMed:22956541). Involved in remodeling processes of adult muscles that occur in response to physiological stimuli (PubMed:9271401, PubMed:22956541). Required to correct temporal orchestration of molecular and cellular events necessary for muscle repair (PubMed:10792059). Represses myogenic differentiation by inhibiting MEFC activity (PubMed:22956541). Positively regulates Wnt/beta-catenin signaling by translocating DVL into the nucleus (By similarity). Reduces virus replication, probably by binding the interferon stimulated response element (ISRE) to promote antiviral gene expression (By similarity). {ECO:0000250|UniProtKB:P85037, ECO:0000269|PubMed:10792059, ECO:0000269|PubMed:12446708, ECO:0000269|PubMed:22956541, ECO:0000269|PubMed:25402684, ECO:0000269|PubMed:29861159, ECO:0000269|PubMed:30700909, ECO:0000269|PubMed:8007964, ECO:0000269|PubMed:9271401}. FUNCTION: Component of the cleavage and polyadenylation specificity factor (CPSF) complex that plays a key role in pre-mRNA 3'-end formation, recognizing the AAUAAA signal sequence and interacting with poly(A) polymerase and other factors to bring about cleavage and poly(A) addition. Has endonuclease activity, and functions as mRNA 3'-end-processing endonuclease. Also involved in the histone 3'-end Cleavage and pre-mRNA processing. U7 snRNP-dependent protein that induces both polyadenylation 684 specificity factor subunit the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a 3 5' to 3' exonuclease for degrading the subsequent downstream cleavage product (DCP) of mature histone mRNAs. Cleavage occurs after the 5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl group on the upstream fragment containing the stem loop (SL) and 5' phosphate on the downstream cleavage product (DCP) starting with CU nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive

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		and degrades the DCP RNA substrate even after complete removal of the
		U7-binding site. Binds to the downstream cleavage product (DCP) of
		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
		(miRNAs) during embryonic stem cell differentiation via its interaction
		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
		primary transcript except miR-92a (PubMed:26255770). Only required
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
		pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
		ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
		FUNCTION: Serine/threonine kinase which acts as an essential
		component of the MAP kinase signal transduction pathway.
		MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an
		important role in the MAPK/ERK cascade. They participate also in a
		signaling cascade initiated by activated KIT and KITLG/SCF. Depending
		on the cellular context, the MAPK/ERK cascade mediates diverse
		biological functions such as cell growth, adhesion, survival and
		differentiation through the regulation of transcription, translation,
		cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role
		in initiation and regulation of meiosis, mitosis, and postmitotic functions
		in differentiated cells by phosphorylating a number of transcription
		factors. About 160 substrates have already been discovered for ERKs.
		Many of these substrates are localized in the nucleus, and seem to
		participate in the regulation of transcription upon stimulation. However,
Mitogen-activated protein		other substrates are found in the cytosol as well as in other cellular
kinase 1	358	organelles, and those are responsible for processes such as translation,
Kinase I		
		mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also
		involved in the regulation of the endosomal dynamics, including
		lysosome processing and endosome cycling through the perinuclear
		recycling compartment (PNRC); as well as in the fragmentation of the
		Golgi apparatus during mitosis. The substrates include transcription
		factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1),
		cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT,
		PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD,
		BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of
		translation (such as EIF4EBP1) and a variety of other signaling-related
		molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases
		(such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3,
		RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2,
		RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and

	1	T
		phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other
		substrates which enable the propagation the MAPK/ERK signal to
		additional cytosolic and nuclear targets, thereby extending the specificity
		of the cascade. Mediates phosphorylation of TPR in response to EGF
		stimulation. May play a role in the spindle assembly checkpoint.
		Phosphorylates PML and promotes its interaction with PIN1, leading to
		PML degradation. Phosphorylates CDK2AP2 (By similarity).
		{ECO:0000250 UniProtKB:P28482, ECO:0000250 UniProtKB:P63086,
		ECO:0000269 PubMed:10753946, ECO:0000269 PubMed:11702783,
		ECO:0000269 PubMed:12134156, ECO:0000303 PubMed:16393692,
		ECO:0000303 PubMed:19565474, ECO:0000303 PubMed:21779493}.;
		FUNCTION: Acts as a transcriptional repressor. Binds to a
		[GC]AAA[GC] consensus sequence. Repress the expression of interferon
		gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1,
		IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1.
		Transcriptional activity is independent of kinase activity.
		{ECO:0000250 UniProtKB:P28482}.
		FUNCTION: RNA-binding protein that acts as a key regulator of
		N6-methyladenosine (m6A) methylation of RNAs, thereby regulating
		different processes, such as hematopoietic cell homeostasis, alternative
		splicing of mRNAs and X chromosome inactivation mediated by Xist
		RNA (PubMed:29535189). Associated component of the WMM
		complex, a complex that mediates N6-methyladenosine (m6A)
		methylation of RNAs, a modification that plays a role in the efficiency of
		mRNA splicing and RNA processing (PubMed:29535189). Plays a key
		role in m6A methylation, possibly by binding target RNAs and recruiting
	962	the WMM complex (PubMed:29535189). Involved in random X
		inactivation mediated by Xist RNA: acts by binding Xist RNA and
		recruiting the WMM complex, which mediates m6A methylation, leading
		to target YTHDC1 reader on Xist RNA and promoting transcription
RNA-binding protein 15		repression activity of Xist (By similarity). Required for the development
		of multiple tissues, such as the maintenance of the homeostasis of
		long-term hematopoietic stem cells and for megakaryocyte (MK) and
		B-cell differentiation (PubMed:17283045, PubMed:17376872,
		PubMed:18981216, PubMed:25468569). Regulates megakaryocyte
		differentiation by regulating alternative splicing of genes important for
		megakaryocyte differentiation; probably regulates alternative splicing via
		m6A regulation (By similarity). Required for placental vascular
		branching morphogenesis and embryonic development of the heart and
		spleen (PubMed:18981216). Acts as a regulator of thrombopoietin
		response in hematopoietic stem cells by regulating alternative splicing of
		MPL (PubMed:25468569). May also function as an mRNA export factor,
		stimulating export and expression of RTE-containing mRNAs which are
		present in many retrotransposons that require to be exported prior to
	i	present in many recommisposons and require to be experted prior to

		splicing (By similarity). High affinity binding of pre-mRNA to RBM15 may allow targeting of the mRNP to the export helicase DBP5 in a manner that is independent of splicing-mediated NXF1 deposition, resulting in export prior to splicing (By similarity). May be implicated in HOX gene regulation (By similarity).  {ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:17283045, ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18981216, ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29535189}.  FUNCTION: Transcription coactivator which associates with nuclear receptors, transcriptional coactivators including EP300, CREBBP and NCOA1, and basal transcription factors like TBP and TFIIA to facilitate
Activating signal cointegrator 1	581	nuclear receptors-mediated transcription. May thereby play an important role in establishing distinct coactivator complexes under different cellular conditions. Plays a role in thyroid hormone receptor and estrogen receptor transactivation (By similarity). Also involved in androgen receptor transactivation (PubMed:12077347). Plays a pivotal role in the transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of transrepression between nuclear receptor and either AP1 or NF-kappa-B. May play a role in the development of neuromuscular junction (By similarity). May play a role in late myogenic differentiation (PubMed:27008887). Also functions as part of the RQC trigger (RQT) complex that activates the ribosome quality control (RQC) pathway, a pathway that degrades nascent peptide chains during problematic translation (By similarity). {ECO:0000250 UniProtKB:Q15650, ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891, ECO:0000269 PubMed:27008887}.
Histone-lysine N-methyltransferase SETD2	2537	FUNCTION: Histone methyltransferase that specifically trimethylates 'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36' (H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By similarity). Represents the main enzyme generating H3K36me3, a specific tag for epigenetic transcriptional activation (PubMed:18157086, PubMed:20133625). Plays a role in chromatin structure modulation during elongation by coordinating recruitment of the FACT complex and by interacting with hyperphosphorylated POLR2A (By similarity). Acts as a key regulator of DNA mismatch repair in G1 and early S phase by generating H3K36me3, a mark required to recruit MSH6 subunit of the MutS alpha complex: early recruitment of the MutS alpha complex to chromatin to be replicated allows a quick identification of mismatch DNA to initiate the mismatch repair reaction (By similarity). Required for DNA double-strand break repair in response to DNA damage: acts by mediating formation of H3K36me3, promoting recruitment of RAD51 and DNA repair via homologous recombination (HR) (By similarity). Acts as a tumor suppressor (By similarity). H3K36me3 also plays an

essential role in the maintenance of a heterochromatic state, by recruiting DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also enhanced in intron-containing genes, suggesting that SETD2 recruitment is enhanced by splicing and that splicing is coupled to recruitment of elongating RNA polymerase (By similarity). Required during angiogenesis (PubMed:20133625). Required for endoderm development by promoting embryonic stem cell differentiation toward endoderm: acts by mediating formation of H3K36me3 in distal promoter regions of FGFR3, leading to regulate transcription initiation of FGFR3 (PubMed:25242323). In addition to histones, also mediates methylation of other proteins, such as tubulins and STAT1 (PubMed:27518565). Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B (alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis and cytokinesis and may be a specific tag in cytoskeletal remodeling (PubMed:27518565). Involved in interferon-alpha-induced antiviral defense by mediating both monomethylation of STAT1 at 'Lys-525' and catalyzing H3K36me3 on promoters of some interferon-stimulated genes (ISGs) to activate gene transcription (By similarity). {ECO:0000250|UniProtKB:Q9BYW2, ECO:0000269|PubMed:18157086, ECO:0000269|PubMed:20133625, ECO:0000269|PubMed:25242323, ECO:0000269|PubMed:27518565}. FUNCTION: RNA-binding protein that plays a central role in myelinization (PubMed:10864952, PubMed:11917126). Also required for visceral endoderm function and blood vessel development (PubMed:11892011, PubMed:16470614). Binds to the 5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence (PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA export, mRNA stability and protein translation, as well as cellular processes including apoptosis, cell cycle, glial cell fate and development (PubMed:10535969, PubMed:12467586, PubMed:11297509, PubMed:11917126, PubMed:15568022). Required to protect and promote stability of mRNAs such as MBP and CDKN1B which promotes 341 oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022). Protein quaking Participates in mRNA transport by regulating the nuclear export of MBP mRNA (PubMed:12467586). May also play a role in smooth muscle development (PubMed:14706070). {ECO:0000269|PubMed:10535969, ECO:0000269|PubMed:10864952, ECO:0000269|PubMed:11297509, ECO:0000269|PubMed:11892011, ECO:0000269|PubMed:11917126, ECO:0000269|PubMed:12467586, ECO:0000269|PubMed:14706070, ECO:0000269|PubMed:15568022, ECO:0000269|PubMed:16041388, ECO:0000269|PubMed:16470614}.; FUNCTION: Isoform 1 is involved in regulation of mRNA splicing of MAG pre-mRNA by acting as a negative regulator of MAG exon 12 alternative splicing. {ECO:0000269|PubMed:11917126}.; FUNCTION: Isoform 3 can induce

TBC1 domain family member 1  Mesenteric	1255	apoptosis, while heterodimerization with other isoforms results in nuclear translocation of isoform 3 and suppression of apoptosis.  {ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.  FUNCTION: May act as a GTPase-activating protein for Rab family protein(s). May play a role in the cell cycle and differentiation of various tissues. Involved in the trafficking and translocation of GLUT4-containing vesicles and insulin-stimulated glucose uptake into cells. {ECO:0000269 PubMed:19740738}.  FUNCTION: Involved in processes that promote adipocyte
estrogen-dependent adipogenesis protein	303	differentiation, lipid accumulation, and glucose uptake in mature adipocytes. {ECO:0000269 PubMed:22510272}.
SWI/SNF complex subunit SMARCC2	1213	FUNCTION: Involved in transcriptional activation and repression of select genes by chromatin remodeling (alteration of DNA-nucleosome topology). Component of SWI/SNF chromatin remodeling complexes that carry out key enzymatic activities, changing chromatin structure by altering DNA-histone contacts within a nucleosome in an ATP-dependent manner. Can stimulate the ATPase activity of the catalytic subunit of these complexes. May be required for CoREST dependent repression of neuronal specific gene promoters in non-neuronal cells. Belongs to the neural progenitors-specific chromatin remodeling complex (npBAF complex) and the neuron-specific chromatin remodeling complex (npBAF complex). During neural development a switch from a stem/progenitor to a postmitotic chromatin remodeling mechanism occurs as neurons exit the cell cycle and become committed to their adult state. The transition from proliferating neural stem/progenitor cells to postmitotic neurons requires a switch in subunit composition of the npBAF and nBAF complexes. As neural progenitors exit mitosis and differentiate into neurons, npBAF complexes which contain ACTL6A/BAF53A and PHF10/BAF45A, are exchanged for homologous alternative ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in neuron-specific complexes (nBAF). The npBAF complex is essential for the self-renewal/proliferative capacity of the multipotent neural stem cells. The nBAF complex along with CREST plays a role regulating the activity of genes essential for dendrite growth (PubMed:17640523). Critical regulator of myeloid differentiation, controlling granulocytopoiesis and the expression of genes involved in neutrophil granule formation (PubMed:28369036). {ECO:0000269 PubMed:31216030, ECO:0000269 PubMed:28369036, ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240, ECO:0000303 PubMed:26601204}.
Protein prune homolog 2	3084	survival and aggressiveness of the tumor cells. {ECO:0000250}.
Ninjurin-1	152	FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion

molecule involved in various processes such as inflammation, cell death, axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008, PubMed:24347169, PubMed:24917672, PubMed:31526566, PubMed:33472215). Promotes cell adhesion by mediating homophilic interactions via its extracellular N-terminal adhesion motif (N-NAM) (PubMed:24917672, PubMed:30510259). Involved in the progression of the inflammatory stress by promoting cell-to-cell interactions between immune cells and endothelial cells (PubMed:24917672, PubMed:30510259). Involved in leukocyte migration during inflammation by promoting transendothelial migration of macrophages via homotypic binding (PubMed:24917672). Promotes the migration of monocytes across the brain endothelium to central nervous system inflammatory lesions (By similarity). Acts as a regulator of Toll-like receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during systemic inflammation; directly binds LPS (PubMed:25860173). Acts as a mediator of both programmed and necrotic cell death (PubMed:19557008, PubMed:33472215). Plays a key role in the induction of plasma membrane rupture during programmed and necrotic cell death: oligomerizes in response to death stimuli to mediate plasma membrane rupture (cytolysis), leading to release intracellular molecules named damage-associated molecular patterns (DAMPs) that propagate the inflammatory response (PubMed:33472215). Plays a role in nerve regeneration by promoting maturation of Schwann cells (PubMed:31526566). Acts as a regulator of angiogenesis (PubMed:25766274, PubMed:30354207). Promotes the formation of new vessels by mediating the interaction between capillary pericyte cells and endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates vascular functions in penile tissue as well as vascular formation (PubMed:24979788). Promotes osteoclasts development by enhancing the survival of prefusion osteoclasts (PubMed:30700695). Also involved in striated muscle growth and differentiation (PubMed:31091274). Also involved in cell senescence in a p53/TP53 manner, possibly by acting as an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620, PubMed:29073078). {ECO:0000250|UniProtKB:Q92982, ECO:0000269|PubMed:19557008, ECO:0000269|PubMed:23690620, ECO:0000269|PubMed:24347169, ECO:0000269|PubMed:24917672, ECO:0000269|PubMed:24979788, ECO:0000269|PubMed:25766274, ECO:0000269|PubMed:25860173, ECO:0000269|PubMed:29073078, ECO:0000269|PubMed:30354207, ECO:0000269|PubMed:30510259, ECO:0000269|PubMed:30700695, ECO:0000269|PubMed:31091274, ECO:0000269|PubMed:31526566, ECO:0000269|PubMed:33472215}.; FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage, which has chemotactic activity (PubMed:23142597). Acts as an anti-inflammatory mediator by promoting monocyte recruitment, thereby

		ameliorating atherosclerosis (PubMed:32883094).
		{ECO:0000269 PubMed:23142597, ECO:0000269 PubMed:32883094}.
		FUNCTION: Phosphorylates a large number of substrates in the
		cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B,
		ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9
		and VASP (PubMed:10805756, PubMed:19223768). Regulates the
		abundance of compartmentalized pools of its regulatory subunits through
		phosphorylation of PJA2 which binds and ubiquitinates these subunits,
		leading to their subsequent proteolysis (By similarity). RORA is activated
		by phosphorylation. Required for glucose-mediated adipogenic
		differentiation increase and osteogenic differentiation inhibition from
		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
		circulating platelets in a resting state by phosphorylating proteins in
		numerous platelet inhibitory pathways when in complex with
		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
		thrombin and collagen disrupt these complexes and free active PRKACA
		stimulates platelets and leads to platelet aggregation by phosphorylating
		VASP. RYR2 channel activity is potentiated by phosphorylation in
		presence of luminal Ca(2+), leading to reduced amplitude and increased
cAMP-dependent protein		frequency of store overload-induced Ca(2+) release (SOICR)
kinase catalytic subunit	351	characterized by an increased rate of Ca(2+) release and propagation
alpha		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
		ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.;
		FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm
		flagellum to promote spermatozoa capacitation.
		{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.
Interleukin-4 receptor		FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples
subunit alpha	810	to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in
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factors RELA and RELB (PubMed:2602823). Required for antigen-specific T-cell proliferation response (PubMed:8627154).  {ECO-0000250[UniProtKB-P48452, ECO:0000250[UniProtKB-P63329, ECO:0000250[UniProtKB-P63329, ECO:0000250]UniProtKB-P63329, ECO:0000250[PubMed:15509543, ECO:0000269]PubMed:15509543, ECO:0000269[PubMed:15509543, ECO:0000269]PubMed:1626032, ECO:0000269[PubMed:16668888, ECO:0000269]PubMed:2602823, ECO:0000269[PubMed:26028924]. ECO:0000269[PubMed:26028924]. ECO:0000269[PubMed:26028924]. ECO:0000269[PubMed:26028924]. ECO:0000269[PubMed:8627154].  FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by home- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, Sl12D1A/SAP and/or Sl12D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on Sl12D1A and Sl12D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and Sl12D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a Sl12D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell:B-cell contact, optimal T-follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:23801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling: independent of Sl12D1A and SH2D1B but implicating FES and PTPNGSHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretio	Г	1	
(ECO-0000250[UniProtkB:P48452, ECO-0000250[UniProtkB:P63329, ECO-0000250[UniProtkB:P0809, ECO-0000250[PubMed:10200317, ECO-0000250[PubMed:15509543, ECO-0000260]PubMed:16509543, ECO-0000260[PubMed:16735444, ECO-0000260]PubMed:16735444, ECO-0000260[PubMed:16968888, ECO-0000260]PubMed:26029823, ECO-0000260[PubMed:2435446, ECO-0000260]PubMed:26029823, ECO-0000260[PubMed:2435446, ECO-0000260]PubMed:26029823, ECO-0000260[PubMed:26029824], ECO-0000260[PubMed:3627154].  FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by home- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cells-E-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling; independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappuB activation and modulates LPS-induced cytokine secretion; involving ITSM 2 (PubMed:20028063). Positively regulates macroautophagy in primary dendritic cell			factors RELA and RELB (PubMed:26029823). Required for
ECO:0000250 UniProtKB:Q08209, ECO:0000269 PubMed:10200317, ECO:0000269 PubMed:1573574, ECO:0000269 PubMed:15735744, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:26021542.  FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell-B-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:235320). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:23601429). In mast cells negatively regulates high affinity immunoglobulin opsilon receptor signaling; independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretion; involving ITSM2 (PubMed:26268063). Positively regulates macroautophagy in primary dendritic cells via stabilization of IRF8; inhibi			antigen-specific T-cell proliferation response (PubMed:8627154).
ECO:0000269 PubMed:12773574, ECO:0000269 PubMed:15509543, ECO:0000269 PubMed:16286645, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:3627154].  FUNCTION: SclF-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by home- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1A and SH2D1B/CMAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFMG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell:B-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretion; involving ITSM 2 (PubMed:26028063), Positively regulates macroautophagy in primary dendritic cells via stabilization of IRF8; inhibits TRIM21-mediated proteasomal degradation of IRF8 (By similarity). (ECO:0000269 PubMed:20620963), Positively PubMed:20962259, ECO:0000269 PubMed:25801429, ECO:0000269 PubMed:20962259, EC			{ECO:0000250 UniProtKB:P48452, ECO:0000250 UniProtKB:P63329,
ECO:0000269 PubMed:16286645, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16968888, ECO:0000269 PubMed:19626032, ECO:0000269 PubMed:21435446, ECO:0000269 PubMed:26029823, ECO:0000269 PubMed:26794871, ECO:0000269 PubMed:26799872, ECO:0000269 PubMed:3627154}.  FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell-B-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling; independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretion; involving ITSM 2 (PubMed:20628063). Positively regulates macroautophagy in primary dendritic cells via stabilization of IRF8; inhibits TRIM21-mediated proteasomal degradation of IRF8 (By similarity). (ECO:0000269 PubMed:206208063, ECO:00000269 PubMed:205259, ECO:0000269 PubMed:20520063, ECO:0000269 Pub			ECO:0000250 UniProtKB:Q08209, ECO:0000269 PubMed:10200317,
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	protein 1		patterning during development (By similarity). May be involved in
cartilage and bone development (By similarity). May play a role in the			cartilage and bone development (By similarity). May play a role in the

