Table SI. The genes in OSgset.

Human symbol	Name	gene ID	Uniprot ID
ACTN3	Actinin alpha 3	89	Q08043
ADAMTS18	ADAM metallopeptidase with thrombospondin type 1 motif 18	170692	Q8TE60
ADCY10	Adenylate cyclase 10	55811	Q96PN6
ADIPOQ	Adiponectin, C1Q and collagen domain containing	9370	Q96A54
ADRA2A	Adrenoceptor alpha 2A	150	P08913
AGTR2	Angiotensin II receptor type 2	186	P50052
AKAP11	A-kinase anchoring protein 11	11215	Q9UKA4
AKAP13	A-kinase anchoring protein 13	11214	Q12802
AKR1A1	Aldo-keto reductase family 1 member A1	10327	P14550
ALOX15	Arachidonate 15-lipoxygenase	246	P16050
ALOX5	Arachidonate 5-lipoxygenase	240	P09917
ALPL	Alkaline phosphatase, liver/bone/kidney	249	P05186
ANXA6	Annexin A6	309	P08133
APC	APC, WNT signaling pathway regulator	324	P25054
AKR1B1	Aldo-keto reductase family 1 member B	231	P15121
ARHGAP1	Rho GTPase activating protein 1	392	Q07960
ARHGEF3	Rho guanine nucleotide exchange factor 3	50650	Q9NR81
ATP5F1E	ATP synthase F1 subunit epsilon	514	P56381
ATP6V1G1	ATPase H+ transporting V1 subunit G1	9550	O75348
ATP6V1H	ATPase H+ transporting V1 subunit H	51606	Q9UI12
AVP	Arginine vasopressin	551	P01185
B2M	Beta-2-microglobulin	567	P61769
BDNF	Brain derived neurotrophic factor	627	P23560
BMP2	Bone morphogenetic protein 2	650	P12643
BMP7	Bone morphogenetic protein 7	655	P18075
BMPR1B	Bone morphogenetic protein receptor type 1B	658	O00238
IBSP	Integrin binding sialoprotein	3381	P21815
CCDC170	Coiled-coil domain containing 170	80129	Q8IYT3
CA10	Carbonic anhydrase 10	56934	Q9NS85
CA8	Carbonic anhydrase 8	767	P35219
CALM1	Calmodulin 1	801	P0DP23
CASR	Calcium sensing receptor	846	P41180
CAT	Catalase	847	P04040
CNR1	Cannabinoid receptor 1	1268	P21554
CCNE1	Cyclin E1	898	P24864
REL	REL proto-oncogene, NF-kB subunit	5966	Q00653
CCR2	C-C motif chemokine receptor 2	729230	P41597
CD200	CD200 molecule	4345	P41217
CD40	CD40 molecule	958	P25942
CD40LG	CD40 ligand	959	P29965
CER1	Cerberus 1, DAN family BMP antagonist	9350	O95813
CFTR	Cystic fibrosis transmembrane conductance regulator	1080	P13569
CHD2	Chromodomain helicase DNA binding protein 2	1106	O14647
CIITA	Class II major histocompatibility complex transactivator	4261	P33076
CLCN7	Chloride voltage-gated channel 7	1186	P51798
CLDN14	Claudin 14	23562	O95500
CLEC16A	C-type lectin domain containing 16A	23274	Q2KHT3
CNOT7	CCR4-NOT transcription complex subunit 7	29883	Q9UIV1
CNR2	Cannabinoid receptor 2	1269	P34972
COL1A1	Collagen type I alpha 1 chain	1277	P02452
COL6A1	Collagen type VI alpha 1 chain	1291	P12109
COL9A1	Collagen type IX alpha 1 chain	1297	P20849
MYO5A	Myosin VA	4644	Q9Y4I1
COMT	Catechol-O-methyltransferase	1312	P21964
CPB2	Carboxypeptidase B2	1361	Q96IY4
CRHR1	Corticotropin releasing hormone receptor 1	1394	P34998
CRTAP	Cartilage associated protein	10491	O75718
CSTA	Cystatin A	1475	P01040
TYROBP	TYRO protein tyrosine kinase binding protein	7305	O43914

Table SI. Continued.

