

Figure S1. Transfection efficiency of knockdown or overexpression was further quantified by measuring the density of the band of western blots. Student's t-test was used to evaluate the difference between two groups. (A) TRIM67 levels were upregulated with the transfection of TRIM67 plasmid compared with the corresponding controls. Results are expressed as the mean \pm SD. (B) Quantitative data demonstrating that TRIM67 levels were significantly downregulated with the transfection of the TRIM67 siRNA. Results are expressed as the mean \pm SD. ***P<0.001.

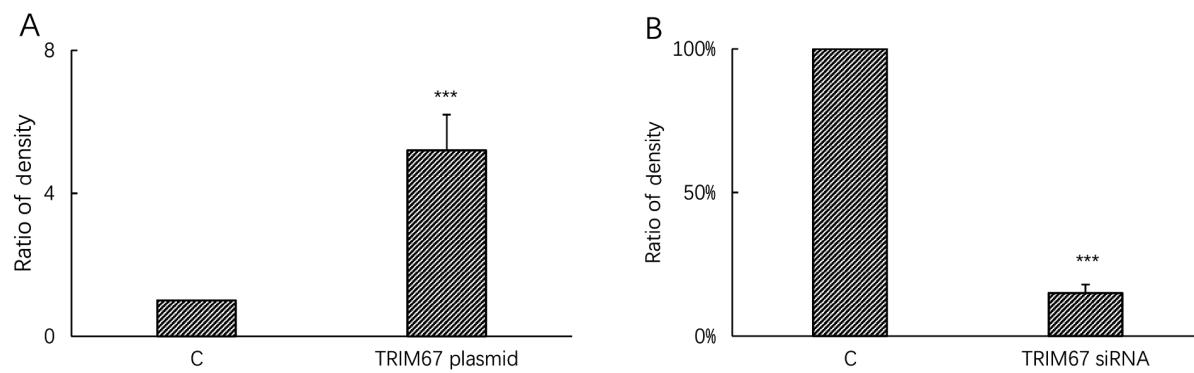


Figure S2. Identified differentially expressed genes were uploaded to Ingenuity Pathway Analysis tools and pathway analysis was performed. The enriched pathways are presented. Green represents downregulated genes. Red represents upregulated genes.