	Т	
		differentiation of cranial neural crest cells (By similarity).
		{ECO:0000250 UniProtKB:A2BIE7,
		ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
		FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm
		diameter microfibrils of the extracellular matrix, which conveys both
		structural and regulatory properties to load-bearing connective tissues.
		Fibrillin-1-containing microfibrils provide long-term force bearing
		structural support. In tissues such as the lung, blood vessels and skin,
		microfibrils form the periphery of the elastic fiber, acting as a scaffold for
		the deposition of elastin. In addition, microfibrils can occur as
		elastin-independent networks in tissues such as the ciliary zonule, tendon,
		cornea and glomerulus where they provide tensile strength and have
		anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis
		through specific interactions with growth factors, such as the bone
		morphogenetic proteins (BMPs), growth and differentiation factors
		(GDFs) and latent transforming growth factor-beta-binding proteins
		(LTBPs), cell-surface integrins and other extracellular matrix protein and
		proteoglycan components (By similarity). Regulates osteoblast
		maturation by controlling TGF-beta bioavailability and calibrating
		TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively
		regulates osteoclastogenesis by binding and sequestering an osteoclast
		differentiation and activation factor TNFSF11. This leads to disruption of
		TNFSF11-induced Ca(2+) signaling and impairment of
Fibrillin-1	2873	TNFSF11-mediated nuclear translocation and activation of transcription
		factor NFATC1 which regulates genes important for osteoclast
		differentiation and function (PubMed:24039232). Mediates cell adhesion
		via its binding to cell surface receptors integrins ITGAV:ITGB3 and
		ITGA5:ITGB1. Binds heparin and this interaction plays an important role
		in the assembly of microfibrils (By similarity).
		{ECO:0000250 UniProtKB:P35555, ECO:0000269 PubMed:20855508,
		ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine
		secreted by white adipose tissue that plays an important regulatory role in
		the glucose metabolism of liver, muscle and pancreas
		(PubMed:31230984, PubMed:30997682). Hormone that targets the liver
		in response to fasting to increase plasma glucose levels
		(PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface
		of hepatocytes and promotes hepatocyte glucose release by activating the
		protein kinase A activity in the liver, resulting in rapid glucose release
		into the circulation (PubMed:31230984). May act as a regulator of
		adaptive thermogenesis by inhibiting browning and energy consumption,
		while increasing lipid deposition in white adipose tissue
		(PubMed:33705351). Also acts as an orexigenic hormone that increases
		appetite: crosses the blood brain barrier and exerts effects on the hypothalamus (PubMed:29106398). In the arcuate nucleus of the

		hypothalamus, asprosin directly activates orexigenic AgRP neurons and indirectly inhibits anorexigenic POMC neurons, resulting in appetite stimulation (PubMed:29106398, PubMed:32337066). Activates orexigenic AgRP neurons via binding to the olfactory receptor Olfr734 (PubMed:32337066). May also play a role in sperm motility in testis via interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682, ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959, ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
Versican core protein	3357	FUNCTION: May play a role in intercellular signaling and in connecting cells with the extracellular matrix. May take part in the regulation of cell motility, growth and differentiation. Binds hyaluronic acid.
All-trans-retinol 13,14-reductase	609	FUNCTION: Catalyzes the saturation of all-trans-retinol to all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779, PubMed:19139408). Does not exhibit any activity toward all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers (PubMed:15358783). May play a role in the metabolism of vitamin A (PubMed:15358783, PubMed:17253779). Independently of retinol conversion, may regulate liver metabolism upstream of MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This effect seems not to mimic the in vivo situation in which animals show increased adiposity in the absence of RETSAT (PubMed:19940255). {ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779, ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
Calcium-transporting ATPase type 2C member 1	918	FUNCTION: ATP-driven pump that supplies the Golgi apparatus with Ca(2+) and Mn(2+) ions, both essential cofactors for processing and trafficking of newly synthesized proteins in the secretory pathway (By similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on the cytoplasmic side of the membrane and delivers them to the lumenal side. The transfer of ions across the membrane is coupled to ATP hydrolysis and is associated with a transient phosphorylation that shifts the pump conformation from inward-facing to outward-facing state (By similarity). Plays a primary role in the maintenance of Ca(2+) homeostasis in the trans-Golgi compartment with a functional impact on Golgi and post-Golgi protein sorting as well as a structural impact on cisternae morphology. Responsible for loading the Golgi stores with Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation and epidermis integrity (By similarity). Participates in Ca(2+) and Mn(2+) ions uptake into the Golgi store of hippocampal neurons and regulates protein trafficking required for neural polarity (PubMed:19793975). May also play a role in the maintenance of Ca(2+) and Mn(2+) homeostasis and signaling in the cytosol while preventing

Exopolyphosphatase PRUNE1	454	cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194, ECO:0000269 PubMed:19793975}.  FUNCTION: Phosphodiesterase (PDE) that has higher activity toward cAMP than cGMP, as substrate. Plays a role in cell proliferation, migration and differentiation, and acts as a negative regulator of NME1. Plays a role in the regulation of neurogenesis. Involved in the regulation of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma membrane-associated protein	415	FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.
Fibroblast growth factor 23	251	FUNCTION: Regulator of phosphate homeostasis (By similarity). Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
P2X purinoceptor 4	388	FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central nervous system physiology (PubMed:26456657, PubMed:35119925).  Plays a key role in initial steps of T-cell activation and Ca(2+) microdomain formation (PubMed:35119925). Participates also in basal T-cell activity without TCR/CD3 stimulation (PubMed:35119925).  Promotes the differentiation and activation of Th17 cells via expression of retinoic acid-related orphan receptor C/RORC (By similarity). Upon activation, drives microglia motility via the PI3K/Akt pathway (PubMed:17299767). {ECO:0000250 UniProtKB:Q99571, ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:35119925}.
Exostosin-like 3	918	FUNCTION: Glycosyltransferase which regulates the biosynthesis of heparan sulfate (HS). Important for both skeletal development and hematopoiesis, through the formation of HS proteoglycans (HSPGs). Required for the function of REG3A in regulating keratinocyte proliferation and differentiation (By similarity). {ECO:0000250 UniProtKB:O43909}.
Vacuolar protein sorting-associated protein 37B	285	FUNCTION: Component of the ESCRT-I complex, a regulator of vesicular trafficking process. Required for the sorting of endocytic ubiquitinated cargos into multivesicular bodies. May be involved in cell growth and differentiation (By similarity). {ECO:0000250}.
Ubiquitin-conjugating enzyme E2 variant 1	147	FUNCTION: Has no ubiquitin ligase activity on its own. The UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical poly-ubiquitin chains that are linked through 'Lys-63'. This type of poly-ubiquitination activates IKK and does not seem to involve protein degradation by the proteasome. Plays a role in the activation of

		NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates
		transcriptional activation of target genes. Plays a role in the control of
		progress through the cell cycle and differentiation (By similarity). Plays a
		role in the error-free DNA repair pathway and contributes to the survival
		of cells after DNA damage. Promotes TRIM5 capsid-specific restriction
		activity and the UBE2V1-UBE2N heterodimer acts in concert with
		TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate
		the MAP3K7/TAK1 complex which in turn results in the induction and
		expression of NF-kappa-B and MAPK-responsive inflammatory genes
		(By similarity). Together with RNF135 and UBE2N, catalyzes the viral
		RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to
		activate the downstream signaling pathway that leads to interferon beta
		production (By similarity). UBE2V1-UBE2N together with TRAF3IP2
		E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6,
		a component of IL17A-mediated signaling pathway. {ECO:0000250,
		ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
		FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties
		conjugated to substrates and thus, functions to process newly synthesized
Ubiquitin		Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains
1 1	1055	
carboxyl-terminal	1055	and prevents proteasomal degradation of substrates. Hydrolyzes both
hydrolase 25		'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
		{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
		may have a role in the regulation of muscular differentiation and function.
		FUNCTION: Transcriptional regulator involved in different processes
		such as glucose metabolism, aerobic glycolysis, muscle cell
		differentiation and autophagy (PubMed:25402684, PubMed:29861159,
		PubMed:30700909). Recognizes and binds the forkhead DNA sequence
		motif (5'-GTAAACA-3') and can both act as a transcription activator or
		repressor, depending on the context (PubMed:25402684,
		PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
		key regulator of metabolic reprogramming towards aerobic glycolysis, a
		process in which glucose is converted to lactate in the presence of oxygen
		(PubMed:30700909). Acts by promoting expression of enzymes for
Forkhead box protein K1	719	glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
		kinase (PKLR) and lactate dehydrogenase), while suppressing further
		oxidation of pyruvate in the mitochondria by up-regulating pyruvate
		dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
		plays a role in gluconeogenesis during overnight fasting, when lactate
		from white adipose tissue and muscle is the main substrate
		(PubMed:30700909). Involved in mTORC1-mediated metabolic
		reprogramming: in response to mTORC1 signaling, translocates into the
		nucleus and regulates the expression of genes associated with glycolysis
		and downstream anabolic pathways, such as HIF1A, thereby regulating
		glucose metabolism (PubMed:29861159). Together with FOXK2, acts as

		a negative regulator of autophagy in skeletal muscle: in response to
		starvation, enters the nucleus, binds the promoters of autophagy genes
		and represses their expression, preventing proteolysis of skeletal muscle
		proteins (PubMed:25402684). Acts as a transcriptional regulator of the
		myogenic progenitor cell population in skeletal muscle
		(PubMed:8007964, PubMed:9271401, PubMed:12446708,
		PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
		of myoglobin (MB) gene, regulating the myogenic progenitor cell
		population (PubMed:8007964, PubMed:9271401). Promotes muscle
		progenitor cell proliferation by repressing the transcriptional activity of
		FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
		PubMed:22956541). Involved in remodeling processes of adult muscles
		that occur in response to physiological stimuli (PubMed:9271401,
		PubMed:22956541). Required to correct temporal orchestration of
		molecular and cellular events necessary for muscle repair
		(PubMed:10792059). Represses myogenic differentiation by inhibiting
		MEFC activity (PubMed:22956541). Positively regulates
		Wnt/beta-catenin signaling by translocating DVL into the nucleus (By
		similarity). Reduces virus replication, probably by binding the interferon
		stimulated response element (ISRE) to promote antiviral gene expression
		(By similarity). {ECO:0000250 UniProtKB:P85037,
		ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:12446708,
		ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:25402684,
		ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:30700909,
		ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.
		FUNCTION: Component of the cleavage and polyadenylation specificity
		factor (CPSF) complex that plays a key role in pre-mRNA 3'-end
		formation, recognizing the AAUAAA signal sequence and interacting
		with poly(A) polymerase and other factors to bring about cleavage and
		poly(A) addition. Has endonuclease activity, and functions as mRNA
		3'-end-processing endonuclease. Also involved in the histone 3'-end
		pre-mRNA processing. U7 snRNP-dependent protein that induces both
Classes and		the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a
Cleavage and		5' to 3' exonuclease for degrading the subsequent downstream cleavage
polyadenylation	684	product (DCP) of mature histone mRNAs. Cleavage occurs after the
specificity factor subunit		5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl
3		group on the upstream fragment containing the stem loop (SL) and 5'
		phosphate on the downstream cleavage product (DCP) starting with CU
		nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive
		and degrades the DCP RNA substrate even after complete removal of the
		U7-binding site. Binds to the downstream cleavage product (DCP) of
		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
		(miRNAs) during embryonic stem cell differentiation via its interaction
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		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
		primary transcript except miR-92a (PubMed:26255770). Only required
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
		pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
		ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
		FUNCTION: Serine/threonine kinase which acts as an essential
		component of the MAP kinase signal transduction pathway.
		MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an
		important role in the MAPK/ERK cascade. They participate also in a
		signaling cascade initiated by activated KIT and KITLG/SCF. Depending
		on the cellular context, the MAPK/ERK cascade mediates diverse
		biological functions such as cell growth, adhesion, survival and
		differentiation through the regulation of transcription, translation,
		cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role
		in initiation and regulation of meiosis, mitosis, and postmitotic functions
		in differentiated cells by phosphorylating a number of transcription
		factors. About 160 substrates have already been discovered for ERKs.
		Many of these substrates are localized in the nucleus, and seem to
		participate in the regulation of transcription upon stimulation. However,
		other substrates are found in the cytosol as well as in other cellular
		organelles, and those are responsible for processes such as translation,
Mitogen-activated protein	250	mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also
kinase 1	358	involved in the regulation of the endosomal dynamics, including
		lysosome processing and endosome cycling through the perinuclear
		recycling compartment (PNRC); as well as in the fragmentation of the
		Golgi apparatus during mitosis. The substrates include transcription
		factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1),
		cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT,
		PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD,
		BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of
		translation (such as EIF4EBP1) and a variety of other signaling-related
		molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases
		(such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3,
		RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2,
		RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and
		phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other
		substrates which enable the propagation the MAPK/ERK signal to
		additional cytosolic and nuclear targets, thereby extending the specificity
		of the cascade. Mediates phosphorylation of TPR in response to EGF
		stimulation. May play a role in the spindle assembly checkpoint.
	L	1 717 1 7 1

		Phosphorylates PML and promotes its interaction with PIN1, leading to PML degradation. Phosphorylates CDK2AP2 (By similarity).  {ECO:0000250 UniProtKB:P28482, ECO:0000250 UniProtKB:P63086, ECO:0000269 PubMed:10753946, ECO:0000269 PubMed:11702783, ECO:0000269 PubMed:12134156, ECO:0000303 PubMed:16393692, ECO:0000303 PubMed:19565474, ECO:0000303 PubMed:21779493}.; FUNCTION: Acts as a transcriptional repressor. Binds to a [GC]AAA[GC] consensus sequence. Repress the expression of interferon gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1, IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1. Transcriptional activity is independent of kinase activity.  {ECO:0000250 UniProtKB:P28482}.
RNA-binding protein 15	962	FUNCTION: RNA-binding protein that acts as a key regulator of N6-methyladenosine (m6A) methylation of RNAs, thereby regulating different processes, such as hematopoietic cell homeostasis, alternative splicing of mRNAs and X chromosome inactivation mediated by Xist RNA (PubMed:29535189). Associated component of the WMM complex, a complex that mediates N6-methyladenosine (m6A) methylation of RNAs, a modification that plays a role in the efficiency of mRNA splicing and RNA processing (PubMed:29535189). Plays a key role in m6A methylation, possibly by binding target RNAs and recruiting the WMM complex (PubMed:29535189). Involved in random X inactivation mediated by Xist RNA: acts by binding Xist RNA and recruiting the WMM complex, which mediates m6A methylation, leading to target YTHDC1 reader on Xist RNA and promoting transcription repression activity of Xist (By similarity). Required for the development of multiple tissues, such as the maintenance of the homeostasis of long-term hematopoietic stem cells and for megakaryocyte (MK) and B-cell differentiation (PubMed:17283045, PubMed:17376872, PubMed:18981216, PubMed:25468569). Regulates megakaryocyte differentiation by regulating alternative splicing of genes important for megakaryocyte differentiation; probably regulates alternative splicing via m6A regulation (By similarity). Required for placental vascular branching morphogenesis and embryonic development of the heart and spleen (PubMed:18981216). Acts as a regulator of thrombopoietin response in hematopoietic stem cells by regulating alternative splicing of MPL (PubMed:25468569). May also function as an mRNA export factor, stimulating export and expression of RTE-containing mRNAs which are present in many retrotransposons that require to be exported prior to splicing (By similarity). High affinity binding of pre-mRNA to RBM15 may allow targeting of the mRNP to the export helicase DBP5 in a manner that is independent of splicing-mediated NXF1 deposition, resulting in export prior to splicing (By similarity). May

	1	(ECO.0000250HL::D.::4VD-00/T27-ECO.00002(0ID-134-117202045
		{ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:17283045,
		ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18981216,
		ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29535189}.
		FUNCTION: Transcription coactivator which associates with nuclear
		receptors, transcriptional coactivators including EP300, CREBBP and
		NCOA1, and basal transcription factors like TBP and TFIIA to facilitate
		nuclear receptors-mediated transcription. May thereby play an important
		role in establishing distinct coactivator complexes under different cellular
		conditions. Plays a role in thyroid hormone receptor and estrogen
		receptor transactivation (By similarity). Also involved in androgen
		receptor transactivation (PubMed:12077347). Plays a pivotal role in the
Activating signal	581	transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of
cointegrator 1	361	transrepression between nuclear receptor and either AP1 or NF-kappa-B.
		May play a role in the development of neuromuscular junction (By
		similarity). May play a role in late myogenic differentiation
		(PubMed:27008887). Also functions as part of the RQC trigger (RQT)
		complex that activates the ribosome quality control (RQC) pathway, a
		pathway that degrades nascent peptide chains during problematic
		translation (By similarity). {ECO:0000250 UniProtKB:Q15650,
		ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
		ECO:0000269 PubMed:27008887}.
		FUNCTION: Histone methyltransferase that specifically trimethylates
		'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36'
		(H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is
		capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
		similarity). Represents the main enzyme generating H3K36me3, a
		specific tag for epigenetic transcriptional activation (PubMed:18157086,
		PubMed:20133625). Plays a role in chromatin structure modulation
		during elongation by coordinating recruitment of the FACT complex and
		by interacting with hyperphosphorylated POLR2A (By similarity). Acts
		as a key regulator of DNA mismatch repair in G1 and early S phase by
Histone-lysine		generating H3K36me3, a mark required to recruit MSH6 subunit of the
N-methyltransferase	2537	MutS alpha complex: early recruitment of the MutS alpha complex to
SETD2	2337	chromatin to be replicated allows a quick identification of mismatch
SETD2		
		DNA to initiate the mismatch repair reaction (By similarity). Required for
		DNA double-strand break repair in response to DNA damage: acts by
		mediating formation of H3K36me3, promoting recruitment of RAD51
		and DNA repair via homologous recombination (HR) (By similarity).
		Acts as a tumor suppressor (By similarity). H3K36me3 also plays an
		essential role in the maintenance of a heterochromatic state, by recruiting
		DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also
		enhanced in intron-containing genes, suggesting that SETD2 recruitment
		is enhanced by splicing and that splicing is coupled to recruitment of
		elongating RNA polymerase (By similarity). Required during
	L	

		angiogenesis (PubMed:20133625). Required for endoderm development
		by promoting embryonic stem cell differentiation toward endoderm: acts
		by mediating formation of H3K36me3 in distal promoter regions of
		FGFR3, leading to regulate transcription initiation of FGFR3
		(PubMed:25242323). In addition to histones, also mediates methylation
		of other proteins, such as tubulins and STAT1 (PubMed:27518565).
		Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B
		(alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis
		and cytokinesis and may be a specific tag in cytoskeletal remodeling
		(PubMed:27518565). Involved in interferon-alpha-induced antiviral
		defense by mediating both monomethylation of STAT1 at 'Lys-525' and
		catalyzing H3K36me3 on promoters of some interferon-stimulated genes
		(ISGs) to activate gene transcription (By similarity).
		{ECO:0000250 UniProtKB:Q9BYW2,
		ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625,
		ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.
		FUNCTION: RNA-binding protein that plays a central role in
		myelinization (PubMed:10864952, PubMed:11917126). Also required for
		visceral endoderm function and blood vessel development
		(PubMed:11892011, PubMed:16470614). Binds to the
		5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence
		(PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA
		export, mRNA stability and protein translation, as well as cellular
		processes including apoptosis, cell cycle, glial cell fate and development
		(PubMed:10535969, PubMed:12467586, PubMed:11297509,
		PubMed:11917126, PubMed:15568022). Required to protect and promote
		stability of mRNAs such as MBP and CDKN1B which promotes
		oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022).
		Participates in mRNA transport by regulating the nuclear export of MBP
Protein quaking	341	mRNA (PubMed: 12467586). May also play a role in smooth muscle
1 Totem quaking	341	development (PubMed:14706070). {ECO:0000269 PubMed:10535969,
		ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509,
		ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126,
		ECO:0000269 FubMed:11492011, ECO:0000269 FubMed:11471120, ECO:0000269 PubMed:12467586, ECO:0000269 PubMed:14706070,
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388,
		ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved
		in regulation of mRNA splicing of MAG pre-mRNA by acting as a
		negative regulator of MAG exon 12 alternative splicing.
		{ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can induce
		apoptosis, while heterodimerization with other isoforms results in nuclear
		translocation of isoform 3 and suppression of apoptosis.
		{ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a
		translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.
TBC1 domain family	1255	FUNCTION: May act as a GTPase-activating protein for Rab family

member 1		protein(s). May play a role in the cell cycle and differentiation of various
		tissues. Involved in the trafficking and translocation of
		GLUT4-containing vesicles and insulin-stimulated glucose uptake into
		cells. {ECO:0000269 PubMed:19740738}.
Mesenteric		FUNCTION: Involved in processes that promote adipocyte
estrogen-dependent	303	differentiation, lipid accumulation, and glucose uptake in mature
adipogenesis protein		adipocytes. {ECO:0000269 PubMed:22510272}.
		FUNCTION: Involved in transcriptional activation and repression of
		select genes by chromatin remodeling (alteration of DNA-nucleosome
		topology). Component of SWI/SNF chromatin remodeling complexes
		that carry out key enzymatic activities, changing chromatin structure by
		altering DNA-histone contacts within a nucleosome in an ATP-dependent
		manner. Can stimulate the ATPase activity of the catalytic subunit of
		these complexes. May be required for CoREST dependent repression of
		neuronal specific gene promoters in non-neuronal cells. Belongs to the
		neural progenitors-specific chromatin remodeling complex (npBAF
		complex) and the neuron-specific chromatin remodeling complex (nBAF
		complex). During neural development a switch from a stem/progenitor to
		a postmitotic chromatin remodeling mechanism occurs as neurons exit
	1213	the cell cycle and become committed to their adult state. The transition
CNII/CNIE 1		from proliferating neural stem/progenitor cells to postmitotic neurons
SWI/SNF complex		requires a switch in subunit composition of the npBAF and nBAF
subunit SMARCC2		complexes. As neural progenitors exit mitosis and differentiate into
		neurons, npBAF complexes which contain ACTL6A/BAF53A and
		PHF10/BAF45A, are exchanged for homologous alternative
		ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in
		neuron-specific complexes (nBAF). The npBAF complex is essential for
		the self-renewal/proliferative capacity of the multipotent neural stem
		cells. The nBAF complex along with CREST plays a role regulating the
		activity of genes essential for dendrite growth (PubMed:17640523).
		Critical regulator of myeloid differentiation, controlling
		granulocytopoiesis and the expression of genes involved in neutrophil
		granule formation (PubMed:28369036).
		{ECO:0000269 PubMed:17640523, ECO:0000269 PubMed:28369036,
		ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240,
		ECO:0000303 PubMed:26601204}.
Protein prune homolog 2	3084	FUNCTION: May play an important role in regulating differentiation,
1 rotein prune nomotog 2	3004	survival and aggressiveness of the tumor cells. {ECO:0000250}.
Ninjurin-1		FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion
	152	molecule involved in various processes such as inflammation, cell death,
		axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008,
		PubMed:24347169, PubMed:24917672, PubMed:31526566,
		PubMed:33472215). Promotes cell adhesion by mediating homophilic
		interactions via its extracellular N-terminal adhesion motif (N-NAM)