Human symbol	Name	gene ID	Uniprot ID
CTHRC1	Collagen triple helix repeat containing 1	115908	Q96CG8
CTNNB1	Catenin beta 1	1499	P35222
CALCR	Calcitonin receptor	799	P30988
CTSZ	Cathepsin Z	1522	Q9UBR2
CXCR4	C-X-C motif chemokine receptor 4	7852	P61073
CYLD	CYLD lysine 63 deubiquitinase	1540	Q9NQC7
CYP17A1	Cytochrome P450 family 17 subfamily A member 1	1586	P05093
CYP19A1	Cytochrome P450 family 19 subfamily A member 1	1588	P11511
CYP1A1	Cytochrome P450 family 1 subfamily A member 1	1543	P04798
CYP1B1	Cytochrome P450 family 1 subfamily B member 1	1545	Q16678
CYP24A1	Cytochrome P450 family 24 subfamily A member 1	1591	Q07973
DBP	D-box binding PAR bZIP transcription factor	1628	Q10586
DCDC1	Doublecortin domain containing 1	341019	Q6ZRR9
DICER1	Dicer 1, ribonuclease III	23405	Q9UPY3
DKK1	Dickkopf WNT signaling pathway inhibitor 1	22943	O94907
DKK2	Dickkopf WNT signaling pathway inhibitor 2	27123	Q9UBU2
DLX5	Distal-less homeobox 5	1749	P56178
DMP1	Dentin matrix acidic phosphoprotein 1	1758	Q13316
ENPP1	Ectonucleotide pyrophosphatase/phosphodiesterase 1	5167	P22413
ESR1	Estrogen receptor 1	2099	P03372
ESRRA	Estrogen related receptor alpha	2101	P11474
FABP3	Fatty acid binding protein 3	2170	P05413
FAM210A	Family with sequence similarity 210 member A	125228	Q96ND0
FAM3C	Family with sequence similarity 3 member C	10447	Q92520
FGF20	Fibroblast growth factor 20	26281	Q9NP95
FGFR1	Fibroblast growth factor receptor 1	2260	P11362
FGFR2	Fibroblast growth factor receptor 2	2263	P21802
FGFRL1	Fibroblast growth factor receptor like 1	53834	Q8N441
FLNB	Filamin B	2317	O75369
FLT1	Fms related tyrosine kinase 1	2321	P17948
BRD2	Bromodomain containing 2	6046	P25440
FTCDNL1	Formiminotransferase cyclodeaminase N-terminal like	348751	E5RQL4
FOXC2	Forkhead box C2	2303	Q99958
FOXL1	Forkhead box L1	2300	Q12952
FRZB	Frizzled related protein	2487	Q92765
FTO	FTO, alpha-ketoglutarate dependent dioxygenase	79068	Q9C0B1
FZD1	Frizzled class receptor 1	8321	Q9UP38
FZD6	Frizzled class receptor 6	8323	O60353
GALNT3	Polypeptide N-acetylgalactosaminyltransferase 3	2591	Q14435
GDF5	Growth differentiation factor 5	8200	P43026
GHRH	Growth hormone releasing hormone	2691	P01286
GIP	Gastric inhibitory polypeptide	2695	P09681
GIPR	Gastric inhibitory polypeptide receptor	2696	P48546
GSTM3	Glutathione S-transferase mu 3	2947	P21266
GPC6	Glypican 6	10082	Q9Y625
GPNMB	Glycoprotein nmb	10457	Q14956
WLS	wntless Wnt ligand secretion mediator	79971	Q5T9L3
GPER1	G protein-coupled estrogen receptor 1	2852	Q99527
ADGRV1	Adhesion G protein-coupled receptor V1	84059	Q8WXG9
NR3C1	Nuclear receptor subfamily 3 group C member 1	2908	P04150
GREM2	Gremlin 2, DAN family BMP antagonist	64388	Q9H772
GSR	Glutathione-disulfide reductase	2936	P00390
GSTP1	Glutathione S-transferase pi 1	2950	P09211
HDAC5	Histone deacetylase 5	10014	Q9UQL6
HIF1A	Hypoxia inducible factor 1 alpha subunit	3091	Q16665
REG3A	Regenerating family member 3 alpha	5068	Q06141
RPL29	Ribosomal protein L29	6159	P47914
HLA-A	Major histocompatibility complex, class I, A	3105	P01892
HLA-B	Major histocompatibility complex, class I, B	3106	P03989

Table SI. Continued.