(PubMed:24917672, PubMed:30510259). Involved in the progression of the inflammatory stress by promoting cell-to-cell interactions between immune cells and endothelial cells (PubMed:24917672, PubMed:30510259). Involved in leukocyte migration during inflammation by promoting transendothelial migration of macrophages via homotypic binding (PubMed:24917672). Promotes the migration of monocytes across the brain endothelium to central nervous system inflammatory lesions (By similarity). Acts as a regulator of Toll-like receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during systemic inflammation; directly binds LPS (PubMed:25860173). Acts as a mediator of both programmed and necrotic cell death (PubMed:19557008, PubMed:33472215). Plays a key role in the induction of plasma membrane rupture during programmed and necrotic cell death: oligomerizes in response to death stimuli to mediate plasma membrane rupture (cytolysis), leading to release intracellular molecules named damage-associated molecular patterns (DAMPs) that propagate the inflammatory response (PubMed:33472215). Plays a role in nerve regeneration by promoting maturation of Schwann cells (PubMed:31526566). Acts as a regulator of angiogenesis (PubMed:25766274, PubMed:30354207). Promotes the formation of new vessels by mediating the interaction between capillary pericyte cells and endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates vascular functions in penile tissue as well as vascular formation (PubMed:24979788). Promotes osteoclasts development by enhancing the survival of prefusion osteoclasts (PubMed:30700695). Also involved in striated muscle growth and differentiation (PubMed:31091274). Also involved in cell senescence in a p53/TP53 manner, possibly by acting as an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620, PubMed:29073078). {ECO:0000250|UniProtKB:Q92982, ECO:0000269|PubMed:19557008, ECO:0000269|PubMed:23690620, ECO:0000269|PubMed:24347169, ECO:0000269|PubMed:24917672, ECO:0000269|PubMed:24979788, ECO:0000269|PubMed:25766274, ECO:0000269|PubMed:25860173, ECO:0000269|PubMed:29073078, ECO:0000269|PubMed:30354207, ECO:0000269|PubMed:30510259, ECO:0000269|PubMed:30700695, ECO:0000269|PubMed:31091274, ECO:0000269|PubMed:31526566, ECO:0000269|PubMed:33472215}.; FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage, which has chemotactic activity (PubMed:23142597). Acts as an anti-inflammatory mediator by promoting monocyte recruitment, thereby ameliorating atherosclerosis (PubMed:32883094). {ECO:0000269|PubMed:23142597, ECO:0000269|PubMed:32883094}. FUNCTION: Phosphorylates a large number of substrates in the cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B, ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9

cAMP-dependent protein kinase catalytic subunit alpha

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		and VASP (PubMed:10805756, PubMed:19223768). Regulates the abundance of compartmentalized pools of its regulatory subunits through
		phosphorylation of PJA2 which binds and ubiquitinates these subunits,
		leading to their subsequent proteolysis (By similarity). RORA is activated
		by phosphorylation. Required for glucose-mediated adipogenic
		differentiation increase and osteogenic differentiation inhibition from
		osteoblasts (By similarity). Involved in chondrogenesis by mediating
		phosphorylation of SOX9 (PubMed:10805756). Involved in the
		regulation of platelets in response to thrombin and collagen; maintains
		circulating platelets in a resting state by phosphorylating proteins in
		numerous platelet inhibitory pathways when in complex with
		NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), but
		thrombin and collagen disrupt these complexes and free active PRKACA
		stimulates platelets and leads to platelet aggregation by phosphorylating
		VASP. RYR2 channel activity is potentiated by phosphorylation in
		presence of luminal Ca(2+), leading to reduced amplitude and increased
		frequency of store overload-induced Ca(2+) release (SOICR)
		characterized by an increased rate of Ca(2+) release and propagation
		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude
		and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
		ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.;
		FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm
		flagellum to promote spermatozoa capacitation.
		{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.
		FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples
	810	to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in
Interleukin-4 receptor		promoting Th2 differentiation. The IL4/IL13 responses are involved in
subunit alpha		regulating IgE production and, chemokine and mucus production at sites
		of allergic inflammation. In certain cell types, can signal through
		activation of insulin receptor substrates, IRS1/IRS2.
Protein NEDD1	660	FUNCTION: Required for mitosis progression. Promotes the nucleation

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		of microtubules from the spindle (By similarity). May play an important
		role during the embryonic development and differentiation of the central
		nervous system (PubMed:1378265).
		{ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
		FUNCTION: Calcium-dependent, calmodulin-stimulated protein
		phosphatase which plays an essential role in the transduction of
		intracellular Ca(2+)-mediated signals (PubMed:7791792,
		PubMed:26794871). Many of the substrates contain a PxIxIT motif
		and/or a LxVP motif (By similarity). In response to increased Ca(2+)
		levels, dephosphorylates and activates phosphatase SSH1 which results in
		cofilin dephosphorylation (By similarity). In response to increased
		Ca(2+) levels following mitochondrial depolarization, dephosphorylates
		DNM1L inducing DNM1L translocation to the mitochondrion (By
		similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+)
		release probability at hippocampal neuronal soma and synaptic terminals
		(By similarity). Dephosphorylates heat shock protein HSPB1 (By
		similarity). Dephosphorylates and activates transcription factor NFATC1
		(By similarity). Dephosphorylates and inactivates transcription factor
		ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May
		dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation
		from 14-3-3 proteins (By similarity). Required for postnatal development
		of the nephrogenic zone and superficial glomeruli in the kidneys, cell
	521	cycle homeostasis in the nephrogenic zone, and ultimately normal kidney
Protein phosphatase 3 catalytic subunit alpha		function (PubMed:15509543). Plays a role in intracellular AQP2
		processing and localization to the apical membrane in the kidney, may
		thereby be required for efficient kidney filtration (PubMed:16735444).
		Required for secretion of salivary enzymes amylase, peroxidase,
		lysozyme and sialic acid via formation of secretory vesicles in the
		submandibular glands (PubMed:21435446). Required for calcineurin
		activity and homosynaptic depotentiation in the hippocampus
		(PubMed:10200317). Required for normal differentiation and survival of
		keratinocytes and therefore required for epidermis superstructure
		formation (PubMed:19626032). Positively regulates osteoblastic bone
		formation, via promotion of osteoblast differentiation
		(PubMed:16286645). Positively regulates osteoclast differentiation,
		potentially via NFATC1 signaling (PubMed:16968888). May play a role
		in skeletal muscle fiber type specification, potentially via NFATC1
		signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK
		signaling via inhibition of nuclear translocation of the transcription
		factors RELA and RELB (PubMed:26029823). Required for
		antigen-specific T-cell proliferation response (PubMed:8627154).
		{ECO:0000250 UniProtKB:P48452, ECO:0000250 UniProtKB:P63329,
		ECO:0000250 UniProtKB:Q08209, ECO:0000269 PubMed:10200317,
		ECO:0000269 PubMed:12773574, ECO:0000269 PubMed:15509543,
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		ECO:0000269 PubMed:16286645, ECO:0000269 PubMed:16735444, ECO:0000269 PubMed:16968888, ECO:0000269 PubMed:19626032, ECO:0000269 PubMed:21435446, ECO:0000269 PubMed:26029823,
		ECO:0000269 PubMed:26794871, ECO:0000269 PubMed:7791792, ECO:0000269 PubMed:8627154}.
SLAM family member 5	329	FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell:B-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling; independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretion; involving ITSM 2 (PubMed:20628063). Positively regulates macroautophagy in primary dendritic cells via stabilization of IRF8; inhibits TRIM21-mediated proteasomal degradation of IRF8 (By similarity). {ECO:0000250 UniProtKB:Q9UIB8, ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259, ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259, ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259, ECO:0000269 PubMed:20628063, ECO:00000369 PubMed:20962259, ECO:0000269 PubMed:25801429, ECO:00000365
Transmembrane anterior posterior transformation protein 1	564	FUNCTION: Plays a role in primary cilia formation (By similarity). May act as a downstream effector of HOXC8 possibly by transducing or transmitting extracellular information required for axial skeletal patterning during development (By similarity). May be involved in cartilage and bone development (By similarity). May play a role in the differentiation of cranial neural crest cells (By similarity). {ECO:0000250 UniProtKB:A2BIE7, ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
Fibrillin-1	2873	FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm diameter microfibrils of the extracellular matrix, which conveys both

structural and regulatory properties to load-bearing connective tissues. Fibrillin-1-containing microfibrils provide long-term force bearing structural support. In tissues such as the lung, blood vessels and skin, microfibrils form the periphery of the elastic fiber, acting as a scaffold for the deposition of elastin. In addition, microfibrils can occur as elastin-independent networks in tissues such as the ciliary zonule, tendon, cornea and glomerulus where they provide tensile strength and have anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis through specific interactions with growth factors, such as the bone morphogenetic proteins (BMPs), growth and differentiation factors (GDFs) and latent transforming growth factor-beta-binding proteins (LTBPs), cell-surface integrins and other extracellular matrix protein and proteoglycan components (By similarity). Regulates osteoblast maturation by controlling TGF-beta bioavailability and calibrating TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively regulates osteoclastogenesis by binding and sequestering an osteoclast differentiation and activation factor TNFSF11. This leads to disruption of TNFSF11-induced Ca(2+) signaling and impairment of TNFSF11-mediated nuclear translocation and activation of transcription factor NFATC1 which regulates genes important for osteoclast differentiation and function (PubMed:24039232). Mediates cell adhesion via its binding to cell surface receptors integrins ITGAV:ITGB3 and ITGA5:ITGB1. Binds heparin and this interaction plays an important role in the assembly of microfibrils (By similarity). {ECO:0000250|UniProtKB:P35555, ECO:0000269|PubMed:20855508, ECO:0000269|PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine secreted by white adipose tissue that plays an important regulatory role in the glucose metabolism of liver, muscle and pancreas (PubMed:31230984, PubMed:30997682). Hormone that targets the liver in response to fasting to increase plasma glucose levels (PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface of hepatocytes and promotes hepatocyte glucose release by activating the protein kinase A activity in the liver, resulting in rapid glucose release into the circulation (PubMed:31230984). May act as a regulator of adaptive thermogenesis by inhibiting browning and energy consumption, while increasing lipid deposition in white adipose tissue (PubMed:33705351). Also acts as an orexigenic hormone that increases appetite: crosses the blood brain barrier and exerts effects on the hypothalamus (PubMed:29106398). In the arcuate nucleus of the hypothalamus, asprosin directly activates orexigenic AgRP neurons and indirectly inhibits anorexigenic POMC neurons, resulting in appetite stimulation (PubMed:29106398, PubMed:32337066). Activates orexigenic AgRP neurons via binding to the olfactory receptor Olfr734 (PubMed:32337066). May also play a role in sperm motility in testis via

		interaction with Olfs724 recentor (PubMed-21700050)
		interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682,
		ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959,
		ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
		FUNCTION: May play a role in intercellular signaling and in connecting
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cell
		motility, growth and differentiation. Binds hyaluronic acid.
		FUNCTION: Catalyzes the saturation of all-trans-retinol to
		all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779,
		PubMed:19139408). Does not exhibit any activity toward
		all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers
		(PubMed:15358783). May play a role in the metabolism of vitamin A
		(PubMed:15358783, PubMed:17253779). Independently of retinol
All-trans-retinol	609	conversion, may regulate liver metabolism upstream of
13,14-reductase	009	MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte
		differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This
		effect seems not to mimic the in vivo situation in which animals show
		increased adiposity in the absence of RETSAT (PubMed:19940255).
		{ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779,
		ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255,
		ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
		FUNCTION: ATP-driven pump that supplies the Golgi apparatus with
		Ca(2+) and Mn(2+) ions, both essential cofactors for processing and
		trafficking of newly synthesized proteins in the secretory pathway (By
		similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on
		the cytoplasmic side of the membrane and delivers them to the lumenal
		side. The transfer of ions across the membrane is coupled to ATP
		hydrolysis and is associated with a transient phosphorylation that shifts
		the pump conformation from inward-facing to outward-facing state (By
		similarity). Plays a primary role in the maintenance of Ca(2+)
Calcium-transporting		homeostasis in the trans-Golgi compartment with a functional impact on
ATPase type 2C member	918	Golgi and post-Golgi protein sorting as well as a structural impact on
1		cisternae morphology. Responsible for loading the Golgi stores with
		Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation
		and epidermis integrity (By similarity). Participates in Ca(2+) and
		Mn(2+) ions uptake into the Golgi store of hippocampal neurons and
		regulates protein trafficking required for neural polarity
		(PubMed:19793975). May also play a role in the maintenance of Ca(2+)
		and Mn(2+) homeostasis and signaling in the cytosol while preventing
		cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194,
		ECO:0000269 PubMed:19793975}.
		FUNCTION: Phosphodiesterase (PDE) that has higher activity toward
Exopolyphosphatase	454	cAMP than cGMP, as substrate. Plays a role in cell proliferation,
PRUNE1	7.74	
		migration and differentiation, and acts as a negative regulator of NME1.

		Plays a role in the regulation of neurogenesis. Involved in the regulation
		of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma		FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl
membrane-associated	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte
protein	713	differentiation. {ECO:0000250}.
protein		FUNCTION: Regulator of phosphate homeostasis (By similarity).
		Inhibits renal tubular phosphate transport by reducing SLC34A1 levels
		(By similarity). Acts directly on the parathyroid to decrease PTH
Fibroblast growth factor	251	secretion (By similarity). Regulator of vitamin-D metabolism (By
23	231	similarity). Negatively regulates osteoblasts differentiation and matrix
		mineralization (By similarity). Up-regulates EGR1 expression in the
		, , , , , , , , , , , , , , , , , , , ,
		presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
l		FUNCTION: Receptor for extracellularly released ATP acting as a
		ligand-gated ion channel that plays multiple role in immunity and central
		nervous system physiology (PubMed:26456657, PubMed:35119925).
		Plays a key role in initial steps of T-cell activation and Ca(2+)
		microdomain formation (PubMed:35119925). Participates also in basal
P2X purinoceptor 4	388	T-cell activity without TCR/CD3 stimulation (PubMed:35119925).
		Promotes the differentiation and activation of Th17 cells via expression
		of retinoic acid-related orphan receptor C/RORC (By similarity). Upon
		activation, drives microglia motility via the PI3K/Akt pathway
		(PubMed:17299767). {ECO:0000250 UniProtKB:Q99571,
		ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:26456657,
		ECO:0000269 PubMed:35119925}.
	918	FUNCTION: Glycosyltransferase which regulates the biosynthesis of
		heparan sulfate (HS). Important for both skeletal development and
Exostosin-like 3		hematopoiesis, through the formation of HS proteoglycans (HSPGs).
	, , ,	Required for the function of REG3A in regulating keratinocyte
		proliferation and differentiation (By similarity).
		{ECO:0000250 UniProtKB:O43909}.
Vacuolar protein		FUNCTION: Component of the ESCRT-I complex, a regulator of
sorting-associated protein	285	vesicular trafficking process. Required for the sorting of endocytic
37B	203	ubiquitinated cargos into multivesicular bodies. May be involved in cell
37 <b>D</b>		growth and differentiation (By similarity). {ECO:0000250}.
		FUNCTION: Has no ubiquitin ligase activity on its own. The
Ubiquitin-conjugating enzyme E2 variant 1		UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical
		poly-ubiquitin chains that are linked through 'Lys-63'. This type of
	147	poly-ubiquitination activates IKK and does not seem to involve protein
		degradation by the proteasome. Plays a role in the activation of
		NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates
		transcriptional activation of target genes. Plays a role in the control of
		progress through the cell cycle and differentiation (By similarity). Plays a
		role in the error-free DNA repair pathway and contributes to the survival
		of cells after DNA damage. Promotes TRIM5 capsid-specific restriction

		activity and the UBE2V1-UBE2N heterodimer acts in concert with
		TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate
		the MAP3K7/TAK1 complex which in turn results in the induction and
		expression of NF-kappa-B and MAPK-responsive inflammatory genes
		(By similarity). Together with RNF135 and UBE2N, catalyzes the viral
		RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to
		activate the downstream signaling pathway that leads to interferon beta
		production (By similarity). UBE2V1-UBE2N together with TRAF3IP2
		E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6,
		a component of IL17A-mediated signaling pathway. {ECO:0000250,
		ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
		FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties
		conjugated to substrates and thus, functions to process newly synthesized
Ubiquitin		Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains
carboxyl-terminal	1055	and prevents proteasomal degradation of substrates. Hydrolyzes both
hydrolase 25		'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
		{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
		may have a role in the regulation of muscular differentiation and function.
		FUNCTION: Transcriptional regulator involved in different processes
		such as glucose metabolism, aerobic glycolysis, muscle cell
		differentiation and autophagy (PubMed:25402684, PubMed:29861159,
		PubMed:30700909). Recognizes and binds the forkhead DNA sequence
	719	motif (5'-GTAAACA-3') and can both act as a transcription activator or
		repressor, depending on the context (PubMed:25402684,
		PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
		key regulator of metabolic reprogramming towards aerobic glycolysis, a
		process in which glucose is converted to lactate in the presence of oxygen
		(PubMed:30700909). Acts by promoting expression of enzymes for
		glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
		kinase (PKLR) and lactate dehydrogenase), while suppressing further
Forkhead box protein K1		oxidation of pyruvate in the mitochondria by up-regulating pyruvate
•		dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
		plays a role in gluconeogenesis during overnight fasting, when lactate
		from white adipose tissue and muscle is the main substrate
		(PubMed:30700909). Involved in mTORC1-mediated metabolic
		reprogramming: in response to mTORC1 signaling, translocates into the
		nucleus and regulates the expression of genes associated with glycolysis
		and downstream anabolic pathways, such as HIF1A, thereby regulating
		glucose metabolism (PubMed:29861159). Together with FOXK2, acts as
		a negative regulator of autophagy in skeletal muscle: in response to
		starvation, enters the nucleus, binds the promoters of autophagy genes
		and represses their expression, preventing proteolysis of skeletal muscle
		proteins (PubMed:25402684). Acts as a transcriptional regulator of the
		myogenic progenitor cell population in skeletal muscle
		myogeme progemior cen population in skeletal musele

	<u> </u>	(D.1) ( 1000 TO ( ) D.1) ( 100 TO ( ) D.1) ( 100 TO ( ) D.1)
		(PubMed:8007964, PubMed:9271401, PubMed:12446708,
		PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
		of myoglobin (MB) gene, regulating the myogenic progenitor cell
		population (PubMed:8007964, PubMed:9271401). Promotes muscle
		progenitor cell proliferation by repressing the transcriptional activity of
		FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
		PubMed:22956541). Involved in remodeling processes of adult muscles
		that occur in response to physiological stimuli (PubMed:9271401,
		PubMed:22956541). Required to correct temporal orchestration of
		molecular and cellular events necessary for muscle repair
		(PubMed:10792059). Represses myogenic differentiation by inhibiting
		MEFC activity (PubMed:22956541). Positively regulates
		Wnt/beta-catenin signaling by translocating DVL into the nucleus (By
		similarity). Reduces virus replication, probably by binding the interferon
		stimulated response element (ISRE) to promote antiviral gene expression
		(By similarity). {ECO:0000250 UniProtKB:P85037,
		ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:12446708,
		ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:25402684,
		ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:30700909,
		ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.
		FUNCTION: Component of the cleavage and polyadenylation specificity
		factor (CPSF) complex that plays a key role in pre-mRNA 3'-end
		formation, recognizing the AAUAAA signal sequence and interacting
		with poly(A) polymerase and other factors to bring about cleavage and
		poly(A) addition. Has endonuclease activity, and functions as mRNA
		3'-end-processing endonuclease. Also involved in the histone 3'-end
		pre-mRNA processing. U7 snRNP-dependent protein that induces both
		the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a
		5' to 3' exonuclease for degrading the subsequent downstream cleavage
		product (DCP) of mature histone mRNAs. Cleavage occurs after the
Cleavage and		5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl
polyadenylation	684	group on the upstream fragment containing the stem loop (SL) and 5'
specificity factor subunit		phosphate on the downstream cleavage product (DCP) starting with CU
3		nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive
		and degrades the DCP RNA substrate even after complete removal of the
		U7-binding site. Binds to the downstream cleavage product (DCP) of
		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
		(miRNAs) during embryonic stem cell differentiation via its interaction
		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
1		primary transcript except miR-92a (PubMed:26255770). Only required
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
		101 the orogeneous of mix-270 and mix-70 from the pri-mix-270-293 and

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		pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
		ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
		FUNCTION: Serine/threonine kinase which acts as an essential
		component of the MAP kinase signal transduction pathway.
		MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an
		important role in the MAPK/ERK cascade. They participate also in a
		signaling cascade initiated by activated KIT and KITLG/SCF. Depending
		on the cellular context, the MAPK/ERK cascade mediates diverse
		biological functions such as cell growth, adhesion, survival and
		differentiation through the regulation of transcription, translation,
		cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role
		in initiation and regulation of meiosis, mitosis, and postmitotic functions
		in differentiated cells by phosphorylating a number of transcription
		factors. About 160 substrates have already been discovered for ERKs.
		Many of these substrates are localized in the nucleus, and seem to
		participate in the regulation of transcription upon stimulation. However,
		other substrates are found in the cytosol as well as in other cellular
		organelles, and those are responsible for processes such as translation,
		mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also
		involved in the regulation of the endosomal dynamics, including
		lysosome processing and endosome cycling through the perinuclear
Mitogen-activated protein		recycling compartment (PNRC); as well as in the fragmentation of the
kinase 1	358	Golgi apparatus during mitosis. The substrates include transcription
Killase 1		factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1),
		cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT,
		PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD,
		BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of
		translation (such as EIF4EBP1) and a variety of other signaling-related
		molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases
		(such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3,
		RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2,
		RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and
		phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other
		substrates which enable the propagation the MAPK/ERK signal to
		additional cytosolic and nuclear targets, thereby extending the specificity
		of the cascade. Mediates phosphorylation of TPR in response to EGF
		stimulation. May play a role in the spindle assembly checkpoint.
		Phosphorylates PML and promotes its interaction with PIN1, leading to
		PML degradation. Phosphorylates CDK2AP2 (By similarity).
		{ECO:0000250 UniProtKB:P28482, ECO:0000250 UniProtKB:P63086,
		ECO:0000269 PubMed:10753946, ECO:0000269 PubMed:11702783,
		ECO:0000269 PubMed:12134156, ECO:0000303 PubMed:16393692,
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		ECO 0000202 P-1-M-1-10565474 ECO 0000202 P-1-M-1-01770402
		ECO:0000303 PubMed:19565474, ECO:0000303 PubMed:21779493}.;
		FUNCTION: Acts as a transcriptional repressor. Binds to a
		[GC]AAA[GC] consensus sequence. Repress the expression of interferon
		gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1,
		IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1.
		Transcriptional activity is independent of kinase activity.
		{ECO:0000250 UniProtKB:P28482}.
		FUNCTION: RNA-binding protein that acts as a key regulator of
		N6-methyladenosine (m6A) methylation of RNAs, thereby regulating
		different processes, such as hematopoietic cell homeostasis, alternative
		splicing of mRNAs and X chromosome inactivation mediated by Xist
		RNA (PubMed:29535189). Associated component of the WMM
		complex, a complex that mediates N6-methyladenosine (m6A)
		methylation of RNAs, a modification that plays a role in the efficiency of
		mRNA splicing and RNA processing (PubMed:29535189). Plays a key
		role in m6A methylation, possibly by binding target RNAs and recruiting
		the WMM complex (PubMed:29535189). Involved in random X
		inactivation mediated by Xist RNA: acts by binding Xist RNA and
		recruiting the WMM complex, which mediates m6A methylation, leading
		to target YTHDC1 reader on Xist RNA and promoting transcription
		repression activity of Xist (By similarity). Required for the development
		of multiple tissues, such as the maintenance of the homeostasis of
		long-term hematopoietic stem cells and for megakaryocyte (MK) and
		B-cell differentiation (PubMed:17283045, PubMed:17376872,
RNA-binding protein 15	962	PubMed:18981216, PubMed:25468569). Regulates megakaryocyte
		differentiation by regulating alternative splicing of genes important for
		megakaryocyte differentiation; probably regulates alternative splicing via
		m6A regulation (By similarity). Required for placental vascular
		branching morphogenesis and embryonic development of the heart and
		spleen (PubMed:18981216). Acts as a regulator of thrombopoietin
		response in hematopoietic stem cells by regulating alternative splicing of
		MPL (PubMed:25468569). May also function as an mRNA export factor,
		stimulating export and expression of RTE-containing mRNAs which are
		present in many retrotransposons that require to be exported prior to
		splicing (By similarity). High affinity binding of pre-mRNA to RBM15
		may allow targeting of the mRNP to the export helicase DBP5 in a
		manner that is independent of splicing-mediated NXF1 deposition,
		resulting in export prior to splicing (By similarity). May be implicated in
		HOX gene regulation (By similarity).
		{ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:17283045,
		ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18981216,
		ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29535189}.
Activating signal	581	FUNCTION: Transcription coactivator which associates with nuclear
cointegrator 1	381	receptors, transcriptional coactivators including EP300, CREBBP and
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		NCOA1, and basal transcription factors like TBP and TFIIA to facilitate
		nuclear receptors-mediated transcription. May thereby play an important
		role in establishing distinct coactivator complexes under different cellular
		conditions. Plays a role in thyroid hormone receptor and estrogen
		receptor transactivation (By similarity). Also involved in androgen
		receptor transactivation (PubMed:12077347). Plays a pivotal role in the
		transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of
		transrepression between nuclear receptor and either AP1 or NF-kappa-B.
		May play a role in the development of neuromuscular junction (By
		similarity). May play a role in late myogenic differentiation
		(PubMed:27008887). Also functions as part of the RQC trigger (RQT)
		complex that activates the ribosome quality control (RQC) pathway, a
		pathway that degrades nascent peptide chains during problematic
		translation (By similarity). {ECO:0000250 UniProtKB:Q15650,
		ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
		ECO:0000269 PubMed:27008887}.
		FUNCTION: Histone methyltransferase that specifically trimethylates
		'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36'
		(H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is
		capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
		similarity). Represents the main enzyme generating H3K36me3, a
		specific tag for epigenetic transcriptional activation (PubMed:18157086,
		PubMed:20133625). Plays a role in chromatin structure modulation
		during elongation by coordinating recruitment of the FACT complex and
		by interacting with hyperphosphorylated POLR2A (By similarity). Acts
		as a key regulator of DNA mismatch repair in G1 and early S phase by
		generating H3K36me3, a mark required to recruit MSH6 subunit of the
	MutS alpha complex: early recruitment of the MutS alpha complex to	
Iliatana lawina		chromatin to be replicated allows a quick identification of mismatch
Histone-lysine	2525	DNA to initiate the mismatch repair reaction (By similarity). Required for
N-methyltransferase	2537	DNA double-strand break repair in response to DNA damage: acts by
SETD2		mediating formation of H3K36me3, promoting recruitment of RAD51
		and DNA repair via homologous recombination (HR) (By similarity).
		Acts as a tumor suppressor (By similarity). H3K36me3 also plays an
		essential role in the maintenance of a heterochromatic state, by recruiting
		DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also
		enhanced in intron-containing genes, suggesting that SETD2 recruitment
		is enhanced by splicing and that splicing is coupled to recruitment of
		elongating RNA polymerase (By similarity). Required during
		angiogenesis (PubMed:20133625). Required for endoderm development
		by promoting embryonic stem cell differentiation toward endoderm: acts
		by mediating formation of H3K36me3 in distal promoter regions of
		FGFR3, leading to regulate transcription initiation of FGFR3
		(PubMed:25242323). In addition to histones, also mediates methylation