Human symbol	Name	gene ID	Uniprot ID
HMGA2	High mobility group AT-hook 2	8091	P52926
HSD11B1	Hydroxysteroid 11-beta dehydrogenase 1	3290	P28845
IDUA	Iduronidase, alpha-L-	3425	P35475
IGF1	Insulin like growth factor 1	3479	P05019
IGFBP2	Insulin like growth factor binding protein 2	3485	P18065
IL10	Interleukin 10	3586	P22301
IL15	Interleukin 15	3600	P40933
IL23A	Interleukin 23 subunit alpha	51561	Q9NPF7
IL23R	Interleukin 23 receptor	149233	Q5VWK5
IL6	Interleukin 6	3569	P05231
IL6R	Interleukin 6 receptor	3570	P08887
IL7	Interleukin 7	3574	P13232
ID4	Inhibitor of DNA binding 4, HLH protein	3400	P47928
SLCO6A1	Solute carrier organic anion transporter family member 6A1	133482	Q86UG4
IRF8	Interferon regulatory factor 8	3394	Q02556
ITGA1	Integrin subunit alpha 1	3672	P56199
JAG1	Jagged 1	182	P78504
JUND	JunD proto-oncogene, AP-1 transcription factor subunit	3727	P17535
LCT	Lactase	3938	P09848
LEPR	Leptin receptor	3953	P48357
LHB	Luteinizing hormone beta polypeptide	3972	P01229
LHCGR	Luteinizing hormone/choriogonadotropin receptor	3973	P22888
LRP1	LDL receptor related protein 1	4035	Q07954
LRP4	LDL receptor related protein 4	4038	O75096
LRP5	LDL receptor related protein 5	4041	O75197
LRP6	LDL receptor related protein 6	4040	O75581
LTBP2	Latent transforming growth factor beta binding protein 2	4053	Q14767
MAP4K4	Mitogen-activated protein kinase kinase kinase kinase 4	9448	O95819
MARK3	Microtubule affinity regulating kinase 3	4140	P27448
GLA	Galactosidase alpha	2717	P06280
CCL2	C-C motif chemokine ligand 2	6347	P13500
IFIH1	Interferon induced with helicase C domain 1	64135	Q9BYX4
ABCB1	ATP binding cassette subfamily B member 1	5243	P08183
MECOM	MDS1 and EVI1 complex locus	2122	Q03112
MECP2	Methyl-CpG binding protein 2	4204	P51608
MEF2C	Myocyte enhancer factor 2C	4208	Q06413
MEPE	Matrix extracellular phosphoglycoprotein	56955	Q9NQ76
MTHFR	Methylenetetrahydrofolate reductase	4524	P42898
MMP2	Matrix metallopeptidase 2	4313	P08253
MSTN	Myostatin	2660	O14793
DECR1	2,4-dienoyl-CoA reductase 1	1666	P30043
NCF1	Neutrophil cytosolic factor 1	653361	P14598
NF1	Neurofibromin 1	4763	P21359
NFATC1	Nuclear factor of activated T cells 1	4772	O95644
NLRC5	NLR family CARD domain containing 5	84166	Q86WI3
ZNF384	Zinc finger protein 384	171017	Q8TF68
NMU	Neuromedin U	10874	P48645
NOG	Noggin	9241	Q13253
NOS3	Nitric oxide synthase 3	4846	P29474
NPY	Neuropeptide Y	4852	P01303
NR1I3	Nuclear receptor subfamily 1 group I member 3	9970	Q14994
CLEC2D	C-type lectin domain family 2 member D	29121	Q9UHP7
ITLN1	Intelectin 1	55600	Q8WWA0
BTF3P11	Basic transcription factor 3 pseudogene 11	690	O00300
OXT	Oxytocin/neurophysin I prepropeptide	5020	X5D7M6
P2RX1	Purinergic receptor P2X 1	5023	P51575
P2RX7	Purinergic receptor P2X 7	5027	Q99572
SERPINE1	Serpin family E member 1	5054	P05121

Table SI. Continued.

Human symbol	Name	gene ID	Uniprot ID
PAPPA	Pappalysin 1	5069	Q13219
PBX1	PBX homeobox 1	5087	P40424
PCSK6	Proprotein convertase subtilisin/kexin type 6	5046	P29122
PECAM1	Platelet and endothelial cell adhesion molecule 1	5175	P16284
PIR	Pirin	8544	O00625
PLOD1	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1	5351	Q02809
PLS3	Plastin 3	5358	P13797
PRL	Prolactin	5617	P01236
PTCH1	Patched 1	5727	Q13635
PTH	Parathyroid hormone	5741	P01270
PTHLH	Parathyroid hormone like hormone	5744	P12272
PTH1R	Parathyroid hormone 1 receptor	5745	Q03431
PTH2R	Parathyroid hormone 2 receptor	5746	P49190
PTMA	Prothymosin alpha	5757	P06454
PTN	Pleiotrophin	5764	P21246
RAC1	Rac family small GTPase 1	5879	P63000
RAC2	Rac family small GTPase 2	5880	P15153
TNFRSF11A	TNF receptor superfamily member 11a	8792	Q9Y6Q6
TNFSF11	TNF superfamily member 11	8600	O14788
RB1	RB transcriptional corepressor 1	5925	P06400
RGMA	Repulsive guidance molecule BMP co-receptor a	56963	Q96B86
PRDM2	PR/SET domain 2	7799	Q13029
ROR2	Receptor tyrosine kinase like orphan receptor 2	4920	Q01974
RSPO3	R-spondin 3	84870	Q9BXY4
RUNX2	Runt related transcription factor 2	860	Q13950
SAA1	Serum amyloid A1	6288	P0DJI8
SATB2	SATB homeobox 2	23314	Q9UPW6
CASP3	Caspase 3	836	P54253
SFRP1	Secreted frizzled related protein 1	6422	Q8N474
SFRP2	Secreted frizzled related protein 2	6423	Q96HF1
SFRP4	Secreted frizzled related protein 4	6424	Q6FHJ7
SGCZ	Sarcoglycan zeta	137868	Q96LD1
SHBG	Sex hormone binding globulin	6462	P04278
SEM1	SEM1, 26S proteasome complex subunit	7979	P60896
SLC25A13	Solute carrier family 25 member 13	10165	Q9UJS0
PRELID3B	PRELI domain containing 3B	51012	Q9Y3B1
SMOC1	SPARC related modular calcium binding 1	64093	Q9H4F8
SOD1	Superoxide dismutase 1	6647	P00441
SOD2	Superoxide dismutase 2	6648	P04179
SOST	Sclerostin	50964	Q9BQB4
SOX4	SRY-box 4	6659	Q06945
SOX6	SRY-box 6	55553	P35712
SOX9	SRY-box 9	6662	P48436
SP7	Sp7 transcription factor	121340	Q8TDD2
SPARC	Secreted protein acidic and cysteine rich	6678	P09486
SPOP	Speckle type BTB/POZ protein	8405	O43791
SPP1	Secreted phosphoprotein 1	6696	P10451
SPP2	Secreted phosphoprotein 2	6694	Q13103
SPRY1	Sprouty RTK signaling antagonist 1	10252	O43609
SPTBN1	Spectrin beta, non-erythrocytic 1	6711	Q01082
NCOA1	Nuclear receptor coactivator 1	8648	Q15788
NCOA2	Nuclear receptor coactivator 2	10499	Q15596
SRD5A2	Steroid 5 alpha-reductase 2	6716	P31213
SREBF1	Sterol regulatory element binding transcription factor 1	6720	P36956
STARD3NL	STARD3 N-terminal like	83930	O95772
SQOR	Sulfide quinone oxidoreductase	58472	Q9Y6N5
TERC	Telomerase RNA component	7012	O14746
TGFBR3	Transforming growth factor beta receptor 3	7049	Q03167