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		of other proteins, such as tubulins and STAT1 (PubMed:27518565).
		Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B
		(alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis
		and cytokinesis and may be a specific tag in cytoskeletal remodeling
		(PubMed:27518565). Involved in interferon-alpha-induced antiviral
		defense by mediating both monomethylation of STAT1 at 'Lys-525' and
		catalyzing H3K36me3 on promoters of some interferon-stimulated genes
		(ISGs) to activate gene transcription (By similarity).
		{ECO:0000250 UniProtKB:Q9BYW2,
		ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625,
		ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.
		FUNCTION: RNA-binding protein that plays a central role in
		myelinization (PubMed:10864952, PubMed:11917126). Also required for
		visceral endoderm function and blood vessel development
		(PubMed:11892011, PubMed:16470614). Binds to the
		5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence
		(PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA
		export, mRNA stability and protein translation, as well as cellular
		processes including apoptosis, cell cycle, glial cell fate and development
		(PubMed:10535969, PubMed:12467586, PubMed:11297509,
		PubMed:11917126, PubMed:15568022). Required to protect and promote
		stability of mRNAs such as MBP and CDKN1B which promotes
		oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022).
		Participates in mRNA transport by regulating the nuclear export of MBP
Protein quaking	341	mRNA (PubMed:12467586). May also play a role in smooth muscle
		development (PubMed:14706070). {ECO:0000269 PubMed:10535969,
		ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509,
		ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126,
		ECO:0000269 PubMed:12467586, ECO:0000269 PubMed:14706070,
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388,
		ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved
		in regulation of mRNA splicing of MAG pre-mRNA by acting as a
		negative regulator of MAG exon 12 alternative splicing.
		{ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can induce
		apoptosis, while heterodimerization with other isoforms results in nuclear
		translocation of isoform 3 and suppression of apoptosis.
		{ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a
		translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.
		FUNCTION: May act as a GTPase-activating protein for Rab family
	1255	protein(s). May play a role in the cell cycle and differentiation of various
TBC1 domain family		tissues. Involved in the trafficking and translocation of
member 1		GLUT4-containing vesicles and insulin-stimulated glucose uptake into
		cells. {ECO:0000269 PubMed:19740738}.
Mesenteric	303	FUNCTION: Involved in processes that promote adipocyte
171CSCITCTIC	303	1 0110 11011. Involved in processes that promote adipocyte

estrogen-dependent		differentiation, lipid accumulation, and glucose uptake in mature
adipogenesis protein		adipocytes. {ECO:0000269 PubMed:22510272}.
SWI/SNF complex subunit SMARCC2	1213	adipocytes. {ECO:0000269 PubMed:22510272}.  FUNCTION: Involved in transcriptional activation and repression of select genes by chromatin remodeling (alteration of DNA-nucleosome topology). Component of SWI/SNF chromatin remodeling complexes that carry out key enzymatic activities, changing chromatin structure by altering DNA-histone contacts within a nucleosome in an ATP-dependent manner. Can stimulate the ATPase activity of the catalytic subunit of these complexes. May be required for CoREST dependent repression of neuronal specific gene promoters in non-neuronal cells. Belongs to the neural progenitors-specific chromatin remodeling complex (npBAF complex) and the neuron-specific chromatin remodeling complex (nBAF complex). During neural development a switch from a stem/progenitor to a postmitotic chromatin remodeling mechanism occurs as neurons exit the cell cycle and become committed to their adult state. The transition from proliferating neural stem/progenitor cells to postmitotic neurons requires a switch in subunit composition of the npBAF and nBAF complexes. As neural progenitors exit mitosis and differentiate into neurons, npBAF complexes which contain ACTL6A/BAF53A and PHF10/BAF45A, are exchanged for homologous alternative ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in neuron-specific complexes (nBAF). The npBAF complex is essential for the self-renewal/proliferative capacity of the multipotent neural stem cells. The nBAF complex along with CREST plays a role regulating the activity of genes essential for dendrite growth (PubMed:17640523). Critical regulator of myeloid differentiation, controlling granulocytopoiesis and the expression of genes involved in neutrophil granule formation (PubMed:28369036). {ECO:0000269 PubMed:31216030, ECO:00000303 PubMed:28369036, ECO:0000303 PubMed:26601204}.
Protein prune homolog 2	3084	FUNCTION: May play an important role in regulating differentiation, survival and aggressiveness of the tumor cells. {ECO:0000250}.
Ninjurin-1	152	FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion molecule involved in various processes such as inflammation, cell death, axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008, PubMed:24347169, PubMed:24917672, PubMed:31526566, PubMed:33472215). Promotes cell adhesion by mediating homophilic interactions via its extracellular N-terminal adhesion motif (N-NAM) (PubMed:24917672, PubMed:30510259). Involved in the progression of the inflammatory stress by promoting cell-to-cell interactions between immune cells and endothelial cells (PubMed:24917672, PubMed:30510259). Involved in leukocyte migration during inflammation by promoting transendothelial migration of macrophages

via homotypic binding (PubMed:24917672). Promotes the migration of monocytes across the brain endothelium to central nervous system inflammatory lesions (By similarity). Acts as a regulator of Toll-like receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during systemic inflammation; directly binds LPS (PubMed:25860173). Acts as a mediator of both programmed and necrotic cell death (PubMed:19557008, PubMed:33472215). Plays a key role in the induction of plasma membrane rupture during programmed and necrotic cell death: oligomerizes in response to death stimuli to mediate plasma membrane rupture (cytolysis), leading to release intracellular molecules named damage-associated molecular patterns (DAMPs) that propagate the inflammatory response (PubMed:33472215). Plays a role in nerve regeneration by promoting maturation of Schwann cells (PubMed:31526566). Acts as a regulator of angiogenesis (PubMed:25766274, PubMed:30354207). Promotes the formation of new vessels by mediating the interaction between capillary pericyte cells and endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates vascular functions in penile tissue as well as vascular formation (PubMed:24979788). Promotes osteoclasts development by enhancing the survival of prefusion osteoclasts (PubMed:30700695). Also involved in striated muscle growth and differentiation (PubMed:31091274). Also involved in cell senescence in a p53/TP53 manner, possibly by acting as an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620, PubMed:29073078). {ECO:0000250|UniProtKB:Q92982, ECO:0000269|PubMed:19557008, ECO:0000269|PubMed:23690620, ECO:0000269|PubMed:24347169, ECO:0000269|PubMed:24917672, ECO:0000269|PubMed:24979788, ECO:0000269|PubMed:25766274, ECO:0000269|PubMed:25860173, ECO:0000269|PubMed:29073078, ECO:0000269|PubMed:30354207, ECO:0000269|PubMed:30510259, ECO:0000269|PubMed:30700695, ECO:0000269|PubMed:31091274, ECO:0000269|PubMed:31526566, ECO:0000269|PubMed:33472215}.; FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage, which has chemotactic activity (PubMed:23142597). Acts as an anti-inflammatory mediator by promoting monocyte recruitment, thereby ameliorating atherosclerosis (PubMed:32883094). {ECO:0000269|PubMed:23142597, ECO:0000269|PubMed:32883094}. FUNCTION: Phosphorylates a large number of substrates in the cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B, ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9 cAMP-dependent protein and VASP (PubMed:10805756, PubMed:19223768). Regulates the kinase catalytic subunit 351 abundance of compartmentalized pools of its regulatory subunits through alpha phosphorylation of PJA2 which binds and ubiquitinates these subunits, leading to their subsequent proteolysis (By similarity). RORA is activated by phosphorylation. Required for glucose-mediated adipogenic

differentiation increase and osteogenic differentiation inhibition of osteoblasts (By similarity). Involved in chondrogenesis by media phosphorylation of SOX9 (PubMed:10805756). Involved in the regulation of platelets in response to thrombin and collagen; main circulating platelets in a resting state by phosphorylating proteins numerous platelet inhibitory pathways when in complex with NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKB thrombin and collagen disrupt these complexes and free active Plastimulates platelets and leads to platelet aggregation by phosphorylation presence of luminal Ca(2+), leading to reduced amplitude and infrequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propaga velocity of spontaneous Ca(2+) waves, despite reduced wave am and resting cytosolic Ca(2+). PSMC5/RPT6 activation by	ntains s in IA), but RKACA rylating in
phosphorylation of SOX9 (PubMed:10805756). Involved in the regulation of platelets in response to thrombin and collagen; main circulating platelets in a resting state by phosphorylating proteins numerous platelet inhibitory pathways when in complex with NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKB thrombin and collagen disrupt these complexes and free active Platimulates platelets and leads to platelet aggregation by phosphorylation VASP. RYR2 channel activity is potentiated by phosphorylation presence of luminal Ca(2+), leading to reduced amplitude and infrequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propaga velocity of spontaneous Ca(2+) waves, despite reduced wave am	ntains s in IA), but RKACA rylating in
regulation of platelets in response to thrombin and collagen; main circulating platelets in a resting state by phosphorylating proteins numerous platelet inhibitory pathways when in complex with NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKB thrombin and collagen disrupt these complexes and free active Platimulates platelets and leads to platelet aggregation by phosphory VASP. RYR2 channel activity is potentiated by phosphorylation presence of luminal Ca(2+), leading to reduced amplitude and in frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propaga velocity of spontaneous Ca(2+) waves, despite reduced wave am	in  IA), but  RKACA  rylating  in
circulating platelets in a resting state by phosphorylating proteins numerous platelet inhibitory pathways when in complex with NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKB thrombin and collagen disrupt these complexes and free active Pl stimulates platelets and leads to platelet aggregation by phosphor VASP. RYR2 channel activity is potentiated by phosphorylation presence of luminal Ca(2+), leading to reduced amplitude and in frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propaga velocity of spontaneous Ca(2+) waves, despite reduced wave am	in  IA), but  RKACA  rylating  in
numerous platelet inhibitory pathways when in complex with NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKB thrombin and collagen disrupt these complexes and free active Platimulates platelets and leads to platelet aggregation by phosphor VASP. RYR2 channel activity is potentiated by phosphorylation presence of luminal Ca(2+), leading to reduced amplitude and interpretation frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propagative velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude and increased rate of Ca(2+) release and propagative velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude and increased rate of Ca(2+) release and propagative velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude and increased rate of Ca(2+) release and propagative velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude and increased rate of Ca(2+) release and propagative velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude and increased rate of Ca(2+) release and propagative velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude and increased rate of Ca(2+) release and propagative velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude and increased rate of Ca(2+) release (SOICR)	IA), but RKACA rylating in
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thrombin and collagen disrupt these complexes and free active Pl stimulates platelets and leads to platelet aggregation by phosphor VASP. RYR2 channel activity is potentiated by phosphorylation presence of luminal Ca(2+), leading to reduced amplitude and interpretation frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propagative velocity of spontaneous Ca(2+) waves, despite reduced wave am	RKACA rylating in
stimulates platelets and leads to platelet aggregation by phosphor VASP. RYR2 channel activity is potentiated by phosphorylation presence of luminal Ca(2+), leading to reduced amplitude and in frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propaga velocity of spontaneous Ca(2+) waves, despite reduced wave am	rylating in
VASP. RYR2 channel activity is potentiated by phosphorylation presence of luminal Ca(2+), leading to reduced amplitude and inc frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propaga velocity of spontaneous Ca(2+) waves, despite reduced wave am	in
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characterized by an increased rate of Ca(2+) release and propaga velocity of spontaneous Ca(2+) waves, despite reduced wave am	
velocity of spontaneous Ca(2+) waves, despite reduced wave am	
	tion
and resting cytosolic Ca(2+). PSMC5/RPT6 activation by	plitude
phosphorylation stimulates proteasome. Negatively regulates tigh	nt
junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation	
NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA b	inding.
Involved in embryonic development by down-regulating the Hed	•
(Hh) signaling pathway that determines embryo pattern formation	-
morphogenesis (By similarity). Prevents meiosis resumption in	
prophase-arrested oocytes via CDC25B inactivation by phosphor	vlation
(PubMed:19223768). May also regulate rapid eye movement (RI	•
sleep in the pedunculopontine tegmental (PPT) (By similarity).	,
Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1:	this
phosphorylation promotes HSF1 nuclear localization and transcri	
activity upon heat shock (By similarity).	1
{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:F	27791.
ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19222	
FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in	
flagellum to promote spermatozoa capacitation.	эрэгин
{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:1950	50455}
FUNCTION: Receptor for both interleukin 4 and interleukin 13.	-
to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in	_
Interleukin-4 receptor promoting Th2 differentiation. The IL4/IL13 responses are involved.	
subunit alpha  810  810  regulating IgE production and, chemokine and mucus production	
of allergic inflammation. In certain cell types, can signal through	
activation of insulin receptor substrates, IRS1/IRS2.	
FUNCTION: Required for mitosis progression. Promotes the nuc	eleation
of microtubules from the spindle (By similarity). May play an im	
Protein NEDD1 660 role during the embryonic development and differentiation of the	_
nervous system (PubMed:1378265).	Cintai
{ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:12	3782651
Protein phosphatase 3 521 FUNCTION: Calcium-dependent, calmodulin-stimulated protein	
1 Town phosphatase 3 321 Force from: Calcium-acpendent, Cambodumi-stimulated protein	

catalytic subunit alpha

phosphatase which plays an essential role in the transduction of intracellular Ca(2+)-mediated signals (PubMed:7791792, PubMed:26794871). Many of the substrates contain a PxIxIT motif and/or a LxVP motif (By similarity). In response to increased Ca(2+) levels, dephosphorylates and activates phosphatase SSH1 which results in cofilin dephosphorylation (By similarity). In response to increased Ca(2+) levels following mitochondrial depolarization, dephosphorylates DNM1L inducing DNM1L translocation to the mitochondrion (By similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+) release probability at hippocampal neuronal soma and synaptic terminals (By similarity). Dephosphorylates heat shock protein HSPB1 (By similarity). Dephosphorylates and activates transcription factor NFATC1 (By similarity). Dephosphorylates and inactivates transcription factor ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation from 14-3-3 proteins (By similarity). Required for postnatal development of the nephrogenic zone and superficial glomeruli in the kidneys, cell cycle homeostasis in the nephrogenic zone, and ultimately normal kidney function (PubMed:15509543). Plays a role in intracellular AQP2 processing and localization to the apical membrane in the kidney, may thereby be required for efficient kidney filtration (PubMed:16735444). Required for secretion of salivary enzymes amylase, peroxidase, lysozyme and sialic acid via formation of secretory vesicles in the submandibular glands (PubMed:21435446). Required for calcineurin activity and homosynaptic depotentiation in the hippocampus (PubMed:10200317). Required for normal differentiation and survival of keratinocytes and therefore required for epidermis superstructure formation (PubMed:19626032). Positively regulates osteoblastic bone formation, via promotion of osteoblast differentiation (PubMed:16286645). Positively regulates osteoclast differentiation, potentially via NFATC1 signaling (PubMed: 16968888). May play a role in skeletal muscle fiber type specification, potentially via NFATC1 signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK signaling via inhibition of nuclear translocation of the transcription factors RELA and RELB (PubMed: 26029823). Required for antigen-specific T-cell proliferation response (PubMed:8627154). {ECO:0000250|UniProtKB:P48452, ECO:0000250|UniProtKB:P63329, ECO:0000250|UniProtKB:Q08209, ECO:0000269|PubMed:10200317, ECO:0000269|PubMed:12773574, ECO:0000269|PubMed:15509543, ECO:0000269|PubMed:16286645, ECO:0000269|PubMed:16735444, ECO:0000269|PubMed:16968888, ECO:0000269|PubMed:19626032, ECO:0000269|PubMed:21435446, ECO:0000269|PubMed:26029823, ECO:0000269|PubMed:26794871, ECO:0000269|PubMed:7791792, ECO:0000269|PubMed:8627154}.

		FINICIDAL C ICI: 1 4 Cd : 1: 1 1 2 2 2
SLAM family member 5	329	FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell:B-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling; independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretion; involving ITSM 2 (PubMed:20628063). Positively regulates macroautophagy in primary dendritic cells via stabilization of IRF8; inhibits TRIM21-mediated proteasomal degradation of IRF8 (By similarity). {ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20153220, ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:2062805, ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:2062259, ECO:0000269 PubMed:25801429, ECO:0000365 .
Transmembrane anterior posterior transformation protein 1	564	FUNCTION: Plays a role in primary cilia formation (By similarity). May act as a downstream effector of HOXC8 possibly by transducing or transmitting extracellular information required for axial skeletal patterning during development (By similarity). May be involved in cartilage and bone development (By similarity). May play a role in the differentiation of cranial neural crest cells (By similarity). {ECO:0000250 UniProtKB:A2BIE7, ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
Fibrillin-1	2873	FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm diameter microfibrils of the extracellular matrix, which conveys both structural and regulatory properties to load-bearing connective tissues. Fibrillin-1-containing microfibrils provide long-term force bearing structural support. In tissues such as the lung, blood vessels and skin, microfibrils form the periphery of the elastic fiber, acting as a scaffold for the deposition of elastin. In addition, microfibrils can occur as

elastin-independent networks in tissues such as the ciliary zonule, tendon, cornea and glomerulus where they provide tensile strength and have anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis through specific interactions with growth factors, such as the bone morphogenetic proteins (BMPs), growth and differentiation factors (GDFs) and latent transforming growth factor-beta-binding proteins (LTBPs), cell-surface integrins and other extracellular matrix protein and proteoglycan components (By similarity). Regulates osteoblast maturation by controlling TGF-beta bioavailability and calibrating TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively regulates osteoclastogenesis by binding and sequestering an osteoclast differentiation and activation factor TNFSF11. This leads to disruption of TNFSF11-induced Ca(2+) signaling and impairment of TNFSF11-mediated nuclear translocation and activation of transcription factor NFATC1 which regulates genes important for osteoclast differentiation and function (PubMed:24039232). Mediates cell adhesion via its binding to cell surface receptors integrins ITGAV:ITGB3 and ITGA5:ITGB1. Binds heparin and this interaction plays an important role in the assembly of microfibrils (By similarity). {ECO:0000250|UniProtKB:P35555, ECO:0000269|PubMed:20855508, ECO:0000269|PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine secreted by white adipose tissue that plays an important regulatory role in the glucose metabolism of liver, muscle and pancreas (PubMed:31230984, PubMed:30997682). Hormone that targets the liver in response to fasting to increase plasma glucose levels (PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface of hepatocytes and promotes hepatocyte glucose release by activating the protein kinase A activity in the liver, resulting in rapid glucose release into the circulation (PubMed:31230984). May act as a regulator of adaptive thermogenesis by inhibiting browning and energy consumption, while increasing lipid deposition in white adipose tissue (PubMed:33705351). Also acts as an orexigenic hormone that increases appetite: crosses the blood brain barrier and exerts effects on the hypothalamus (PubMed:29106398). In the arcuate nucleus of the hypothalamus, asprosin directly activates orexigenic AgRP neurons and indirectly inhibits anorexigenic POMC neurons, resulting in appetite stimulation (PubMed:29106398, PubMed:32337066). Activates orexigenic AgRP neurons via binding to the olfactory receptor Olfr734 (PubMed:32337066). May also play a role in sperm motility in testis via interaction with Olfr734 receptor (PubMed:31798959). {ECO:0000269|PubMed:29106398, ECO:0000269|PubMed:30997682, ECO:0000269|PubMed:31230984, ECO:0000269|PubMed:31798959, ECO:0000269|PubMed:32337066, ECO:0000269|PubMed:33705351}. FUNCTION: May play a role in intercellular signaling and in connecting

		11 14 4 4 11 1 1 3 4 1 1 1 2 4 1 2 4 1
		cells with the extracellular matrix. May take part in the regulation of cell
		motility, growth and differentiation. Binds hyaluronic acid.
		FUNCTION: Catalyzes the saturation of all-trans-retinol to
		all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779,
		PubMed:19139408). Does not exhibit any activity toward
		all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers
		(PubMed:15358783). May play a role in the metabolism of vitamin A
		(PubMed:15358783, PubMed:17253779). Independently of retinol
All-trans-retinol	609	conversion, may regulate liver metabolism upstream of
13,14-reductase	007	MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte
		differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This
		effect seems not to mimic the in vivo situation in which animals show
		increased adiposity in the absence of RETSAT (PubMed:19940255).
		{ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779,
		ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255,
		ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
		FUNCTION: ATP-driven pump that supplies the Golgi apparatus with
		Ca(2+) and Mn(2+) ions, both essential cofactors for processing and
		trafficking of newly synthesized proteins in the secretory pathway (By
		similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on
		the cytoplasmic side of the membrane and delivers them to the lumenal
		side. The transfer of ions across the membrane is coupled to ATP
		hydrolysis and is associated with a transient phosphorylation that shifts
		the pump conformation from inward-facing to outward-facing state (By
		similarity). Plays a primary role in the maintenance of Ca(2+)
Calcium-transporting		homeostasis in the trans-Golgi compartment with a functional impact on
ATPase type 2C member	918	Golgi and post-Golgi protein sorting as well as a structural impact on
1		cisternae morphology. Responsible for loading the Golgi stores with
		Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation
		and epidermis integrity (By similarity). Participates in Ca(2+) and
		Mn(2+) ions uptake into the Golgi store of hippocampal neurons and
		regulates protein trafficking required for neural polarity
		(PubMed:19793975). May also play a role in the maintenance of Ca(2+)
		and Mn(2+) homeostasis and signaling in the cytosol while preventing
		cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194,
		ECO:0000269 PubMed:19793975}.
Exopolyphosphatase PRUNE1		FUNCTION: Phosphodiesterase (PDE) that has higher activity toward
	454	cAMP than cGMP, as substrate. Plays a role in cell proliferation,
		migration and differentiation, and acts as a negative regulator of NME1.
		Plays a role in the regulation of neurogenesis. Involved in the regulation
		of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma		FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl
membrane-associated	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte
protein		differentiation. {ECO:0000250}.
	415	

		FUNCTION: Regulator of phosphate homeostasis (By similarity).
Fibroblast growth factor		Inhibits renal tubular phosphate transport by reducing SLC34A1 levels
		(By similarity). Acts directly on the parathyroid to decrease PTH
23	251	secretion (By similarity). Regulator of vitamin-D metabolism (By
		similarity). Negatively regulates osteoblasts differentiation and matrix
		mineralization (By similarity). Up-regulates EGR1 expression in the
		presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
		FUNCTION: Receptor for extracellularly released ATP acting as a
		ligand-gated ion channel that plays multiple role in immunity and central
		nervous system physiology (PubMed:26456657, PubMed:35119925).
		Plays a key role in initial steps of T-cell activation and Ca(2+)
		microdomain formation (PubMed:35119925). Participates also in basal
DOV	200	T-cell activity without TCR/CD3 stimulation (PubMed:35119925).
P2X purinoceptor 4	388	Promotes the differentiation and activation of Th17 cells via expression
		of retinoic acid-related orphan receptor C/RORC (By similarity). Upon
		activation, drives microglia motility via the PI3K/Akt pathway
		(PubMed:17299767). {ECO:0000250 UniProtKB:Q99571,
		ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:26456657,
		ECO:0000269 PubMed:35119925}.
		FUNCTION: Glycosyltransferase which regulates the biosynthesis of
	918	heparan sulfate (HS). Important for both skeletal development and
		hematopoiesis, through the formation of HS proteoglycans (HSPGs).
Exostosin-like 3		Required for the function of REG3A in regulating keratinocyte
		proliferation and differentiation (By similarity).
		{ECO:0000250 UniProtKB:O43909}.
		FUNCTION: Component of the ESCRT-I complex, a regulator of
Vacuolar protein	285	vesicular trafficking process. Required for the sorting of endocytic
sorting-associated protein		ubiquitinated cargos into multivesicular bodies. May be involved in cell
37B		growth and differentiation (By similarity). {ECO:0000250}.
		FUNCTION: Has no ubiquitin ligase activity on its own. The
		UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical
		poly-ubiquitin chains that are linked through 'Lys-63'. This type of
		poly-ubiquitination activates IKK and does not seem to involve protein
		degradation by the proteasome. Plays a role in the activation of
		NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates
		transcriptional activation of target genes. Plays a role in the control of
Ubiquitin-conjugating	147	progress through the cell cycle and differentiation (By similarity). Plays a
enzyme E2 variant 1	147	role in the error-free DNA repair pathway and contributes to the survival
		of cells after DNA damage. Promotes TRIM5 capsid-specific restriction
		activity and the UBE2V1-UBE2N heterodimer acts in concert with
		TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate
		the MAP3K7/TAK1 complex which in turn results in the induction and
		_
		expression of NF-kappa-B and MAPK-responsive inflammatory genes
		(By similarity). Together with RNF135 and UBE2N, catalyzes the viral

		RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to
		activate the downstream signaling pathway that leads to interferon beta
		production (By similarity). UBE2V1-UBE2N together with TRAF3IP2
		E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6,
		a component of IL17A-mediated signaling pathway. {ECO:0000250,
		ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
		FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties
		conjugated to substrates and thus, functions to process newly synthesized
Ubiquitin		Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains
carboxyl-terminal	1055	and prevents proteasomal degradation of substrates. Hydrolyzes both
hydrolase 25		'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
		{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
		may have a role in the regulation of muscular differentiation and function.
		FUNCTION: Transcriptional regulator involved in different processes
		such as glucose metabolism, aerobic glycolysis, muscle cell
		differentiation and autophagy (PubMed:25402684, PubMed:29861159,
		PubMed:30700909). Recognizes and binds the forkhead DNA sequence
		motif (5'-GTAAACA-3') and can both act as a transcription activator or
		repressor, depending on the context (PubMed:25402684,
		PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
		key regulator of metabolic reprogramming towards aerobic glycolysis, a
		process in which glucose is converted to lactate in the presence of oxygen
		1 1
		(PubMed:30700909). Acts by promoting expression of enzymes for
		glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
		kinase (PKLR) and lactate dehydrogenase), while suppressing further
		oxidation of pyruvate in the mitochondria by up-regulating pyruvate
		dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
		plays a role in gluconeogenesis during overnight fasting, when lactate
Forkhead box protein K1	719	from white adipose tissue and muscle is the main substrate
		(PubMed:30700909). Involved in mTORC1-mediated metabolic
		reprogramming: in response to mTORC1 signaling, translocates into the
		nucleus and regulates the expression of genes associated with glycolysis
		and downstream anabolic pathways, such as HIF1A, thereby regulating
		glucose metabolism (PubMed:29861159). Together with FOXK2, acts as
		a negative regulator of autophagy in skeletal muscle: in response to
		starvation, enters the nucleus, binds the promoters of autophagy genes
		and represses their expression, preventing proteolysis of skeletal muscle
		proteins (PubMed:25402684). Acts as a transcriptional regulator of the
		myogenic progenitor cell population in skeletal muscle
		(PubMed:8007964, PubMed:9271401, PubMed:12446708,
		PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
		of myoglobin (MB) gene, regulating the myogenic progenitor cell
		population (PubMed:8007964, PubMed:9271401). Promotes muscle
		progenitor cell proliferation by repressing the transcriptional activity of
		1 0 1 7 1 0

		EOVO4 4h
		FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
		PubMed:22956541). Involved in remodeling processes of adult muscles
		that occur in response to physiological stimuli (PubMed:9271401,
		PubMed:22956541). Required to correct temporal orchestration of
		molecular and cellular events necessary for muscle repair
		(PubMed:10792059). Represses myogenic differentiation by inhibiting
		MEFC activity (PubMed:22956541). Positively regulates
		Wnt/beta-catenin signaling by translocating DVL into the nucleus (By
		similarity). Reduces virus replication, probably by binding the interferon
		stimulated response element (ISRE) to promote antiviral gene expression
		(By similarity). {ECO:0000250 UniProtKB:P85037,
		ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:12446708,
		ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:25402684,
		ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:30700909,
		ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.
		FUNCTION: Component of the cleavage and polyadenylation specificity
		factor (CPSF) complex that plays a key role in pre-mRNA 3'-end
		formation, recognizing the AAUAAA signal sequence and interacting
		with poly(A) polymerase and other factors to bring about cleavage and
		poly(A) addition. Has endonuclease activity, and functions as mRNA
		3'-end-processing endonuclease. Also involved in the histone 3'-end
		pre-mRNA processing. U7 snRNP-dependent protein that induces both
		the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a
		5' to 3' exonuclease for degrading the subsequent downstream cleavage
		product (DCP) of mature histone mRNAs. Cleavage occurs after the
		5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl
		group on the upstream fragment containing the stem loop (SL) and 5'
Cleavage and		phosphate on the downstream cleavage product (DCP) starting with CU
polyadenylation		nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive
specificity factor subunit	684	and degrades the DCP RNA substrate even after complete removal of the
3		U7-binding site. Binds to the downstream cleavage product (DCP) of
		histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP
		dependent manner. Required for the selective processing of microRNAs
		(miRNAs) during embryonic stem cell differentiation via its interaction
		with ISY1 (PubMed:26255770, PubMed:29804889). Required for
		entering/progressing through S-phase of the cell cycle (By similarity).
		Required for the biogenesis of all miRNAs from the pri-miR-17-92
		primary transcript except miR-92a (PubMed:26255770). Only required
		for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and
		pri-miR-96-183 primary transcripts, respectively (PubMed:29804889).
		{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:16213211,
		ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:19470752,
200	2.50	ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
Mitogen-activated protein	358	FUNCTION: Serine/threonine kinase which acts as an essential

kinase 1

component of the MAP kinase signal transduction pathway. MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an important role in the MAPK/ERK cascade. They participate also in a signaling cascade initiated by activated KIT and KITLG/SCF. Depending on the cellular context, the MAPK/ERK cascade mediates diverse biological functions such as cell growth, adhesion, survival and differentiation through the regulation of transcription, translation, cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role in initiation and regulation of meiosis, mitosis, and postmitotic functions in differentiated cells by phosphorylating a number of transcription factors. About 160 substrates have already been discovered for ERKs. Many of these substrates are localized in the nucleus, and seem to participate in the regulation of transcription upon stimulation. However, other substrates are found in the cytosol as well as in other cellular organelles, and those are responsible for processes such as translation, mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also involved in the regulation of the endosomal dynamics, including lysosome processing and endosome cycling through the perinuclear recycling compartment (PNRC); as well as in the fragmentation of the Golgi apparatus during mitosis. The substrates include transcription factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1), cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT, PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD, BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of translation (such as EIF4EBP1) and a variety of other signaling-related molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases (such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3, RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2, RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other substrates which enable the propagation the MAPK/ERK signal to additional cytosolic and nuclear targets, thereby extending the specificity of the cascade. Mediates phosphorylation of TPR in response to EGF stimulation. May play a role in the spindle assembly checkpoint. Phosphorylates PML and promotes its interaction with PIN1, leading to PML degradation. Phosphorylates CDK2AP2 (By similarity). {ECO:0000250|UniProtKB:P28482, ECO:0000250|UniProtKB:P63086, ECO:0000269|PubMed:10753946, ECO:0000269|PubMed:11702783, ECO:0000269|PubMed:12134156, ECO:0000303|PubMed:16393692, ECO:0000303|PubMed:19565474, ECO:0000303|PubMed:21779493}.; FUNCTION: Acts as a transcriptional repressor. Binds to a [GC]AAA[GC] consensus sequence. Repress the expression of interferon gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1, IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1.

		Transmitting 1 activities in independent of the control of
		Transcriptional activity is independent of kinase activity.
		{ECO:0000250 UniProtKB:P28482}.
		FUNCTION: RNA-binding protein that acts as a key regulator of
		N6-methyladenosine (m6A) methylation of RNAs, thereby regulating
		different processes, such as hematopoietic cell homeostasis, alternative
		splicing of mRNAs and X chromosome inactivation mediated by Xist
		RNA (PubMed:29535189). Associated component of the WMM
		complex, a complex that mediates N6-methyladenosine (m6A)
		methylation of RNAs, a modification that plays a role in the efficiency of
		mRNA splicing and RNA processing (PubMed:29535189). Plays a key
		role in m6A methylation, possibly by binding target RNAs and recruiting
		the WMM complex (PubMed:29535189). Involved in random X
		inactivation mediated by Xist RNA: acts by binding Xist RNA and
		recruiting the WMM complex, which mediates m6A methylation, leading
		to target YTHDC1 reader on Xist RNA and promoting transcription
		repression activity of Xist (By similarity). Required for the development
		of multiple tissues, such as the maintenance of the homeostasis of
		long-term hematopoietic stem cells and for megakaryocyte (MK) and
		B-cell differentiation (PubMed:17283045, PubMed:17376872,
RNA-binding protein 15	962	PubMed:18981216, PubMed:25468569). Regulates megakaryocyte
		differentiation by regulating alternative splicing of genes important for
		megakaryocyte differentiation; probably regulates alternative splicing via
		m6A regulation (By similarity). Required for placental vascular
		branching morphogenesis and embryonic development of the heart and
		spleen (PubMed:18981216). Acts as a regulator of thrombopoietin
		response in hematopoietic stem cells by regulating alternative splicing of
		MPL (PubMed:25468569). May also function as an mRNA export factor,
		stimulating export and expression of RTE-containing mRNAs which are
		present in many retrotransposons that require to be exported prior to
		splicing (By similarity). High affinity binding of pre-mRNA to RBM15
		may allow targeting of the mRNP to the export helicase DBP5 in a
		manner that is independent of splicing-mediated NXF1 deposition,
		resulting in export prior to splicing (By similarity). May be implicated in
		HOX gene regulation (By similarity).
		{ECO:0000250 UniProtKB:Q96T37, ECO:0000269 PubMed:17283045,
		ECO:0000269 PubMed:17376872, ECO:0000269 PubMed:18981216,
		ECO:0000269 PubMed:25468569, ECO:0000269 PubMed:29535189}.
		FUNCTION: Transcription coactivator which associates with nuclear
		receptors, transcriptional coactivators including EP300, CREBBP and
		NCOA1, and basal transcription factors like TBP and TFIIA to facilitate
Activating signal	581	_
cointegrator 1	381	nuclear receptors-mediated transcription. May thereby play an important
		role in establishing distinct coactivator complexes under different cellular
		conditions. Plays a role in thyroid hormone receptor and estrogen
		receptor transactivation (By similarity). Also involved in androgen

		receptor transactivation (PubMed:12077347). Plays a pivotal role in the transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of transrepression between nuclear receptor and either AP1 or NF-kappa-B. May play a role in the development of neuromuscular junction (By similarity). May play a role in late myogenic differentiation (PubMed:27008887). Also functions as part of the RQC trigger (RQT) complex that activates the ribosome quality control (RQC) pathway, a pathway that degrades nascent peptide chains during problematic translation (By similarity). {ECO:0000250 UniProtKB:Q15650,
Histone-lysine N-methyltransferase SETD2	2537	translation (By similarity). {ECO:0000250 UniProtKB:Q15650, ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891, ECO:0000269 PubMed:27008887}.  FUNCTION: Histone methyltransferase that specifically trimethylates 'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36' (H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By similarity). Represents the main enzyme generating H3K36me3, a specific tag for epigenetic transcriptional activation (PubMed:18157086, PubMed:20133625). Plays a role in chromatin structure modulation during elongation by coordinating recruitment of the FACT complex and by interacting with hyperphosphorylated POLR2A (By similarity). Acts as a key regulator of DNA mismatch repair in G1 and early S phase by generating H3K36me3, a mark required to recruit MSH6 subunit of the MutS alpha complex: early recruitment of the MutS alpha complex to chromatin to be replicated allows a quick identification of mismatch DNA to initiate the mismatch repair reaction (By similarity). Required for DNA double-strand break repair in response to DNA damage: acts by mediating formation of H3K36me3, promoting recruitment of RAD51 and DNA repair via homologous recombination (HR) (By similarity). Acts as a tumor suppressor (By similarity). H3K36me3 also plays an essential role in the maintenance of a heterochromatic state, by recruiting DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also enhanced in intron-containing genes, suggesting that SETD2 recruitment is enhanced by splicing and that splicing is coupled to recruitment of elongating RNA polymerase (By similarity). Required during angiogenesis (PubMed:20133625). Required for endoderm development by promoting embryonic stem cell differentiation toward endoderm: acts by mediating formation of H3K36me3 in distal promoter regions of FGFR3, leading to regulate transcription initiation of FGFR3 (PubMed:25242323). In addition to histones, also mediates methylation of other
		(PubMed:27518565). Involved in interferon-alpha-induced antiviral

		defense by mediating both monomethylation of STAT1 at 'Lys-525' and catalyzing H3K36me3 on promoters of some interferon-stimulated genes (ISGs) to activate gene transcription (By similarity).  {ECO:0000250 UniProtKB:Q9BYW2, ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625, ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.  FUNCTION: RNA-binding protein that plays a central role in myelinization (PubMed:10864952, PubMed:11917126). Also required for visceral endoderm function and blood vessel development (PubMed:11892011, PubMed:16470614). Binds to the
Protein quaking	341	5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence (PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA export, mRNA stability and protein translation, as well as cellular processes including apoptosis, cell cycle, glial cell fate and development (PubMed:10535969, PubMed:12467586, PubMed:11297509, PubMed:11917126, PubMed:15568022). Required to protect and promote stability of mRNAs such as MBP and CDKN1B which promotes oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022). Participates in mRNA transport by regulating the nuclear export of MBP mRNA (PubMed:12467586). May also play a role in smooth muscle development (PubMed:14706070). {ECO:0000269 PubMed:10535969, ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509, ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126, ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:14706070, ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved in regulation of mRNA splicing of MAG pre-mRNA by acting as a negative regulator of MAG exon 12 alternative splicing. {ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can induce apoptosis, while heterodimerization with other isoforms results in nuclear translocation of isoform 3 and suppression of apoptosis. {ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.
TBC1 domain family member 1	1255	FUNCTION: May act as a GTPase-activating protein for Rab family protein(s). May play a role in the cell cycle and differentiation of various tissues. Involved in the trafficking and translocation of GLUT4-containing vesicles and insulin-stimulated glucose uptake into cells. {ECO:0000269 PubMed:19740738}.
Mesenteric estrogen-dependent adipogenesis protein	303	FUNCTION: Involved in processes that promote adipocyte differentiation, lipid accumulation, and glucose uptake in mature adipocytes. {ECO:0000269 PubMed:22510272}.
SWI/SNF complex subunit SMARCC2	1213	FUNCTION: Involved in transcriptional activation and repression of select genes by chromatin remodeling (alteration of DNA-nucleosome topology). Component of SWI/SNF chromatin remodeling complexes

		that carry out key enzymatic activities, changing chromatin structure by altering DNA-histone contacts within a nucleosome in an ATP-dependent manner. Can stimulate the ATPase activity of the catalytic subunit of these complexes. May be required for CoREST dependent repression of neuronal specific gene promoters in non-neuronal cells. Belongs to the neural progenitors-specific chromatin remodeling complex (npBAF complex) and the neuron-specific chromatin remodeling complex (nBAF complex). During neural development a switch from a stem/progenitor to a postmitotic chromatin remodeling mechanism occurs as neurons exit the cell cycle and become committed to their adult state. The transition from proliferating neural stem/progenitor cells to postmitotic neurons requires a switch in subunit composition of the npBAF and nBAF complexes. As neural progenitors exit mitosis and differentiate into neurons, npBAF complexes which contain ACTL6A/BAF53A and PHF10/BAF45A, are exchanged for homologous alternative ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in neuron-specific complexes (nBAF). The npBAF complex is essential for the self-renewal/proliferative capacity of the multipotent neural stem cells. The nBAF complex along with CREST plays a role regulating the activity of genes essential for dendrite growth (PubMed:17640523). Critical regulator of myeloid differentiation, controlling granulocytopoiesis and the expression of genes involved in neutrophil granule formation (PubMed:28369036). [ECO:0000269 PubMed:31216030, ECO:0000269 PubMed:28369036, ECO:0000303 PubMed:26601204}.
Protein prune homolog 2	3084	FUNCTION: May play an important role in regulating differentiation, survival and aggressiveness of the tumor cells. {ECO:0000250}.
Ninjurin-1	152	FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion molecule involved in various processes such as inflammation, cell death, axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008, PubMed:24347169, PubMed:24917672, PubMed:31526566, PubMed:33472215). Promotes cell adhesion by mediating homophilic interactions via its extracellular N-terminal adhesion motif (N-NAM) (PubMed:24917672, PubMed:30510259). Involved in the progression of the inflammatory stress by promoting cell-to-cell interactions between immune cells and endothelial cells (PubMed:24917672, PubMed:30510259). Involved in leukocyte migration during inflammation by promoting transendothelial migration of macrophages via homotypic binding (PubMed:24917672). Promotes the migration of monocytes across the brain endothelium to central nervous system inflammatory lesions (By similarity). Acts as a regulator of Toll-like receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during systemic inflammation; directly binds LPS (PubMed:25860173). Acts as