Table SI. Continued.

Human symbol	Name	gene ID	Uniprot ID
THSD4	Thrombospondin type 1 domain containing 4	79875	Q 6 Z M P 0
THSD7A	Thrombospondin type 1 domain containing 7A	221981	Q9UPZ6
TIMP1	TIMP metallopeptidase inhibitor 1	7076	P01033
TIMP2	TIMP metallopeptidase inhibitor 2	7077	P16035
TMEM135	Transmembrane protein 135	65084	Q86UB9
TNF	Tumor necrosis factor	7124	Q5STB3
LTA	Lymphotoxin alpha	4049	P01374
TNFRSF1B	TNF receptor superfamily member 1B	7133	P20333
F2R	Coagulation factor II thrombin receptor	2149	A0A024RAP7
TRPS1	Transcriptional repressor GATA binding 1	7227	Q9UHF7
TRPV4	Transient receptor potential cation channel subfamily V member 4	59341	Q9HBA0
TSHR	Thyroid stimulating hormone receptor	7253	P16473
TUBA1B	Tubulin alpha 1b	10376	P68363
TWIST1	Twist family bHLH transcription factor 1	7291	Q15672
PLAUR	Plasminogen activator, urokinase receptor	5329	Q03405
CYP27B1	Cytochrome P450 family 27 subfamily B member 1	1594	P11473
VEGFA	Vascular endothelial growth factor A	7422	P15692
VPS13B	Vacuolar protein sorting 13 homolog B	157680	Q7Z7G8
DCAF13	DDB1 and CUL4 associated factor 13	25879	Q9NV06
WISP3	WNT1 inducible signaling pathway protein 3	8838	O95389
WNK4	WNK lysine deficient protein kinase 4	65266	Q96J92
WNT1	Wnt family member 1	7471	P04628
WNT10B	Wnt family member 10B	7480	O00744
WNT16	Wnt family member 16	51384	Q9UBV4
WNT3A	Wnt family member 3A	89780	P56704
WNT5B	Wnt family member 5B	81029	Q9H1J7
WNT7B	Wnt family member 7B	7477	P56706
ZBTB40	Zinc finger and BTB domain containing 40	9923	Q9NUA8
ZMPSTE24	Zinc metallopeptidase STE24	10269	O75844
HTR2B	5-hydroxytryptamine receptor 2B	3357	P41595
SNCA	Synuclein alpha	6622	P37840
ADRB2	Adrenoceptor beta 2	154	P07750
ESR2	Estrogen receptor 2	2100	Q92731
FDPS	Farnesyl diphosphate synthase	2224	P14324
GHR	Growth hormone receptor	2690	P10912
MSX1	Msh homeobox 1	4487	P28360
HSD17B2	Hydroxysteroid 17-beta dehydrogenase 2	3294	P37059
IFNG	Interferon gamma	3458	P01579
IL16	Interleukin 16	3603	Q14005
IL17A	Interleukin 17A	3605	Q16552
IL1A	Interleukin 1 alpha	3552	P01583
PGR	Progesterone receptor	5241	P06401
MGP	Matrix Gla protein	4256	P08493
MMRN1	Multimerin 1	22915	Q13201
NOX4	NADPH oxidase 4	50507	Q9NPH5
NELL1	Neural EGFL like 1	4745	Q92832
BGLAP	Bone gamma-carboxyglutamate protein	632	P02818
P2RX4	Purinergic receptor P2X 4	5025	Q99571
PON1	Paraoxonase 1	5444	P27169
PLIN1	Perilipin 1	5346	O60240
PER3	Period circadian regulator 3	8863	P56645
PPARG	Peroxisome proliferator activated receptor gamma	5468	P37231
SLC6A4	Solute carrier family 6 member 4	6532	P31645
MID1	Midline 1	4281	O15344
TGFBI	Transforming growth factor beta induced	7045	O75534
TLR4	Toll like receptor 4	7099	O00206
TRAM2	Translocation associated membrane protein 2	9697	Q15035
TMEM14A	Transmembrane protein 14A	28978	Q9Y6G1

Table SI. Continued.

Human symbol	Name	gene ID	Uniprot ID
VKORC1	Vitamin K epoxide reductase complex subunit 1	79001	Q9BQB6
GC	GC, vitamin D binding protein	2638	P02774

OSgset: osteoporosis-related genes gene set.

Table SIII. Pathways enriched in OSgset.

Pathways	P-value[a]	p_{BH} value[b]	Genes included in the pathway[c]
Ensemble of genes encoding extracellular matrix and extracellular matrix-associated proteins	$3.60x10^{-18}$	$6.05x10^{-15}$	IL10, THSD4, GDF5, IL15, IL16, IL17A, SPARC, SPP1, SMOC1, MSTN, BDNF, BGLAP, MEPE, PTN, WNT5B, WISP3, NELL1, BMP2, BMP7, ADIPOQ, MGP, FGF20, WNT3A, WNT16, CTHRC1, ADAMTS18, CCL2, MMP2, DMP1, PLOD1, COL1A1, VEGFA, COL6A1, COL9A1. SFRP1, SFRP2, SFRP4, WNT1, ITLN1, ANXA6, IBSP, WNT7B, WNT10B, GPC6, IL23A, IFNG, MMRN1, TGFBI, RSPO3, IGF1, TNFSF11, IGFBP2, TIMP1, TIMP2, PCSK6, FRZB, SERPINE1, CLEC2D, CSTA, REG3A, PAPPA, LTA, TNF, LTBP2, IL1A, IL6, PRL, CTSZ, IL7
Wnt signaling pathway	$3.71x10^{-13}$	$6.23x10^{-10}$	FZD1, FZD6, WNT5B, CER1, NFATC1, WNT3A, WNT16, RAC1, RAC2, SOST, SFRP1, SFRP2, SFRP4, WNT1, WNT7B, WNT10B, APC, DKK1, LRP6, LRP5, CTNNB1, DKK2
Breast cancer	$4.29x10^{-13}$	$7.21x10^{-10}$	ESR1, ESR2, PGR, FZD1, FZD6, WNT5B, FGF20, WNT3A, JAG1, WNT16, FGFR1, RB1, WNT1, WNT7B, WNT10B, APC, IGF1, TNFSF11, LRP6, NCOA1, LRP5, CTNNB1
Genes encoding secreted soluble factors	$4.63x10^{-13}$	$7.78x10^{-10}$	IL10, GDF5, IL15, IL16, IL17A, MSTN, BDNF, PTN, WNT5B, BMP2, BMP7, FGF20, WNT3A, WNT16, CCL2, VEGFA, SFRP1, SFRP2, SFRP4, WNT1, WNT7B, WNT10B, IL23A, IFNG, IGF1, TNFSF11, FRZB, LTA, TNF, IL1A, IL6, PRL, IL7
Cytokine-cytokine receptor interaction	$7.86x10^{-13}$	$1.32x10^{-09}$	IL10, GDF5, IL15, IL17A, TNFRSF11A, GHR, CCR2, BMP2, BMP7, BMPR1B, CXCR4, CCL2, IL23R, VEGFA, FLT1, IL23A, LEPR, IFNG, TNFSF11, CD40, CD40LG, LTA, TNF, TNFRSF1B, IL1A, IL6, PRL, IL6R, IL7
Ensemble of genes encoding ECM-associated proteins including ECM-affiliated proteins, ECM regulators and secreted factors	$7.91x10^{-12}$	$1.33x10^{-08}$	IL10, GDF5, IL15, IL16, IL17A, MSTN, BDNF, PTN, WNT5B, BMP2, BMP7, FGF20, WNT3A, WNT16, ADAMTS18, CCL2, MMP2, PLOD1, VEGFA, SFRP1, SFRP2, SFRP4, WNT1, ITLN1, ANXA6, WNT7B, WNT10B, GPC6, IL23A, IFNG, IGF1, TNFSF11, TIMP1, TIMP2, PCSK6, FRZB, SERPINE1, CLEC2D, CSTA, REG3A, PAPPA, LTA, TNF, IL1A, IL6, PRL, CTSZ, IL7
Canonical Wnt signaling	$8.61x10^{-12}$	$1.45x10^{-08}$	FZD1, WNT5B, WNT3A, WNT16, WNT1, WNT7B, WNT10B, APC, DKK1, LRP6 LRP5, CTNNB1, DKK2
Class B/2 (Secretin family receptors)	$1.10x10^{-11}$	$1.85x10^{-08}$	PTCH1, PTH, PTHLH, PTH1R, PTH2R, FZD1, FZD6, GHRH, GIP, GIPR, WNT3A, WNT16, CALCR, WNT1, WNT7B, WNT10B, CRHR1
GPCR ligand binding	$1.14x10^{-11}$	$1.91x10^{-08}$	AVP, TSHR, PTCH1, F2R, PTH, PTHLH, PTH1R, PTH2R, NMU, FZD1, FZD6, GHRH, CCR2, GIP, GIPR, SAA1, ADRA2A, ADRB2, CXCR4, WNT3A, WNT16, AGTR2, CNR1, NPY, CNR2, HTR2B, CALCR, GPER1, WNT1, WNT7B, WNT10B, CASR, CRHR1, LHB, LHCGR, OXT
Interleukin-4 and 13 signaling	$3.51x10^{-11}$	$5.90x10^{-08}$	IL10, HIF1A, IL17A, TWIST1, SAA1, CCL2, MMP2, ALOX5, IL23R, ALOX15, VEGFA, IL23A, TIMP1, TNF, TNFRSF1B, IL1A, IL6, IL6R
Genes related to Wnt-mediated signal transduction	$5.88x10^{-11}$	$9.88x10^{-08}$	B2M, FZD1, FZD6, WNT5B, WNT3A, WNT16, SFRP1, SFRP4, WNT1, WNT7B APC, DKK1, FRZB, LRP6, LRP5, CTNNB1
Proteoglycans in cancer	$7.02x10^{-11}$	$1.18x10^{-07}$	HIF1A, ESR1, PTCH1, TWIST1, FZD1, FZD6, WNT5B, WNT3A, WNT16, PLAUR, FGFR1, MMP2, RAC1, VEGFA, FLNB, WNT1, WNT7B, WNT10B, CASP3, IGF1, TLR4,TNF, CTNNB1
Cytokine Signaling in Immune system	$1.52x10^{-10}$	$2.56x10^{-07}$	IL10, IL15, HIF1A, IL16, IL17A, HLA-A, HLA-B, MARK3, B2M, SPTBN1, TNFRSF11A, TWIST1, GHR, CCR2, SAA1, NF1, CIITA, FGF20, MID1, CCL2, FGFR1, FGFR2, MMP2, ALOX5, IL23R, ALOX15, VEGFA, FLNB, CALM1, SEM1, IRF8, CASP3, IL23A, IFNG, TNFSF11, TIMP1, CD40, CD40LG, LTA, TNF, TNFRSF1B, IL1A, IL6, PRL, IL6R, IL7
Wnt signaling network	$1.69x10^{-10}$	$2.83x10^{-07}$	FZD1, FZD6, WNT3A, CTHRC1, WNT1, WNT7B, ROR2, DKK1, LRP6, LRP5
Cytokine Network	$2.04x10^{-10}$	$3.42x10^{-07}$	IL10, IL15, IL16, IL17A, IFNG, LTA, TNF, IL1A, IL6