a mediator of both programmed and necrotic cell death (PubMed:19557008, PubMed:33472215). Plays a key role in the induction of plasma membrane rupture during programmed and necrotic cell death: oligomerizes in response to death stimuli to mediate plasma membrane rupture (cytolysis), leading to release intracellular molecules named damage-associated molecular patterns (DAMPs) that propagate the inflammatory response (PubMed:33472215). Plays a role in nerve regeneration by promoting maturation of Schwann cells (PubMed:31526566). Acts as a regulator of angiogenesis (PubMed:25766274, PubMed:30354207). Promotes the formation of new vessels by mediating the interaction between capillary pericyte cells and endothelial cells (PubMed:25766274, PubMed:30354207). Also mediates vascular functions in penile tissue as well as vascular formation (PubMed:24979788). Promotes osteoclasts development by enhancing the survival of prefusion osteoclasts (PubMed:30700695). Also involved in striated muscle growth and differentiation (PubMed:31091274). Also involved in cell senescence in a p53/TP53 manner, possibly by acting as an indirect regulator of p53/TP53 mRNA translation (PubMed:23690620, PubMed:29073078). {ECO:0000250|UniProtKB:Q92982, ECO:0000269|PubMed:19557008, ECO:0000269|PubMed:23690620, ECO:0000269|PubMed:24347169, ECO:0000269|PubMed:24917672, ECO:0000269|PubMed:24979788, ECO:0000269|PubMed:25766274, ECO:0000269|PubMed:25860173, ECO:0000269|PubMed:29073078, ECO:0000269|PubMed:30354207, ECO:0000269|PubMed:30510259, ECO:0000269|PubMed:30700695, ECO:0000269|PubMed:31091274, ECO:0000269|PubMed:31526566, ECO:0000269|PubMed:33472215}.; FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage, which has chemotactic activity (PubMed:23142597). Acts as an anti-inflammatory mediator by promoting monocyte recruitment, thereby ameliorating atherosclerosis (PubMed:32883094). {ECO:0000269|PubMed:23142597, ECO:0000269|PubMed:32883094}. FUNCTION: Phosphorylates a large number of substrates in the cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B, ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9 and VASP (PubMed:10805756, PubMed:19223768). Regulates the abundance of compartmentalized pools of its regulatory subunits through phosphorylation of PJA2 which binds and ubiquitinates these subunits, cAMP-dependent protein kinase catalytic subunit 351 leading to their subsequent proteolysis (By similarity). RORA is activated alpha by phosphorylation. Required for glucose-mediated adipogenic differentiation increase and osteogenic differentiation inhibition from osteoblasts (By similarity). Involved in chondrogenesis by mediating phosphorylation of SOX9 (PubMed:10805756). Involved in the regulation of platelets in response to thrombin and collagen; maintains circulating platelets in a resting state by phosphorylating proteins in

numerous platelet inhibitory pathways when in complex with NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), thrombin and collagen disrupt these complexes and free active PRKA stimulates platelets and leads to platelet aggregation by phosphorylation in VASP. RYR2 channel activity is potentiated by phosphorylation in presence of luminal Ca(2+), leading to reduced amplitude and increased frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propagation velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude and the store of the spontaneous Ca(2+) waves, despite reduced wave amplitude and the store of the spontaneous Ca(2+) waves, despite reduced wave amplitude and the store of the spontaneous Ca(2+) waves, despite reduced wave amplitude and the store of the spontaneous Ca(2+) waves, despite reduced wave amplitude and the store of the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous Ca(2+) waves, despite reduced wave amplitude and the spontaneous C	ACA ing sed
thrombin and collagen disrupt these complexes and free active PRKA stimulates platelets and leads to platelet aggregation by phosphorylation in VASP. RYR2 channel activity is potentiated by phosphorylation in presence of luminal Ca(2+), leading to reduced amplitude and increa frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propagation velocity of spontaneous Ca(2+) waves, despite reduced wave amplitudes	ACA ing sed
stimulates platelets and leads to platelet aggregation by phosphorylat VASP. RYR2 channel activity is potentiated by phosphorylation in presence of luminal Ca(2+), leading to reduced amplitude and increa frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propagation velocity of spontaneous Ca(2+) waves, despite reduced wave amplitudes	ing sed
VASP. RYR2 channel activity is potentiated by phosphorylation in presence of luminal Ca(2+), leading to reduced amplitude and increa frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propagation velocity of spontaneous Ca(2+) waves, despite reduced wave amplitudes	sed
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and antique of the COO DOMOS/DRTC of the	
and resting cytosolic Ca(2+). PSMC5/RPT6 activation by	
phosphorylation stimulates proteasome. Negatively regulates tight	
junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.	
NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA bindi	ıg.
Involved in embryonic development by down-regulating the Hedgeh	_
(Hh) signaling pathway that determines embryo pattern formation an	_
morphogenesis (By similarity). Prevents meiosis resumption in	
prophase-arrested oocytes via CDC25B inactivation by phosphorylat	ion
(PubMed:19223768). May also regulate rapid eye movement (REM)	
sleep in the pedunculopontine tegmental (PPT) (By similarity).	
Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this	;
phosphorylation promotes HSF1 nuclear localization and transcription	
activity upon heat shock (By similarity).	
{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P277	91
ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768	
FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in spe	1
flagellum to promote spermatozoa capacitation.	
{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:1956045	(5)
FUNCTION: Receptor for both interleukin 4 and interleukin 13. Cou	
to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in	pies
Interleukin-4 receptor promoting Th2 differentiation. The IL4/IL13 response are involved	in
810	
subunit alpha regulating IgE production and, chemokine and mucus production at s	nes
of allergic inflammation. In certain cell types, can signal through	
activation of insulin receptor substrates, IRS1/IRS2.	
FUNCTION: Required for mitosis progression. Promotes the nucleat	
of microtubules from the spindle (By similarity). May play an import	
Protein NEDD1 660 role during the embryonic development and differentiation of the cer	tral
nervous system (PubMed:1378265).	
{ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:13782	265}.
FUNCTION: Calcium-dependent, calmodulin-stimulated protein	
phosphatase which plays an essential role in the transduction of	
Protein phosphatase 3 intracellular Ca(2+)-mediated signals (PubMed:7791792,	
catalytic subunit alpha PubMed:26794871). Many of the substrates contain a PxIxIT motif	
and/or a LxVP motif (By similarity). In response to increased Ca(2+)	
levels, dephosphorylates and activates phosphatase SSH1 which resu	lts in

cofilin dephosphorylation (By similarity). In response to increased Ca(2+) levels following mitochondrial depolarization, dephosphorylates DNM1L inducing DNM1L translocation to the mitochondrion (By similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+) release probability at hippocampal neuronal soma and synaptic terminals (By similarity). Dephosphorylates heat shock protein HSPB1 (By similarity). Dephosphorylates and activates transcription factor NFATC1 (By similarity). Dephosphorylates and inactivates transcription factor ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation from 14-3-3 proteins (By similarity). Required for postnatal development of the nephrogenic zone and superficial glomeruli in the kidneys, cell cycle homeostasis in the nephrogenic zone, and ultimately normal kidney function (PubMed:15509543). Plays a role in intracellular AQP2 processing and localization to the apical membrane in the kidney, may thereby be required for efficient kidney filtration (PubMed:16735444). Required for secretion of salivary enzymes amylase, peroxidase, lysozyme and sialic acid via formation of secretory vesicles in the submandibular glands (PubMed:21435446). Required for calcineurin activity and homosynaptic depotentiation in the hippocampus (PubMed:10200317). Required for normal differentiation and survival of keratinocytes and therefore required for epidermis superstructure formation (PubMed:19626032). Positively regulates osteoblastic bone formation, via promotion of osteoblast differentiation (PubMed:16286645). Positively regulates osteoclast differentiation, potentially via NFATC1 signaling (PubMed:16968888). May play a role in skeletal muscle fiber type specification, potentially via NFATC1 signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK signaling via inhibition of nuclear translocation of the transcription factors RELA and RELB (PubMed:26029823). Required for antigen-specific T-cell proliferation response (PubMed:8627154). {ECO:0000250|UniProtKB:P48452, ECO:0000250|UniProtKB:P63329, ECO:0000250|UniProtKB:Q08209, ECO:0000269|PubMed:10200317, ECO:0000269|PubMed:12773574, ECO:0000269|PubMed:15509543, ECO:0000269|PubMed:16286645, ECO:0000269|PubMed:16735444, ECO:0000269|PubMed:16968888, ECO:0000269|PubMed:19626032, ECO:0000269|PubMed:21435446, ECO:0000269|PubMed:26029823, ECO:0000269|PubMed:26794871, ECO:0000269|PubMed:7791792, ECO:0000269|PubMed:8627154}. FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or SLAM family member 5 329 heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune

		response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not seen be required for this process. Homophilic interactions enhance interferon gamma/IFNG secretion in lymphocytes and induce platelet stimulation via a SH2D1A/SAP-dependent pathway. May serve as a marker for hematopoietic progenitor cells (By similarity). Required for a prolonged T-cell:B-cell contact, optimal T follicular helper function, and germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity immunoglobulin epsilon receptor signaling; independent of SH2D1A and SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and NF-kappaB activation and modulates LPS-induced cytokine secretion; involving ITSM 2 (PubMed:20628063). Positively regulates macroautophagy in primary dendritic cells via stabilization of IRF8; inhibits TRIM21-mediated proteasomal degradation of IRF8 (By similarity). {ECO:0000250 UniProtKB:Q9UIB8,
		germinal center formation (PubMed:20153220). In germinal centers involved in maintaining B cell tolerance and in preventing autoimmunity (PubMed:25801429). In mast cells negatively regulates high affinity
		SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In macrophages enhances LPS-induced MAPK phosphorylation and
		macroautophagy in primary dendritic cells via stabilization of IRF8; inhibits TRIM21-mediated proteasomal degradation of IRF8 (By
		ECO:0000269 PubMed:16037392, ECO:0000269 PubMed:20153220, ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259, ECO:0000269 PubMed:25801429, ECO:0000305}.
Transmembrane anterior posterior transformation protein 1	564	FUNCTION: Plays a role in primary cilia formation (By similarity). May act as a downstream effector of HOXC8 possibly by transducing or transmitting extracellular information required for axial skeletal patterning during development (By similarity). May be involved in cartilage and bone development (By similarity). May play a role in the differentiation of cranial neural crest cells (By similarity).
		{ECO:0000250 UniProtKB:A2BIE7, ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
Eleilie 1	2972	FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm diameter microfibrils of the extracellular matrix, which conveys both structural and regulatory properties to load-bearing connective tissues.  Fibrillin-1-containing microfibrils provide long-term force bearing structural support. In tissues such as the lung, blood vessels and skin, microfibrils form the periphery of the elastic fiber, acting as a scaffold for
Fibrillin-1	2873	the deposition of elastin. In addition, microfibrils can occur as elastin-independent networks in tissues such as the ciliary zonule, tendon, cornea and glomerulus where they provide tensile strength and have anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis through specific interactions with growth factors, such as the bone morphogenetic proteins (BMPs), growth and differentiation factors

		(GDFs) and latent transforming growth factor-beta-binding proteins
		(LTBPs), cell-surface integrins and other extracellular matrix protein and
		proteoglycan components (By similarity). Regulates osteoblast
		maturation by controlling TGF-beta bioavailability and calibrating
		TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively
		regulates osteoclastogenesis by binding and sequestering an osteoclast
		differentiation and activation factor TNFSF11. This leads to disruption of
		TNFSF11-induced Ca(2+) signaling and impairment of
		TNFSF11-mediated nuclear translocation and activation of transcription
		factor NFATC1 which regulates genes important for osteoclast
		differentiation and function (PubMed:24039232). Mediates cell adhesion
		via its binding to cell surface receptors integrins ITGAV:ITGB3 and
		ITGA5:ITGB1. Binds heparin and this interaction plays an important role in the assembly of microfibile (By similarity)
		in the assembly of microfibrils (By similarity).
		{ECO:0000250 UniProtKB:P35555, ECO:0000269 PubMed:20855508,
		ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipoking
		secreted by white adipose tissue that plays an important regulatory role in
		the glucose metabolism of liver, muscle and pancreas
		(PubMed:31230984, PubMed:30997682). Hormone that targets the liver
		in response to fasting to increase plasma glucose levels
		(PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface
		of hepatocytes and promotes hepatocyte glucose release by activating the
		protein kinase A activity in the liver, resulting in rapid glucose release
		into the circulation (PubMed:31230984). May act as a regulator of
		adaptive thermogenesis by inhibiting browning and energy consumption,
		while increasing lipid deposition in white adipose tissue
		(PubMed:33705351). Also acts as an orexigenic hormone that increases
		appetite: crosses the blood brain barrier and exerts effects on the
		hypothalamus (PubMed:29106398). In the arcuate nucleus of the
		hypothalamus, asprosin directly activates orexigenic AgRP neurons and
		indirectly inhibits anorexigenic POMC neurons, resulting in appetite
		stimulation (PubMed:29106398, PubMed:32337066). Activates
		orexigenic AgRP neurons via binding to the olfactory receptor Olfr734
		(PubMed:32337066). May also play a role in sperm motility in testis via
		interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682,
		ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959,
		ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
		FUNCTION: May play a role in intercellular signaling and in connecting
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cell
		motility, growth and differentiation. Binds hyaluronic acid.
A11 / 2 1		FUNCTION: Catalyzes the saturation of all-trans-retinol to
All-trans-retinol	609	all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779,
13,14-reductase		PubMed:19139408). Does not exhibit any activity toward

	1	
		all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers
		(PubMed:15358783). May play a role in the metabolism of vitamin A
		(PubMed:15358783, PubMed:17253779). Independently of retinol
		conversion, may regulate liver metabolism upstream of
		MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte
		differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This
		effect seems not to mimic the in vivo situation in which animals show
		increased adiposity in the absence of RETSAT (PubMed:19940255).
		{ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779,
		ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255,
		ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
		FUNCTION: ATP-driven pump that supplies the Golgi apparatus with
		Ca(2+) and Mn(2+) ions, both essential cofactors for processing and
		trafficking of newly synthesized proteins in the secretory pathway (By
		similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on
		the cytoplasmic side of the membrane and delivers them to the lumenal
		side. The transfer of ions across the membrane is coupled to ATP
		hydrolysis and is associated with a transient phosphorylation that shifts
		the pump conformation from inward-facing to outward-facing state (By
	918	similarity). Plays a primary role in the maintenance of Ca(2+)
Calcium-transporting		homeostasis in the trans-Golgi compartment with a functional impact on
ATPase type 2C member		Golgi and post-Golgi protein sorting as well as a structural impact on
1		cisternae morphology. Responsible for loading the Golgi stores with
		Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation
		and epidermis integrity (By similarity). Participates in Ca(2+) and
		Mn(2+) ions uptake into the Golgi store of hippocampal neurons and
		regulates protein trafficking required for neural polarity
		(PubMed:19793975). May also play a role in the maintenance of Ca(2+)
		and Mn(2+) homeostasis and signaling in the cytosol while preventing
		cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194,
		ECO:0000269 PubMed:19793975}.
		FUNCTION: Phosphodiesterase (PDE) that has higher activity toward
	454	cAMP than cGMP, as substrate. Plays a role in cell proliferation,
Exopolyphosphatase		migration and differentiation, and acts as a negative regulator of NME1.
PRUNE1	434	Plays a role in the regulation of neurogenesis. Involved in the regulation
		of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
A dimension mla arres		
Adipocyte plasma	415	FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl
membrane-associated	415	acetate and phenyl acetate (By similarity). May play a role in adipocyte
protein		differentiation. {ECO:0000250}.
Fibroblast growth factor 23	251	FUNCTION: Regulator of phosphate homeostasis (By similarity).
		Inhibits renal tubular phosphate transport by reducing SLC34A1 levels
		(By similarity). Acts directly on the parathyroid to decrease PTH
	l	secretion (By similarity). Regulator of vitamin-D metabolism (By
		similarity). Negatively regulates osteoblasts differentiation and matrix

		T
		mineralization (By similarity). Up-regulates EGR1 expression in the
		presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
P2X purinoceptor 4	388	FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central nervous system physiology (PubMed:26456657, PubMed:35119925).  Plays a key role in initial steps of T-cell activation and Ca(2+) microdomain formation (PubMed:35119925). Participates also in basal T-cell activity without TCR/CD3 stimulation (PubMed:35119925).  Promotes the differentiation and activation of Th17 cells via expression of retinoic acid-related orphan receptor C/RORC (By similarity). Upon activation, drives microglia motility via the PI3K/Akt pathway (PubMed:17299767). {ECO:0000250 UniProtKB:Q99571, ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:35119925}.
Exostosin-like 3	918	FUNCTION: Glycosyltransferase which regulates the biosynthesis of heparan sulfate (HS). Important for both skeletal development and hematopoiesis, through the formation of HS proteoglycans (HSPGs). Required for the function of REG3A in regulating keratinocyte proliferation and differentiation (By similarity). {ECO:0000250 UniProtKB:O43909}.
Vacuolar protein sorting-associated protein 37B	285	FUNCTION: Component of the ESCRT-I complex, a regulator of vesicular trafficking process. Required for the sorting of endocytic ubiquitinated cargos into multivesicular bodies. May be involved in cell growth and differentiation (By similarity). {ECO:0000250}.
Ubiquitin-conjugating enzyme E2 variant 1	147	FUNCTION: Has no ubiquitin ligase activity on its own. The UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical poly-ubiquitin chains that are linked through 'Lys-63'. This type of poly-ubiquitination activates IKK and does not seem to involve protein degradation by the proteasome. Plays a role in the activation of NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates transcriptional activation of target genes. Plays a role in the control of progress through the cell cycle and differentiation (By similarity). Plays a role in the error-free DNA repair pathway and contributes to the survival of cells after DNA damage. Promotes TRIM5 capsid-specific restriction activity and the UBE2V1-UBE2N heterodimer acts in concert with TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate the MAP3K7/TAK1 complex which in turn results in the induction and expression of NF-kappa-B and MAPK-responsive inflammatory genes (By similarity). Together with RNF135 and UBE2N, catalyzes the viral RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to activate the downstream signaling pathway that leads to interferon beta production (By similarity). UBE2V1-UBE2N together with TRAF3IP2 E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6, a component of IL17A-mediated signaling pathway. {ECO:0000250,

		ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
		FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties
		conjugated to substrates and thus, functions to process newly synthesized
Ubiquitin		Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains
carboxyl-terminal	1055	and prevents proteasomal degradation of substrates. Hydrolyzes both
hydrolase 25	1033	'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
hydroiase 25		{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
		may have a role in the regulation of muscular differentiation and function.
		FUNCTION: Transcriptional regulator involved in different processes
		such as glucose metabolism, aerobic glycolysis, muscle cell
		differentiation and autophagy (PubMed:25402684, PubMed:29861159,
		PubMed:30700909). Recognizes and binds the forkhead DNA sequence
		motif (5'-GTAAACA-3') and can both act as a transcription activator or
		repressor, depending on the context (PubMed:25402684,
		PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
		key regulator of metabolic reprogramming towards aerobic glycolysis, a
		process in which glucose is converted to lactate in the presence of oxygen
		(PubMed:30700909). Acts by promoting expression of enzymes for
		glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
		kinase (PKLR) and lactate dehydrogenase), while suppressing further
		oxidation of pyruvate in the mitochondria by up-regulating pyruvate
		dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
		plays a role in gluconeogenesis during overnight fasting, when lactate
		from white adipose tissue and muscle is the main substrate
		(PubMed:30700909). Involved in mTORC1-mediated metabolic
	719	reprogramming: in response to mTORC1 signaling, translocates into the
Forkhead box protein K1		nucleus and regulates the expression of genes associated with glycolysis
		and downstream anabolic pathways, such as HIF1A, thereby regulating
		glucose metabolism (PubMed:29861159). Together with FOXK2, acts as
		a negative regulator of autophagy in skeletal muscle: in response to
		starvation, enters the nucleus, binds the promoters of autophagy genes
		and represses their expression, preventing proteolysis of skeletal muscle
		proteins (PubMed:25402684). Acts as a transcriptional regulator of the
		myogenic progenitor cell population in skeletal muscle
		(PubMed:8007964, PubMed:9271401, PubMed:12446708,
		PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
		of myoglobin (MB) gene, regulating the myogenic progenitor cell
		population (PubMed:8007964, PubMed:9271401). Promotes muscle
		progenitor cell proliferation by repressing the transcriptional activity of
		FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
		PubMed:22956541). Involved in remodeling processes of adult muscles
		that occur in response to physiological stimuli (PubMed:9271401,
		PubMed:22956541). Required to correct temporal orchestration of
		molecular and cellular events necessary for muscle repair
		morecular and centular events necessary for muscle repair

		(PubMed:10792059). Represses myogenic differentiation by inhibiting MEFC activity (PubMed:22956541). Positively regulates Wnt/beta-catenin signaling by translocating DVL into the nucleus (By similarity). Reduces virus replication, probably by binding the interferon stimulated response element (ISRE) to promote antiviral gene expression (By similarity). {ECO:0000250 UniProtKB:P85037, ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:12446708, ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:25402684, ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:30700909,
Cleavage and polyadenylation specificity factor subunit 3	684	ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401}.  FUNCTION: Component of the cleavage and polyadenylation specificity factor (CPSF) complex that plays a key role in pre-mRNA 3'-end formation, recognizing the AAUAAA signal sequence and interacting with poly(A) polymerase and other factors to bring about cleavage and poly(A) addition. Has endonuclease activity, and functions as mRNA 3'-end-processing endonuclease. Also involved in the histone 3'-end pre-mRNA processing. U7 snRNP-dependent protein that induces both the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts as a 5' to 3' exonuclease for degrading the subsequent downstream cleavage product (DCP) of mature histone mRNAs. Cleavage occurs after the 5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydroxyl group on the upstream fragment containing the stem loop (SL) and 5' phosphate on the downstream cleavage product (DCP) starting with CU nucleotides. The U7-dependent 5' to 3' exonuclease activity is processive and degrades the DCP RNA substrate even after complete removal of the U7-binding site. Binds to the downstream cleavage product (DCP) of histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 snRNP dependent manner. Required for the selective processing of microRNAs (miRNAs) during embryonic stem cell differentiation via its interaction with ISY1 (PubMed:26255770, PubMed:29804889). Required for entering/progressing through S-phase of the cell cycle (By similarity). Required for the biogenesis of all miRNAs from the pri-miR-17-92 primary transcript except miR-92a (PubMed:26255770). Only required for the biogenesis of miR-290 and miR-96 from the pri-miR-290-295 and pri-miR-96-183 primary transcripts, respectively (PubMed:29804889). {ECO:0000269 PubMed:1895505, ECO:0000269 PubMed:19470752, ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:29804889}.
Mitogen-activated protein kinase 1	358	FUNCTION: Serine/threonine kinase which acts as an essential component of the MAP kinase signal transduction pathway.  MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play an important role in the MAPK/ERK cascade. They participate also in a signaling cascade initiated by activated KIT and KITLG/SCF. Depending on the cellular context, the MAPK/ERK cascade mediates diverse

biological functions such as cell growth, adhesion, survival and differentiation through the regulation of transcription, translation, cytoskeletal rearrangements. The MAPK/ERK cascade also plays a role in initiation and regulation of meiosis, mitosis, and postmitotic functions in differentiated cells by phosphorylating a number of transcription factors. About 160 substrates have already been discovered for ERKs. Many of these substrates are localized in the nucleus, and seem to participate in the regulation of transcription upon stimulation. However, other substrates are found in the cytosol as well as in other cellular organelles, and those are responsible for processes such as translation, mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also involved in the regulation of the endosomal dynamics, including lysosome processing and endosome cycling through the perinuclear recycling compartment (PNRC); as well as in the fragmentation of the Golgi apparatus during mitosis. The substrates include transcription factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1), cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT, PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD, BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of translation (such as EIF4EBP1) and a variety of other signaling-related molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases (such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3, RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2, RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other substrates which enable the propagation the MAPK/ERK signal to additional cytosolic and nuclear targets, thereby extending the specificity of the cascade. Mediates phosphorylation of TPR in response to EGF stimulation. May play a role in the spindle assembly checkpoint. Phosphorylates PML and promotes its interaction with PIN1, leading to PML degradation. Phosphorylates CDK2AP2 (By similarity). {ECO:0000250|UniProtKB:P28482, ECO:0000250|UniProtKB:P63086, ECO:0000269|PubMed:10753946, ECO:0000269|PubMed:11702783, ECO:0000269|PubMed:12134156, ECO:0000303|PubMed:16393692, ECO:0000303|PubMed:19565474, ECO:0000303|PubMed:21779493}.; FUNCTION: Acts as a transcriptional repressor. Binds to a [GC]AAA[GC] consensus sequence. Repress the expression of interferon gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1, IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1. Transcriptional activity is independent of kinase activity. {ECO:0000250|UniProtKB:P28482}. FUNCTION: RNA-binding protein that acts as a key regulator of N6-methyladenosine (m6A) methylation of RNAs, thereby regulating