Table SIII. Continued.

Pathways	P-value[a]	p_{BH} value[b]	Genes included in the pathway[c]
Negative regulation of TCF-dependent signaling by WNT ligand antagonists	$2.35x10^{-10}$	$3.95x10^{-07}$	WNT3A, SOST, SFRP1, SFRP2, DKK1, LRP6, LRP5, DKK2
Rheumatoid arthritis	$7.22x10^{-10}$	$1.21x10^{-06}$	IL15, IL17A, TNFRSF11A, CCL2, VEGFA, FLT1, ATP6V1G1, IL23A, IFNG, ATP6V1H, TNFSF11, TLR4, TNF, IL1A, IL6
Signaling by Wnt	$1.07x10^{-09}$	$1.80x10^{-06}$	SOX4, SOX9, WLS, FZD1, FZD6, WNT5B, NFATC1, WNT3A,WNT16, RAC1, RAC2, SOX6, SOST, SFRP1, SFRP2, CALM1, SEM1, WNT1, WNT7B, ROR2, WNT10B, APC, RSPO3, DKK1, LRP6, LRP5, CTNNB1, DKK2
Fluid shear stress and atherosclerosis	$1.43x10^{-09}$	$2.40x10^{-06}$	PECAM1, NCF1, MEF2C, BMPR1B, CCL2, MMP2, NOS3, RAC1, RAC2, VEGFA, CALM1, IFNG, GSTM3, GSTP1, TRPV4, TNF, CTNNB1, IL1A
Basal cell carcinoma	$1.49x10^{-09}$	$2.51x10^{-06}$	PTCH1, FZD1, FZD6, WNT5B, BMP2, WNT3A, WNT16, WNT1, WNT7B, WNT10B, APC, CTNNB1
Pathways in cancer	$1.81x10^{-09}$	$3.05x10^{-06}$	HIF1A, MECOM, PTCH1, F2R, FZD1, FZD6, WNT5B, BMP2, FGF20, CXCR4, WNT3A, WNT16, FGFR1, FGFR2, MMP2, RAC1, RAC2, VEGFA, RB1, WNT1, WNT7B, WNT10B, APC, CASP3, PPARG, CCNE1, GSTP1, IGF1, CTNNB1, IL6
Alzheimer disease-presenilin pathway	$1.83x10^{-08}$	$3.08x10^{-05}$	FZD1, FZD6, WNT5B, WNT3A, WNT16, MMP2, WNT1, WNT7B, WNT10B, PCSK6, LRP1, LRP4, LRP6, LRP5, CTNNB1
Validated transcriptional targets of AP1 family members Fra1 and Fra2	$2.84x10^{-08}$	$4.78x10^{-05}$	BGLAP, JUND, MGP, NFATC1, CCL2, PLAUR, MMP2, NOS3, IL6
Signaling pathways regulating pluripotency of stem cells	$4.81x10^{-08}$	$8.09x10^{-05}$	FZD1, FZD6, WNT5B, BMPR1B, WNT3A, WNT16, FGFR1, DLX5, FGFR2, WNT1, WNT7B, WNT10B, APC, ID4, IGF1, CTNNB1
ALK in cardiac myocytes	$6.37x10^{-08}$	$1.07x10^{-04}$	NOG, MEF2C, FZD1, BMP2, BMP7, WNT1, APC, TGFBR3, CTNNB1
Malaria	$7.09x10^{-08}$	$1.19x10^{-04}$	IL10, PECAM1, CCL2, IFNG, TLR4, CD40, CD40LG, LRP1, TNF, IL6
Cytokines and Inflammatory Response	$1.21x10^{-07}$	$2.03x10^{-04}$	IL10, IL15, IFNG, LTA, TNF, IL1A, IL6, IL7
Neuroactive ligand-receptor interaction	$1.45x10^{-07}$	$2.44x10^{-04}$	TSHR, F2R, PTH1R, PTH2R, GHR, GIPR, ADRA2A, ADRB2, AGTR2, CNR1, CNR2, HTR2B, CALCR, NR3C1, LEPR, CRHR1, LHB, LHCGR, P2RX1, P2RX4, P2RX7, PRL
HTLV-I infection	$1.54x10^{-07}$	$2.59x10^{-04}$	IL15, HLA-A, HLA-B, FZD1, FZD6, WNT5B, NFATC1, FDPS, WNT3A, WNT16, RB1, WNT1, WNT7B, WNT10B, APC, MSX1, CD40, LTA, TNF, CTNNB1, IL6
Genes encoding structural ECM glycoproteins	$2.30x10^{-07}$	$3.86x10^{-04}$	THSD4, SPARC, SPP1, SMOC1, BGLAP, MEPE, WISP3, NELL1, ADIPOQ, MGP, CTHRC1, DMP1, IBSP, MMRN1, TGFBI, RSPO3, IGFBP2, LTBP2
Metabolism of steroid hormones	$2.79x10^{-07}$	$4.69x10^{-04}$	CYP17A1, CYP19A1, SRD5A2, HSD11B1, HSD17B2, AKR1B1, LHB, STARD3NL
Signaling by Interleukins	$4.17x10^{-07}$	$7.02x10^{-04}$	IL10, IL15, HIF1A, IL16, IL17A, MARK3, SPTBN1, TWIST1, CCR2, SAA1, NF1, FGF20, CCL2, FGFR1, FGFR2, MMP2, ALOX5, IL23R, ALOX15, VEGFA, CALM1, SEM1, CASP3, IL23A, TIMP1, TNF, TNFRSF1B, IL1A, IL6, IL6R, IL7
Extracellular matrix organization	$4.82x10^{-07}$	$8.11x10^{-04}$	GDF5, SPARC, SPP1, PECAM1, ITGA1, BMP2, BMP7, ADAMTS18, MMP2, DMP1, PLOD1, CRTAP, COL1A1, COL6A1, COL9A1, IBSP, CASP3, TIMP1, TIMP2, SERPINE1, LRP4, LTBP2
Ensemble of genes encoding core extracellular matrix including ECM glycoproteins, collagens and proteoglycans	$5.09x10^{-07}$	$8.56x10^{-04}$	THSD4, SPARC, SPP1, SMOC1, BGLAP, MEPE, WISP3, NELL1, ADIPOQ, MGP, CTHRC1, DMP1, COL1A1, COL6A1, COL9A1, IBSP, MMRN1, TGFBI, RSPO3, IGFBP2, LTBP2

Table SIII. Continued.