RNA-binding protein 15

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different processes, such as hematopoietic cell homeostasis, alternative

splicing of mRNAs and X chromosome inactivation mediated by Xist RNA (PubMed:29535189). Associated component of the WMM complex, a complex that mediates N6-methyladenosine (m6A) methylation of RNAs, a modification that plays a role in the efficiency of mRNA splicing and RNA processing (PubMed:29535189). Plays a key role in m6A methylation, possibly by binding target RNAs and recruiting the WMM complex (PubMed:29535189). Involved in random X inactivation mediated by Xist RNA: acts by binding Xist RNA and recruiting the WMM complex, which mediates m6A methylation, leading to target YTHDC1 reader on Xist RNA and promoting transcription repression activity of Xist (By similarity). Required for the development of multiple tissues, such as the maintenance of the homeostasis of long-term hematopoietic stem cells and for megakaryocyte (MK) and B-cell differentiation (PubMed:17283045, PubMed:17376872, PubMed:18981216, PubMed:25468569). Regulates megakaryocyte differentiation by regulating alternative splicing of genes important for megakaryocyte differentiation; probably regulates alternative splicing via m6A regulation (By similarity). Required for placental vascular branching morphogenesis and embryonic development of the heart and spleen (PubMed:18981216). Acts as a regulator of thrombopoietin response in hematopoietic stem cells by regulating alternative splicing of MPL (PubMed:25468569). May also function as an mRNA export factor, stimulating export and expression of RTE-containing mRNAs which are present in many retrotransposons that require to be exported prior to splicing (By similarity). High affinity binding of pre-mRNA to RBM15 may allow targeting of the mRNP to the export helicase DBP5 in a manner that is independent of splicing-mediated NXF1 deposition, resulting in export prior to splicing (By similarity). May be implicated in HOX gene regulation (By similarity). {ECO:0000250|UniProtKB:Q96T37, ECO:0000269|PubMed:17283045, ECO:0000269|PubMed:17376872, ECO:0000269|PubMed:18981216, ECO:0000269|PubMed:25468569, ECO:0000269|PubMed:29535189\. FUNCTION: Transcription coactivator which associates with nuclear receptors, transcriptional coactivators including EP300, CREBBP and NCOA1, and basal transcription factors like TBP and TFIIA to facilitate nuclear receptors-mediated transcription. May thereby play an important role in establishing distinct coactivator complexes under different cellular Activating signal conditions. Plays a role in thyroid hormone receptor and estrogen 581 cointegrator 1 receptor transactivation (By similarity). Also involved in androgen receptor transactivation (PubMed:12077347). Plays a pivotal role in the transactivation of NF-kappa-B, SRF and AP1. Acts as a mediator of transrepression between nuclear receptor and either AP1 or NF-kappa-B. May play a role in the development of neuromuscular junction (By similarity). May play a role in late myogenic differentiation

	1	
		(PubMed:27008887). Also functions as part of the RQC trigger (RQT)
		complex that activates the ribosome quality control (RQC) pathway, a
		pathway that degrades nascent peptide chains during problematic
		translation (By similarity). {ECO:0000250 UniProtKB:Q15650,
		ECO:0000269 PubMed:12077347, ECO:0000269 PubMed:12390891,
		ECO:0000269 PubMed:27008887}.
		FUNCTION: Histone methyltransferase that specifically trimethylates
		'Lys-36' of histone H3 (H3K36me3) using dimethylated 'Lys-36'
		(H3K36me2) as substrate (PubMed:18157086, PubMed:20133625). It is
		capable of trimethylating unmethylated H3K36 (H3K36me0) in vitro (By
		similarity). Represents the main enzyme generating H3K36me3, a
		specific tag for epigenetic transcriptional activation (PubMed:18157086,
		PubMed:20133625). Plays a role in chromatin structure modulation
		during elongation by coordinating recruitment of the FACT complex and
		by interacting with hyperphosphorylated POLR2A (By similarity). Acts
		as a key regulator of DNA mismatch repair in G1 and early S phase by
		generating H3K36me3, a mark required to recruit MSH6 subunit of the
		MutS alpha complex: early recruitment of the MutS alpha complex to
		chromatin to be replicated allows a quick identification of mismatch
		DNA to initiate the mismatch repair reaction (By similarity). Required for
	2537	DNA double-strand break repair in response to DNA damage: acts by
		mediating formation of H3K36me3, promoting recruitment of RAD51
		and DNA repair via homologous recombination (HR) (By similarity).
		Acts as a tumor suppressor (By similarity). H3K36me3 also plays an
Histone-lysine		essential role in the maintenance of a heterochromatic state, by recruiting
N-methyltransferase		DNA methyltransferase DNMT3A (By similarity). H3K36me3 is also
SETD2		enhanced in intron-containing genes, suggesting that SETD2 recruitment
		is enhanced by splicing and that splicing is coupled to recruitment of
		elongating RNA polymerase (By similarity). Required during
		angiogenesis (PubMed:20133625). Required for endoderm development
		by promoting embryonic stem cell differentiation toward endoderm: acts
		by mediating formation of H3K36me3 in distal promoter regions of
		FGFR3, leading to regulate transcription initiation of FGFR3
		(PubMed:25242323). In addition to histones, also mediates methylation
		of other proteins, such as tubulins and STAT1 (PubMed:27518565).
		Trimethylates 'Lys-40' of alpha-tubulins such as TUBA1B
		(alpha-TubK40me3); alpha-TubK40me3 is required for normal mitosis
		and cytokinesis and may be a specific tag in cytoskeletal remodeling
		(PubMed:27518565). Involved in interferon-alpha-induced antiviral
		defense by mediating both monomethylation of STAT1 at 'Lys-525' and
		catalyzing H3K36me3 on promoters of some interferon-stimulated genes
		(ISGs) to activate gene transcription (By similarity).
		{ECO:0000250 UniProtKB:Q9BYW2,
		ECO:0000269 PubMed:18157086, ECO:0000269 PubMed:20133625,
		•

		ECO:0000269 PubMed:25242323, ECO:0000269 PubMed:27518565}.
		FUNCTION: RNA-binding protein that plays a central role in
		myelinization (PubMed:10864952, PubMed:11917126). Also required for
		visceral endoderm function and blood vessel development
		(PubMed:11892011, PubMed:16470614). Binds to the
		5'-NACUAAY-N(1,20)-UAAY-3' RNA core sequence
		(PubMed:16041388). Acts by regulating pre-mRNA splicing, mRNA
		export, mRNA stability and protein translation, as well as cellular
		processes including apoptosis, cell cycle, glial cell fate and development
		(PubMed:10535969, PubMed:12467586, PubMed:11297509,
		PubMed:11917126, PubMed:15568022). Required to protect and promote
		stability of mRNAs such as MBP and CDKN1B which promotes
		oligodendrocyte differentiation (PubMed:10535969, PubMed:15568022).
		Participates in mRNA transport by regulating the nuclear export of MBP
Protein quaking	341	mRNA (PubMed: 12467586). May also play a role in smooth muscle
1 Totem quaking	341	development (PubMed:14706070). {ECO:0000269 PubMed:10535969,
		ECO:0000269 PubMed:10864952, ECO:0000269 PubMed:11297509,
		ECO:0000269 PubMed:11892011, ECO:0000269 PubMed:11917126,
		ECO:0000269 PubMed:12467586, ECO:0000269 PubMed:14706070,
		ECO:0000269 PubMed:15568022, ECO:0000269 PubMed:16041388,
		ECO:0000269 PubMed:16470614}.; FUNCTION: Isoform 1 is involved
		in regulation of mRNA splicing of MAG pre-mRNA by acting as a
		negative regulator of MAG exon 12 alternative splicing.
		{ECO:0000269 PubMed:11917126}.; FUNCTION: Isoform 3 can induce
		apoptosis, while heterodimerization with other isoforms results in nuclear
		translocation of isoform 3 and suppression of apoptosis.
		{ECO:0000269 PubMed:11297509}.; FUNCTION: Isoform 4 acts as a
		translational repressor for GLI1. {ECO:0000269 PubMed:16198329}.
		FUNCTION: May act as a GTPase-activating protein for Rab family
		protein(s). May play a role in the cell cycle and differentiation of various
TBC1 domain family	1255	tissues. Involved in the trafficking and translocation of
member 1	1233	GLUT4-containing vesicles and insulin-stimulated glucose uptake into
		cells. {ECO:0000269 PubMed:19740738}.
Mesenteric		FUNCTION: Involved in processes that promote adipocyte
estrogen-dependent	303	differentiation, lipid accumulation, and glucose uptake in mature
adipogenesis protein	303	adipocytes. {ECO:0000269 PubMed:22510272}.
adipogenesis protein		FUNCTION: Involved in transcriptional activation and repression of
		select genes by chromatin remodeling (alteration of DNA-nucleosome
		topology). Component of SWI/SNF chromatin remodeling complexes
SWI/SNF compley		that carry out key enzymatic activities, changing chromatin structure by
SWI/SNF complex subunit SMARCC2	1213	altering DNA-histone contacts within a nucleosome in an ATP-dependent
SUUUIII SWIARCC2		manner. Can stimulate the ATPase activity of the catalytic subunit of
		these complexes. May be required for CoREST dependent repression of
	<u> </u>	neuronal specific gene promoters in non-neuronal cells. Belongs to the

		neural progenitors-specific chromatin remodeling complex (npBAF
		complex) and the neuron-specific chromatin remodeling complex (nBAF
		complex). During neural development a switch from a stem/progenitor to
		a postmitotic chromatin remodeling mechanism occurs as neurons exit
		the cell cycle and become committed to their adult state. The transition
		from proliferating neural stem/progenitor cells to postmitotic neurons
		requires a switch in subunit composition of the npBAF and nBAF
		complexes. As neural progenitors exit mitosis and differentiate into
		neurons, npBAF complexes which contain ACTL6A/BAF53A and
		PHF10/BAF45A, are exchanged for homologous alternative
		ACTL6B/BAF53B and DPF1/BAF45B or DPF3/BAF45C subunits in
		neuron-specific complexes (nBAF). The npBAF complex is essential for
		the self-renewal/proliferative capacity of the multipotent neural stem
		cells. The nBAF complex along with CREST plays a role regulating the
		activity of genes essential for dendrite growth (PubMed:17640523).
		Critical regulator of myeloid differentiation, controlling
		granulocytopoiesis and the expression of genes involved in neutrophil
		granule formation (PubMed:28369036).
		{ECO:0000269 PubMed:17640523, ECO:0000269 PubMed:28369036,
		ECO:0000269 PubMed:31216030, ECO:0000303 PubMed:22952240,
		ECO:0000303 PubMed:26601204}.
		FUNCTION: May play an important role in regulating differentiation,
Protein prune homolog 2	3084	survival and aggressiveness of the tumor cells. {ECO:0000250}.
		FUNCTION: [Ninjurin-1]: Homophilic transmembrane adhesion
		molecule involved in various processes such as inflammation, cell death,
		axonal growth, cell chemotaxis and angiogenesis (PubMed:19557008,
		PubMed:24347169, PubMed:24917672, PubMed:31526566,
		PubMed:33472215). Promotes cell adhesion by mediating homophilic
		interactions via its extracellular N-terminal adhesion motif (N-NAM)
		(PubMed:24917672, PubMed:30510259). Involved in the progression of
		the inflammatory stress by promoting cell-to-cell interactions between
		immune cells and endothelial cells (PubMed:24917672,
		PubMed:30510259). Involved in leukocyte migration during
Ninjurin-1	152	inflammation by promoting transendothelial migration of macrophages
1 my min 1	102	via homotypic binding (PubMed:24917672). Promotes the migration of
		monocytes across the brain endothelium to central nervous system
		inflammatory lesions (By similarity). Acts as a regulator of Toll-like
		receptor 4 (TLR4) signaling triggered by lipopolysaccharide (LPS) during
		systemic inflammation; directly binds LPS (PubMed:25860173). Acts as
		a mediator of both programmed and necrotic cell death
		(PubMed:19557008, PubMed:33472215). Plays a key role in the
		induction of plasma membrane rupture during programmed and necrotic
		cell death: oligomerizes in response to death stimuli to mediate plasma
		membrane rupture (cytolysis), leading to release intracellular molecules

named damage-associated molecular patterns (DAMPs) that propagate the inflammatory response (PubMed:33472215). Plays a role in nerve regeneration by promoting maturation of Schwann cells (PubMed:31526566). Acts as a regulator of angiogenesis (PubMed:25766274, PubMed:30354207). Promotes the formation of ne vessels by mediating the interaction between capillary pericyte cells and endothelial cells (PubMed:25766274, PubMed:30354207). Also mediat vascular functions in penile tissue as well as vascular formation
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vascular functions in penile tissue as well as vascular formation
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(PubMed:24979788). Promotes osteoclasts development by enhancing
the survival of prefusion osteoclasts (PubMed:30700695). Also involve
in striated muscle growth and differentiation (PubMed:31091274). Also
involved in cell senescence in a p53/TP53 manner, possibly by acting a
an indirect regulator of p53/TP53 mRNA translation (PubMed:2369062
PubMed:29073078). {ECO:0000250 UniProtKB:Q92982,
ECO:0000269 PubMed:19557008, ECO:0000269 PubMed:23690620,
ECO:0000269 PubMed:24347169, ECO:0000269 PubMed:24917672,
ECO:0000269 PubMed:24979788, ECO:0000269 PubMed:25766274,
ECO:0000269 PubMed:25860173, ECO:0000269 PubMed:29073078,
ECO:0000269 PubMed:30354207, ECO:0000269 PubMed:30510259,
ECO:0000269 PubMed:30700695, ECO:0000269 PubMed:31091274,
ECO:0000269 PubMed:31526566, ECO:0000269 PubMed:33472215}
FUNCTION: [Secreted ninjurin-1]: Secreted form generated by cleavage
which has chemotactic activity (PubMed:23142597). Acts as an
anti-inflammatory mediator by promoting monocyte recruitment, thereby
ameliorating atherosclerosis (PubMed:32883094).
{ECO:0000269 PubMed:23142597, ECO:0000269 PubMed:32883094}
FUNCTION: Phosphorylates a large number of substrates in the
cytoplasm and the nucleus (By similarity). Phosphorylates CDC25B,
ABL1, NFKB1, CLDN3, PSMC5/RPT6, PJA2, RYR2, RORA, SOX9
and VASP (PubMed:10805756, PubMed:19223768). Regulates the
abundance of compartmentalized pools of its regulatory subunits through
phosphorylation of PJA2 which binds and ubiquitinates these subunits,
leading to their subsequent proteolysis (By similarity). RORA is activat
by phosphorylation. Required for glucose-mediated adipogenic
cAMP-dependent protein
kinase catalytic subunit  differentiation increase and osteogenic differentiation inhibition from
osteoblasts (By similarity). Involved in chondrogenesis by mediating
phosphorylation of SOX9 (PubMed:10805756). Involved in the
regulation of platelets in response to thrombin and collagen; maintains
circulating platelets in a resting state by phosphorylating proteins in
numerous platelet inhibitory pathways when in complex with
NF-kappa-B (NFKB1 and NFKB2) and I-kappa-B-alpha (NFKBIA), bu
thrombin and collagen disrupt these complexes and free active PRKAC
stimulates platelets and leads to platelet aggregation by phosphorylating
VASP. RYR2 channel activity is potentiated by phosphorylation in

		presence of luminal Ca(2+), leading to reduced amplitude and increased frequency of store overload-induced Ca(2+) release (SOICR) characterized by an increased rate of Ca(2+) release and propagation
		velocity of spontaneous Ca(2+) waves, despite reduced wave amplitude and resting cytosolic Ca(2+). PSMC5/RPT6 activation by
		phosphorylation stimulates proteasome. Negatively regulates tight
		junctions (TJs) in ovarian cancer cells via CLDN3 phosphorylation.
		NFKB1 phosphorylation promotes NF-kappa-B p50-p50 DNA binding.
		Involved in embryonic development by down-regulating the Hedgehog
		(Hh) signaling pathway that determines embryo pattern formation and
		morphogenesis (By similarity). Prevents meiosis resumption in
		prophase-arrested oocytes via CDC25B inactivation by phosphorylation
		(PubMed:19223768). May also regulate rapid eye movement (REM)
		sleep in the pedunculopontine tegmental (PPT) (By similarity).
		Phosphorylates APOBEC3G and AICDA. Phosphorylates HSF1; this
		phosphorylation promotes HSF1 nuclear localization and transcriptional
		activity upon heat shock (By similarity).
		{ECO:0000250 UniProtKB:P17612, ECO:0000250 UniProtKB:P27791,
		ECO:0000269 PubMed:10805756, ECO:0000269 PubMed:19223768}.;
		FUNCTION: [Isoform 2]: Phosphorylates and activates ABL1 in sperm flagellum to promote spermatozoa capacitation.
		{ECO:0000269 PubMed:15340140, ECO:0000269 PubMed:19560455}.
		FUNCTION: Receptor for both interleukin 4 and interleukin 13. Couples
		to the JAK1/2/3-STAT6 pathway. The IL4 response is involved in
Interleukin-4 receptor	810	promoting Th2 differentiation. The IL4/IL13 responses are involved in
subunit alpha		regulating IgE production and, chemokine and mucus production at sites
		of allergic inflammation. In certain cell types, can signal through
		activation of insulin receptor substrates, IRS1/IRS2.
		FUNCTION: Required for mitosis progression. Promotes the nucleation
		of microtubules from the spindle (By similarity). May play an important
Protein NEDD1	660	role during the embryonic development and differentiation of the central
		nervous system (PubMed:1378265).
		{ECO:0000250 UniProtKB:Q8NHV4, ECO:0000269 PubMed:1378265}.
		FUNCTION: Calcium-dependent, calmodulin-stimulated protein
		phosphatase which plays an essential role in the transduction of
		intracellular Ca(2+)-mediated signals (PubMed:7791792,
		PubMed:26794871). Many of the substrates contain a PxIxIT motif
Protein phosphatase 3		and/or a LxVP motif (By similarity). In response to increased Ca(2+)
catalytic subunit alpha	521	levels, dephosphorylates and activates phosphatase SSH1 which results in
		cofilin dephosphorylation (By similarity). In response to increased
		Ca(2+) levels following mitochondrial depolarization, dephosphorylates
		DNM1L inducing DNM1L translocation to the mitochondrion (By
		similarity). Positively regulates the CACNA1B/CAV2.2-mediated Ca(2+)
		release probability at hippocampal neuronal soma and synaptic terminals

(By similarity). Dephosphorylates heat shock protein HSPB1 (By similarity). Dephosphorylates and activates transcription factor NFATC1 (By similarity). Dephosphorylates and inactivates transcription factor ELK1 (By similarity). Dephosphorylates DARPP32 (By similarity). May dephosphorylate CRTC2 at 'Ser-171' resulting in CRTC2 dissociation from 14-3-3 proteins (By similarity). Required for postnatal development of the nephrogenic zone and superficial glomeruli in the kidneys, cell cycle homeostasis in the nephrogenic zone, and ultimately normal kidney function (PubMed:15509543). Plays a role in intracellular AQP2 processing and localization to the apical membrane in the kidney, may thereby be required for efficient kidney filtration (PubMed:16735444). Required for secretion of salivary enzymes amylase, peroxidase, lysozyme and sialic acid via formation of secretory vesicles in the submandibular glands (PubMed:21435446). Required for calcineurin activity and homosynaptic depotentiation in the hippocampus (PubMed:10200317). Required for normal differentiation and survival of keratinocytes and therefore required for epidermis superstructure formation (PubMed:19626032). Positively regulates osteoblastic bone formation, via promotion of osteoblast differentiation (PubMed:16286645). Positively regulates osteoclast differentiation, potentially via NFATC1 signaling (PubMed:16968888). May play a role in skeletal muscle fiber type specification, potentially via NFATC1 signaling (PubMed:12773574). Negatively regulates MAP3K14/NIK signaling via inhibition of nuclear translocation of the transcription factors RELA and RELB (PubMed:26029823). Required for antigen-specific T-cell proliferation response (PubMed:8627154). {ECO:0000250|UniProtKB:P48452, ECO:0000250|UniProtKB:P63329, ECO:0000250|UniProtKB:Q08209, ECO:0000269|PubMed:10200317, ECO:0000269|PubMed:12773574, ECO:0000269|PubMed:15509543, ECO:0000269|PubMed:16286645, ECO:0000269|PubMed:16735444, ECO:0000269|PubMed:16968888, ECO:0000269|PubMed:19626032, ECO:0000269|PubMed:21435446, ECO:0000269|PubMed:26029823, ECO:0000269|PubMed:26794871, ECO:0000269|PubMed:7791792, ECO:0000269|PubMed:8627154}. FUNCTION: Self-ligand receptor of the signaling lymphocytic activation molecule (SLAM) family. SLAM receptors triggered by homo- or heterotypic cell-cell interactions are modulating the activation and differentiation of a wide variety of immune cells and thus are involved in the regulation and interconnection of both innate and adaptive immune 329 SLAM family member 5 response. Activities are controlled by presence or absence of small cytoplasmic adapter proteins, SH2D1A/SAP and/or SH2D1B/EAT-2 (PubMed:20962259). Can mediate natural killer (NK) cell cytotoxicity dependent on SH2D1A and SH2D1B (PubMed:20962259). Increases proliferative responses of activated T-cells and SH2D1A/SAP does not

		seen be required for this process. Homophilic interactions enhance
		interferon gamma/IFNG secretion in lymphocytes and induce platelet
		stimulation via a SH2D1A/SAP-dependent pathway. May serve as a
		marker for hematopoietic progenitor cells (By similarity). Required for a
		prolonged T-cell:B-cell contact, optimal T follicular helper function, and
		germinal center formation (PubMed:20153220). In germinal centers
		involved in maintaining B cell tolerance and in preventing autoimmunity
		(PubMed:25801429). In mast cells negatively regulates high affinity
		immunoglobulin epsilon receptor signaling; independent of SH2D1A and
		SH2D1B but implicating FES and PTPN6/SHP-1 (By similarity). In
		macrophages enhances LPS-induced MAPK phosphorylation and
		NF-kappaB activation and modulates LPS-induced cytokine secretion;
		involving ITSM 2 (PubMed:20628063). Positively regulates
		macroautophagy in primary dendritic cells via stabilization of IRF8;
		inhibits TRIM21-mediated proteasomal degradation of IRF8 (By
		similarity). {ECO:0000250 UniProtKB:Q9UIB8,
		ECO:0000269 PubMed:16037392, ECO:0000269 PubMed:20153220,
		ECO:0000269 PubMed:20628063, ECO:0000269 PubMed:20962259,
		ECO:0000269 PubMed:25801429, ECO:0000305}.
		FUNCTION: Plays a role in primary cilia formation (By similarity). May
		act as a downstream effector of HOXC8 possibly by transducing or
		transmitting extracellular information required for axial skeletal
Transmembrane anterior		patterning during development (By similarity). May be involved in
posterior transformation	564	cartilage and bone development (By similarity). May play a role in the
protein 1		differentiation of cranial neural crest cells (By similarity).
		{ECO:0000250 UniProtKB:A2BIE7,
		ECO:0000250 UniProtKB:Q6NXT6, ECO:0000269 PubMed:17151244}.
		FUNCTION: [Fibrillin-1]: Structural component of the 10-12 nm
		diameter microfibrils of the extracellular matrix, which conveys both
		structural and regulatory properties to load-bearing connective tissues.
		Fibrillin-1-containing microfibrils provide long-term force bearing
		structural support. In tissues such as the lung, blood vessels and skin,
		microfibrils form the periphery of the elastic fiber, acting as a scaffold for
		the deposition of elastin. In addition, microfibrils can occur as
		elastin-independent networks in tissues such as the ciliary zonule, tendon,
Fibrillin-1	2873	cornea and glomerulus where they provide tensile strength and have
		anchoring roles. Fibrillin-1 also plays a key role in tissue homeostasis
		through specific interactions with growth factors, such as the bone
		morphogenetic proteins (BMPs), growth and differentiation factors
		(GDFs) and latent transforming growth factor-beta-binding proteins
		(LTBPs), cell-surface integrins and other extracellular matrix protein and
		proteoglycan components (By similarity). Regulates osteoblast
		maturation by controlling TGF-beta bioavailability and calibrating
		TGF-beta and BMP levels, respectively (PubMed:20855508). Negatively
	l	

		regulates osteoclastogenesis by binding and sequestering an osteoclast
		differentiation and activation factor TNFSF11. This leads to disruption of
		TNFSF11-induced Ca(2+) signaling and impairment of
		TNFSF11-mediated nuclear translocation and activation of transcription
		factor NFATC1 which regulates genes important for osteoclast
		differentiation and function (PubMed:24039232). Mediates cell adhesion
		via its binding to cell surface receptors integrins ITGAV:ITGB3 and
		ITGA5:ITGB1. Binds heparin and this interaction plays an important role
		in the assembly of microfibrils (By similarity).
		{ECO:0000250 UniProtKB:P35555, ECO:0000269 PubMed:20855508,
		ECO:0000269 PubMed:24039232}.; FUNCTION: [Asprosin]: Adipokine
		secreted by white adipose tissue that plays an important regulatory role in
		the glucose metabolism of liver, muscle and pancreas
		(PubMed:31230984, PubMed:30997682). Hormone that targets the liver
		in response to fasting to increase plasma glucose levels
		(PubMed:31230984). Binds the olfactory receptor Olfr734 at the surface
		of hepatocytes and promotes hepatocyte glucose release by activating the
		protein kinase A activity in the liver, resulting in rapid glucose release
		into the circulation (PubMed:31230984). May act as a regulator of
		adaptive thermogenesis by inhibiting browning and energy consumption,
		while increasing lipid deposition in white adipose tissue
		(PubMed:33705351). Also acts as an orexigenic hormone that increases
		appetite: crosses the blood brain barrier and exerts effects on the
		hypothalamus (PubMed:29106398). In the arcuate nucleus of the
		hypothalamus, asprosin directly activates orexigenic AgRP neurons and
		indirectly inhibits anorexigenic POMC neurons, resulting in appetite
		stimulation (PubMed:29106398, PubMed:32337066). Activates
		orexigenic AgRP neurons via binding to the olfactory receptor Olfr734
		(PubMed:32337066). May also play a role in sperm motility in testis via
		interaction with Olfr734 receptor (PubMed:31798959).
		{ECO:0000269 PubMed:29106398, ECO:0000269 PubMed:30997682,
		ECO:0000269 PubMed:31230984, ECO:0000269 PubMed:31798959,
		ECO:0000269 PubMed:32337066, ECO:0000269 PubMed:33705351}.
		FUNCTION: May play a role in intercellular signaling and in connecting
Versican core protein	3357	cells with the extracellular matrix. May take part in the regulation of cell
		motility, growth and differentiation. Binds hyaluronic acid.
		FUNCTION: Catalyzes the saturation of all-trans-retinol to
		all-trans-13,14-dihydroretinol (PubMed:15358783, PubMed:17253779,
		PubMed:19139408). Does not exhibit any activity toward
All-trans-retinol	609	all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers
13,14-reductase	009	(PubMed:15358783). May play a role in the metabolism of vitamin A
		(PubMed:15358783, PubMed:17253779). Independently of retinol
		conversion, may regulate liver metabolism upstream of
		MLXIPL/ChREBP (PubMed:28855500). Required for adipocyte

		1100
		differentiation in a 3T3-L1 cell culture model (PubMed:19139408). This effect seems not to mimic the in vivo situation in which animals show increased adiposity in the absence of RETSAT (PubMed:19940255). {ECO:0000269 PubMed:15358783, ECO:0000269 PubMed:17253779, ECO:0000269 PubMed:19139408, ECO:0000269 PubMed:19940255, ECO:0000269 PubMed:28855500, ECO:0000305 PubMed:19940255}.
Calcium-transporting ATPase type 2C member 1	918	FUNCTION: ATP-driven pump that supplies the Golgi apparatus with Ca(2+) and Mn(2+) ions, both essential cofactors for processing and trafficking of newly synthesized proteins in the secretory pathway (By similarity). Within a catalytic cycle, acquires Ca(2+) or Mn(2+) ions on the cytoplasmic side of the membrane and delivers them to the lumenal side. The transfer of ions across the membrane is coupled to ATP hydrolysis and is associated with a transient phosphorylation that shifts the pump conformation from inward-facing to outward-facing state (By similarity). Plays a primary role in the maintenance of Ca(2+) homeostasis in the trans-Golgi compartment with a functional impact on Golgi and post-Golgi protein sorting as well as a structural impact on cisternae morphology. Responsible for loading the Golgi stores with Ca(2+) ions in keratinocytes, contributing to keratinocyte differentiation and epidermis integrity (By similarity). Participates in Ca(2+) and Mn(2+) ions uptake into the Golgi store of hippocampal neurons and regulates protein trafficking required for neural polarity (PubMed:19793975). May also play a role in the maintenance of Ca(2+) and Mn(2+) homeostasis and signaling in the cytosol while preventing cytotoxicity (By similarity). {ECO:0000250 UniProtKB:P98194, ECO:0000269 PubMed:19793975}.
Exopolyphosphatase PRUNE1	454	FUNCTION: Phosphodiesterase (PDE) that has higher activity toward cAMP than cGMP, as substrate. Plays a role in cell proliferation, migration and differentiation, and acts as a negative regulator of NME1. Plays a role in the regulation of neurogenesis. Involved in the regulation of microtubule polymerization. {ECO:0000250 UniProtKB:Q86TP1}.
Adipocyte plasma membrane-associated protein	415	FUNCTION: Exhibits strong arylesterase activity with beta-naphthyl acetate and phenyl acetate (By similarity). May play a role in adipocyte differentiation. {ECO:0000250}.
Fibroblast growth factor 23	251	FUNCTION: Regulator of phosphate homeostasis (By similarity). Inhibits renal tubular phosphate transport by reducing SLC34A1 levels (By similarity). Acts directly on the parathyroid to decrease PTH secretion (By similarity). Regulator of vitamin-D metabolism (By similarity). Negatively regulates osteoblasts differentiation and matrix mineralization (By similarity). Up-regulates EGR1 expression in the presence of KL. {ECO:0000250, ECO:0000269 PubMed:17086194}.
P2X purinoceptor 4	388	FUNCTION: Receptor for extracellularly released ATP acting as a ligand-gated ion channel that plays multiple role in immunity and central nervous system physiology (PubMed:26456657, PubMed:35119925).

		Plays a key role in initial steps of T-cell activation and Ca(2+) microdomain formation (PubMed:35119925). Participates also in basal T-cell activity without TCR/CD3 stimulation (PubMed:35119925). Promotes the differentiation and activation of Th17 cells via expression of retinoic acid-related orphan receptor C/RORC (By similarity). Upon activation, drives microglia motility via the PI3K/Akt pathway (PubMed:17299767). {ECO:0000250 UniProtKB:Q99571, ECO:0000269 PubMed:17299767, ECO:0000269 PubMed:35119925}.
Exostosin-like 3	918	FUNCTION: Glycosyltransferase which regulates the biosynthesis of heparan sulfate (HS). Important for both skeletal development and hematopoiesis, through the formation of HS proteoglycans (HSPGs).  Required for the function of REG3A in regulating keratinocyte proliferation and differentiation (By similarity).  {ECO:0000250 UniProtKB:O43909}.
Vacuolar protein sorting-associated protein 37B	285	FUNCTION: Component of the ESCRT-I complex, a regulator of vesicular trafficking process. Required for the sorting of endocytic ubiquitinated cargos into multivesicular bodies. May be involved in cell growth and differentiation (By similarity). {ECO:0000250}.
Ubiquitin-conjugating enzyme E2 variant 1	147	FUNCTION: Has no ubiquitin ligase activity on its own. The UBE2V1-UBE2N heterodimer catalyzes the synthesis of non-canonical poly-ubiquitin chains that are linked through 'Lys-63'. This type of poly-ubiquitination activates IKK and does not seem to involve protein degradation by the proteasome. Plays a role in the activation of NF-kappa-B mediated by IL1B, TNF, TRAF6 and TRAF2. Mediates transcriptional activation of target genes. Plays a role in the control of progress through the cell cycle and differentiation (By similarity). Plays a role in the error-free DNA repair pathway and contributes to the survival of cells after DNA damage. Promotes TRIM5 capsid-specific restriction activity and the UBE2V1-UBE2N heterodimer acts in concert with TRIM5 to generate 'Lys-63'-linked polyubiquitin chains which activate the MAP3K7/TAK1 complex which in turn results in the induction and expression of NF-kappa-B and MAPK-responsive inflammatory genes (By similarity). Together with RNF135 and UBE2N, catalyzes the viral RNA-dependent 'Lys-63'-linked polyubiquitination of RIG-I/DDX58 to activate the downstream signaling pathway that leads to interferon beta production (By similarity). UBE2V1-UBE2N together with TRAF3IP2 E3 ubiquitin ligase mediate 'Lys-63'-linked polyubiquitination of TRAF6, a component of IL17A-mediated signaling pathway. {ECO:0000250, ECO:0000250 UniProtKB:Q13404, ECO:0000269 PubMed:11406273}.
Ubiquitin carboxyl-terminal hydrolase 25	1055	FUNCTION: Deubiquitinating enzyme that hydrolyzes ubiquitin moieties conjugated to substrates and thus, functions to process newly synthesized Ubiquitin, to recycle ubiquitin molecules or to edit polyubiquitin chains and prevents proteasomal degradation of substrates. Hydrolyzes both

	T	
		'Lys-48'- and 'Lys-63'-linked tetraubiquitin chains (By similarity).
		{ECO:0000250}.; FUNCTION: The muscle-specific isoform (USP25m)
		may have a role in the regulation of muscular differentiation and function.
		FUNCTION: Transcriptional regulator involved in different processes
		such as glucose metabolism, aerobic glycolysis, muscle cell
		differentiation and autophagy (PubMed:25402684, PubMed:29861159,
		PubMed:30700909). Recognizes and binds the forkhead DNA sequence
		motif (5'-GTAAACA-3') and can both act as a transcription activator or
		repressor, depending on the context (PubMed:25402684,
		PubMed:29861159, PubMed:30700909). Together with FOXK2, acts as a
		key regulator of metabolic reprogramming towards aerobic glycolysis, a
		process in which glucose is converted to lactate in the presence of oxygen
		(PubMed:30700909). Acts by promoting expression of enzymes for
		glycolysis (such as hexokinase-2 (HK2), phosphofructokinase, pyruvate
		kinase (PKLR) and lactate dehydrogenase), while suppressing further
		oxidation of pyruvate in the mitochondria by up-regulating pyruvate
		dehydrogenase kinases PDK1 and PDK4 (PubMed:30700909). Probably
		plays a role in gluconeogenesis during overnight fasting, when lactate
		from white adipose tissue and muscle is the main substrate
		(PubMed:30700909). Involved in mTORC1-mediated metabolic
		reprogramming: in response to mTORC1 signaling, translocates into the
		nucleus and regulates the expression of genes associated with glycolysis
		and downstream anabolic pathways, such as HIF1A, thereby regulating
Forkhead box protein K1	719	glucose metabolism (PubMed:29861159). Together with FOXK2, acts as
		a negative regulator of autophagy in skeletal muscle: in response to
		starvation, enters the nucleus, binds the promoters of autophagy genes
		and represses their expression, preventing proteolysis of skeletal muscle
		proteins (PubMed:25402684). Acts as a transcriptional regulator of the
		myogenic progenitor cell population in skeletal muscle
		(PubMed:8007964, PubMed:9271401, PubMed:12446708,
		PubMed:22956541). Binds to the upstream enhancer region (CCAC box)
		of myoglobin (MB) gene, regulating the myogenic progenitor cell
		population (PubMed:8007964, PubMed:9271401). Promotes muscle
		progenitor cell proliferation by repressing the transcriptional activity of
		FOXO4, thereby inhibiting myogenic differentiation (PubMed:12446708,
		PubMed:22956541). Involved in remodeling processes of adult muscles
		that occur in response to physiological stimuli (PubMed:9271401,
		PubMed:22956541). Required to correct temporal orchestration of
		molecular and cellular events necessary for muscle repair
		(PubMed:10792059). Represses myogenic differentiation by inhibiting
		MEFC activity (PubMed:22956541). Positively regulates
		Wnt/beta-catenin signaling by translocating DVL into the nucleus (By
1		
		similarity). Reduces virus replication, probably by binding the interferon
		that occur in response to physiological stimuli (PubMed:9271401, PubMed:22956541). Required to correct temporal orchestration of molecular and cellular events necessary for muscle repair (PubMed:10792059). Represses myogenic differentiation by inhibiting MEFC activity (PubMed:22956541). Positively regulates Wnt/beta-catenin signaling by translocating DVL into the nucleus (By

(By similarity). {ECO:0000250 UniProtKB:P85037, ECO:0000269 PubMed:10792059, ECO:0000269 PubMed:124467 ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:254026 ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:307009 ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401	84, 09,
ECO:0000269 PubMed:22956541, ECO:0000269 PubMed:254026 ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:307009	84, 09,
ECO:0000269 PubMed:29861159, ECO:0000269 PubMed:307009	09,
ECO:0000269 PubMed:8007964, ECO:0000269 PubMed:9271401	<b>}</b> .
FUNCTION: Component of the cleavage and polyadenylation spec	ificity
factor (CPSF) complex that plays a key role in pre-mRNA 3'-end	
formation, recognizing the AAUAAA signal sequence and interact	ng
with poly(A) polymerase and other factors to bring about cleavage	and
poly(A) addition. Has endonuclease activity, and functions as mRN	A
3'-end-processing endonuclease. Also involved in the histone 3'-end	i
pre-mRNA processing. U7 snRNP-dependent protein that induces	ooth
the 3' endoribonucleolytic cleavage of histone pre-mRNAs and acts	as a
5' to 3' exonuclease for degrading the subsequent downstream clear	age
product (DCP) of mature histone mRNAs. Cleavage occurs after the	e
5'-ACCCA-3' sequence in the histone pre-mRNA leaving a 3'hydro	xyl
group on the upstream fragment containing the stem loop (SL) and	
Cleavage and phosphate on the downstream cleavage product (DCP) starting with	
polyadenylation nucleotides. The U7-dependent 5' to 3' exonuclease activity is proc	
specificity factor subunit and degrades the DCP RNA substrate even after complete removal	
3 U7-binding site. Binds to the downstream cleavage product (DCP)	
histone pre-mRNAs and the cleaved DCP RNA substrate in a U7 st	
dependent manner. Required for the selective processing of microR	
(miRNAs) during embryonic stem cell differentiation via its interaction	
with ISY1 (PubMed:26255770, PubMed:29804889). Required for	tion
entering/progressing through S-phase of the cell cycle (By similarit	w)
Required for the biogenesis of all miRNAs from the pri-miR-17-92	
primary transcript except miR-92a (PubMed:26255770). Only requ	
for the biogenesis of miR-290 and miR-96 from the pri-miR-290-2	
pri-miR-96-183 primary transcripts, respectively (PubMed:298048	,
{ECO:0000250 UniProtKB:Q9UKF6, ECO:0000269 PubMed:162	
ECO:0000269 PubMed:18955505, ECO:0000269 PubMed:194707	
ECO:0000269 PubMed:26255770, ECO:0000269 PubMed:298048	89}.
FUNCTION: Serine/threonine kinase which acts as an essential	
component of the MAP kinase signal transduction pathway.	
MAPK1/ERK2 and MAPK3/ERK1 are the 2 MAPKs which play a	
important role in the MAPK/ERK cascade. They participate also in	
Mitogen-activated protein signaling cascade initiated by activated KIT and KITLG/SCF. Dep	ending
sinase 1 358 on the cellular context, the MAPK/ERK cascade mediates diverse	
biological functions such as cell growth, adhesion, survival and	
differentiation through the regulation of transcription, translation,	
cytoskeletal rearrangements. The MAPK/ERK cascade also plays a	role
in initiation and regulation of meiosis, mitosis, and postmitotic fund	ctions
in differentiated cells by phosphorylating a number of transcription	

factors. About 160 substrates have already been discovered for ERKs. Many of these substrates are localized in the nucleus, and seem to participate in the regulation of transcription upon stimulation. However, other substrates are found in the cytosol as well as in other cellular organelles, and those are responsible for processes such as translation, mitosis and apoptosis. Moreover, the MAPK/ERK cascade is also involved in the regulation of the endosomal dynamics, including lysosome processing and endosome cycling through the perinuclear recycling compartment (PNRC); as well as in the fragmentation of the Golgi apparatus during mitosis. The substrates include transcription factors (such as ATF2, BCL6, ELK1, ERF, FOS, HSF4 or SPZ1), cytoskeletal elements (such as CANX, CTTN, GJA1, MAP2, MAPT, PXN, SORBS3 or STMN1), regulators of apoptosis (such as BAD, BTG2, CASP9, DAPK1, IER3, MCL1 or PPARG), regulators of translation (such as EIF4EBP1) and a variety of other signaling-related molecules (like ARHGEF2, DCC, FRS2 or GRB10). Protein kinases (such as RAF1, RPS6KA1/RSK1, RPS6KA3/RSK2, RPS6KA2/RSK3, RPS6KA6/RSK4, SYK, MKNK1/MNK1, MKNK2/MNK2, RPS6KA5/MSK1, RPS6KA4/MSK2, MAPKAPK3 or MAPKAPK5) and phosphatases (such as DUSP1, DUSP4, DUSP6 or DUSP16) are other substrates which enable the propagation the MAPK/ERK signal to additional cytosolic and nuclear targets, thereby extending the specificity of the cascade. Mediates phosphorylation of TPR in response to EGF stimulation. May play a role in the spindle assembly checkpoint. Phosphorylates PML and promotes its interaction with PIN1, leading to PML degradation. Phosphorylates CDK2AP2 (By similarity). {ECO:0000250|UniProtKB:P28482, ECO:0000250|UniProtKB:P63086, ECO:0000269|PubMed:10753946, ECO:0000269|PubMed:11702783, ECO:0000269|PubMed:12134156, ECO:0000303|PubMed:16393692, ECO:0000303|PubMed:19565474, ECO:0000303|PubMed:21779493}.; FUNCTION: Acts as a transcriptional repressor. Binds to a [GC]AAA[GC] consensus sequence. Repress the expression of interferon gamma-induced genes. Seems to bind to the promoter of CCL5, DMP1, IFIH1, IFITM1, IRF7, IRF9, LAMP3, OAS1, OAS2, OAS3 and STAT1. Transcriptional activity is independent of kinase activity. {ECO:0000250|UniProtKB:P28482}. FUNCTION: RNA-binding protein that acts as a key regulator of N6-methyladenosine (m6A) methylation of RNAs, thereby regulating different processes, such as hematopoietic cell homeostasis, alternative splicing of mRNAs and X chromosome inactivation mediated by Xist RNA-binding protein 15 962 RNA (PubMed:29535189). Associated component of the WMM complex, a complex that mediates N6-methyladenosine (m6A) methylation of RNAs, a modification that plays a role in the efficiency of mRNA splicing and RNA processing (PubMed:29535189). Plays a key

role in m6A methylation, possibly by binding target RNAs and recruiting the WMM complex (PubMed:29535189). Involved in random X inactivation mediated by Xist RNA: acts by binding Xist RNA and recruiting the WMM complex, which mediates m6A methylation, leading to target YTHDC1 reader on Xist RNA and promoting transcription repression activity of Xist (By similarity). Required for the development of multiple tissues, such as the maintenance of the homeostasis of long-term hematopoietic stem cells and for megakaryocyte (MK) and B-cell differentiation (PubMed:17283045, PubMed:17376872, PubMed:18981216, PubMed:25468569). Regulates megakaryocyte differentiation by regulating alternative splicing of genes important for megakaryocyte differentiation; probably regulates alternative splicing via m6A regulation (By similarity). Required for placental vascular branching morphogenesis and embryonic development of the heart and spleen (PubMed:18981216). Acts as a regulator of thrombopoietin response in hematopoietic stem cells by regulating alternative splicing of MPL (PubMed:25468569). May also function as an mRNA export factor, stimulating export and expression of RTE-containing mRNAs which are present in many retrotransposons that require to be exported prior to splicing (By similarity). High affinity binding of pre-mRNA to RBM15 may allow targeting of the mRNP to the export helicase DBP5 in a manner that is independent of splicing-mediated NXF1 deposition, resulting in export prior to splicing (By similarity). May be implicated in HOX gene regulation (By similarity). {ECO:0000250|UniProtKB:Q96T37, ECO:0000269|PubMed:17283045,

ECO:0000269|PubMed:25468569, ECO:0000269|PubMed:29535189}.

BDEs, bile duct epithelial cells; Ger, generation; HOCs, hepatic oval cells; NCBI, National Center for

Biotechnology Information.

ECO:0000269|PubMed:17376872, ECO:0000269|PubMed:18981216,