Pathways	P-value[a]	p_{BH} value[b]	Genes included in the pathway[c]
Signaling by WNT in cancer	$5.91x10^{-07}$	$9.93x10^{-04}$	FZD6, WNT3A, APC, DKK1, LRP6, LRP5, CTNNB1, DKK2
Wnt signaling pathway	$7.16x10^{-07}$	$1.20x10^{-03}$	FZD1, FZD6, WNT5B, CER1, BMPR1B, NFATC1, WNT3A, WNT16, SFRP1, SFRP2, SFRP4, WNT1, WNT7B, WNT10B, APC, DKK1, FRZB, LRP6, LRP5, TNF, CTNNB1, DKK2
Angiogenesis	$8.07x10^{-07}$	$1.36x10^{-03}$	HIF1A, FZD1, WNT5B, JAG1, FGFR1, NOS3, VEGFA, SFRP1, WNT1, WNT7B, WNT10B, APC, ARHGAP1, FRZB, CTNNB1
Ovarian steroidogenesis	$1.00x10^{-06}$	$1.69x10^{-03}$	CYP1A1, CYP1B1, CYP17A1, CYP19A1, HSD17B2, ALOX5, LHB, LHCGR, IGF1
Hippo signaling pathway	$1.13x10^{-06}$	$1.90x10^{-03}$	GDF5, FZD1, FZD6, WNT5B, BMP2, BMP7, BMPR1B, WNT3A, WNT16, WNT1, WNT7B, WNT10B, APC, SERPINE1, CTNNB1
Inflammatory bowel disease (IBD)	$1.14x10^{-06}$	$1.92x10^{-03}$	IL10, IL17A, NFATC1, IL23R, IL23A, IFNG, TLR4, TNF, IL1A, IL6
WNT ligand biogenesis and trafficking	$1.22x10^{-06}$	$2.05x10^{-03}$	WLS, WNT5B, WNT3A, WNT16, WNT1, WNT7B, WNT10B
AGE-RAGE signaling pathway in diabetic complications	$1.36x10^{-06}$	$2.28x10^{-03}$	NFATC1, CCL2, MMP2, NOS3, RAC1, COL1A1, VEGFA, CASP3, SERPINE1, TNF, IL1A, IL6
G alpha (s) signalling events	$3.12x10^{-06}$	$5.24x10^{-03}$	AVP, TSHR, PTH, PTHLH, PTH1R, PTH2R, GHRH, GIP, GIPR, ADRB2, CALCR, CRHR1, LHB, LHCGR
Disassembly of the destruction complex and recruitment of AXIN to the membrane	$4.21x10^{-06}$	$7.07x10^{-03}$	FZD1, WNT3A, WNT1, APC, LRP6, LRP5, CTNNB1
Osteoclast differentiation	$4.42x10^{-06}$	$7.44x10^{-03}$	CYLD,NCF1,TNFRSF11A,TYROBP, JUND, NFATC1, RAC1, CALCR, PPARG, IFNG, TNFSF11, TNF, IL1A
mTOR signaling pathway	$4.64x10^{-06}$	$7.80x10^{-03}$	FZD1, FZD6, WNT5B, WNT3A, WNT16, WNT1, WNT7B, WNT10B, ATP6V1G1, ATP6V1H, IGF1, LRP6, LRP5, TNF
PI3K-Akt signaling pathway	$4.74x10^{-06}$	$7.98x10^{-03}$	SPP1, ITGA1, F2R, GHR,FGF20, FGFR1, FGFR2, NOS3, RAC1, COL1A1, VEGFA, COL6A1, COL9A1, FLT1, IBSP, CCNE1, IGF1, TLR4, IL6, PRL, IL6R, IL7
TCF dependent signaling in response to WNT	$4.92x10^{-06}$	$8.27x10^{-03}$	SOX4, SOX9, FZD1, FZD6, WNT3A, SOX6, SOST, SFRP1, SFRP2, SEM1, WNT1, APC, RSPO3, DKK1, LRP6, LRP5, CTNNB1, DKK2
Wnt/beta-catenin Pathway	$6.48x10^{-06}$	$1.09x10^{-02}$	CER1, SFRP1, APC, DKK1, LRP1, CTNNB1, DKK2
Interleukin-10 signaling	$8.72x10^{-06}$	$1.47x10^{-02}$	IL10, CCR2, CCL2, TIMP1, TNF, TNFRSF1B, IL1A, IL6
Glucocorticoid receptor regulatory network	$9.88x10^{-06}$	$1.66x10^{-02}$	BGLAP, NFATC1, NR1I3, NCOA2, NR3C1, IFNG, NCOA1, PBX1, IL6, PRL
HIF-1 signaling pathway	$1.07x10^{-05}$	$1.80x10^{-02}$	HIF1A, NOS3, VEGFA, FLT1, IFNG, IGF1, TIMP1, TLR4, SERPINE1, IL6, IL6R
The IGF-1 Receptor and Longevity	$1.12x10^{-05}$	$1.88x10^{-02}$	GHR, CAT, IGF1, SOD1, SOD2
IL23-mediated signaling events	$1.17x10^{-05}$	$1.97x10^{-02}$	IL17A, CCL2, IL23R, IL23A, IFNG, TNF, IL6
Detoxification of Reactive Oxygen Species	$1.41x10^{-05}$	$2.37x10^{-02}$	NCF1, NOX4, CAT, GSR, GSTP1, SOD1, SOD2
Allograft rejection	$1.41x10^{-05}$	$2.37x10^{-02}$	IL10, HLA-A, HLA-B, IFNG, CD40, CD40LG,TNF
Circadian Clock	$2.01x10^{-05}$	$3.38x10^{-02}$	HIF1A, AVP, SREBF1, DBP, MEF2C, NCOA2, NR3C1, SERPINE1, NCOA1
RNF mutants show enhanced WNT signaling and proliferation	$2.43x10^{-05}$	$4.08x10^{-02}$	FZD6, WNT3A, LRP6, LRP5

OSgset: osteoporosis-related genes gene set. [a]P-values were calculated by Fisher's exact test. [b]PBH values were adjusted by Benjamini and Hochberg (BH) method. [c]Two hundred ninty-four OS-related genes included in the pathway