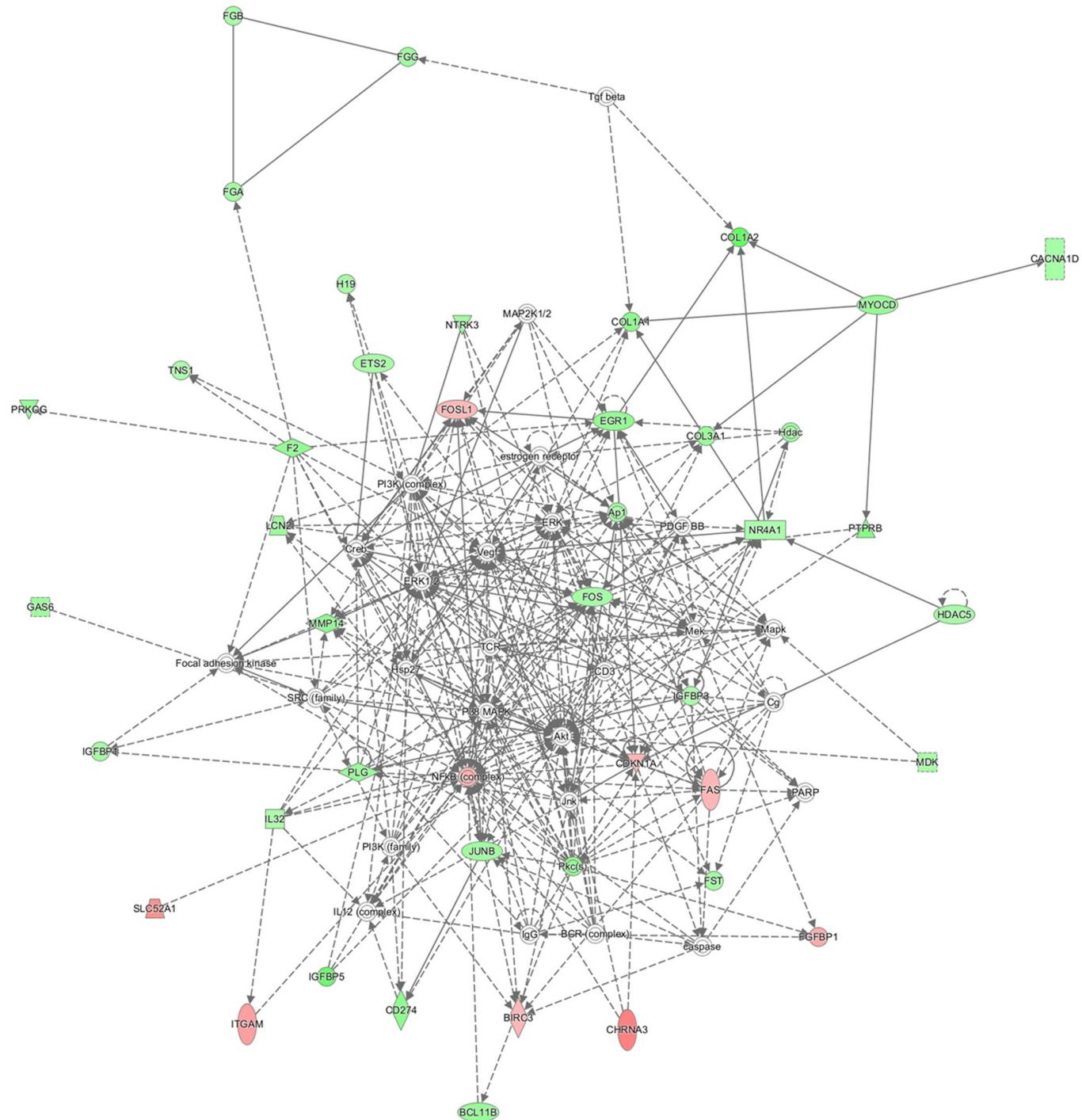


Figure S3. Representative figures of Annexin V staining for detection of apoptosis. (A) Cells were transfected with non-targeting control siRNA or TRIM67 siRNA and treated with control vehicles or GA-13315. Cell flow cytometry was performed to measure the levels of Annexin V-positive cells. TRIM67 siRNA decreased the levels of GA-13315-induced apoptosis in A549 and H460 cell lines. (B) Cells were treated with C, GA-13315 or GA-13315 + NBD (GA + NBD), and apoptotic cells were measured by Annexin V assay. siRNA, small interfering RNA; TRIM67, tripartite motif containing 67; GA/GA-13315, 13-chlorine-3,15-dioxy-gibberellic acid methyl ester; C, control vehicle; NBD, NEMO-binding domain; FITC, fluorescein isothiocyanate; PE, phycoerythrin; PI, propidium iodide.

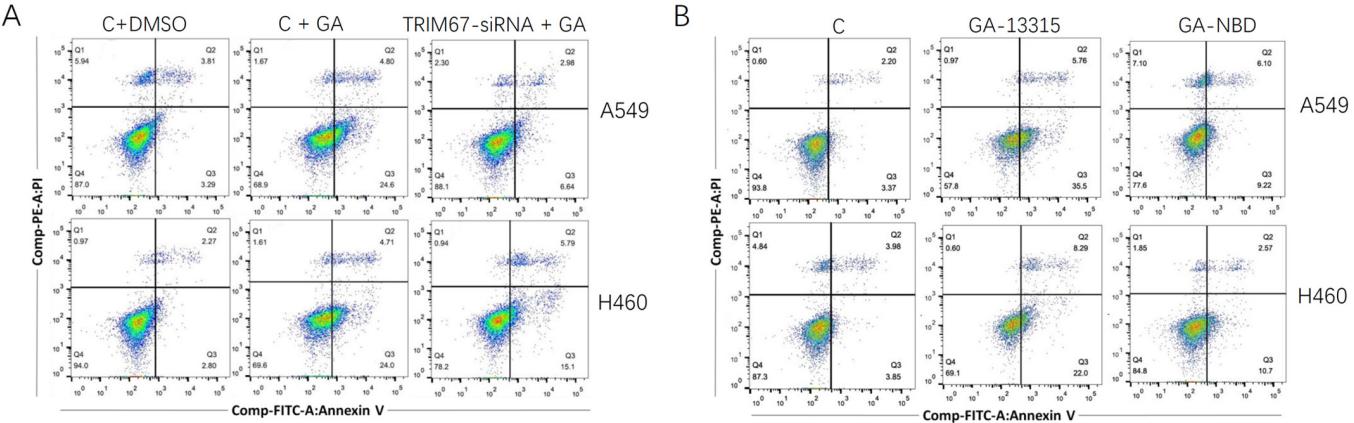


Table SI. Forward and reverse primer pairs used in quantitative polymerase chain reaction.

Gene	Genbank ID	Forward	Reverse
TRIM67	NM_001004342.3	5' TCTGACTTTGGACAGCGAGC	5' GGTGGCACCCCTACATTCAT
FBXO15	NM_152676.2	5' CCGCTCTCTTCACCGTGTAT	5' GCCCCTTCCTCTCACGTT
NFKB2	NM_001077494.3	5' AAAAGAGGGAGGAGGGCCTTA	5' CGTGGATCCGAGTGTCTCG
FAS	NM_000043.5	5' ACTGTGACCCTTGACCAAAA	5' AGACAAAGCCACCCCCAAGTT
BIRC3	NM_001165.4	5' GGGCAGCAGGTTACAAAGG	5' TCCCCTTAAGGATTAGGTCTCCA
PDK1	NM_002610.4	5' ATCCTCTTCCACCATCAAGGC	5' AGTGAAGCCCCCTAACATTACC
CDKN2D	NM_079421.2	5' CGAGGAGGAGGGAGGGC	5' TGCAAACATCATGACCTGC
FOS	NM_005252.3	5' CAGACTACGAGGCGTCATCC	5' TCTGCGGGTGAGTGGTAGTA
JUNB	NM_002229.2	5' CCACCTCCCGTTACACCAA	5' GAGGTAGCTGATGGTGGTCG
BCL11B	NM_138576.3	5' CGGGCGATGCCAGAATAGAT	5' CTCCACATGGTCAGCCTCTG

Table SII. Significantly differentially expressed genes identified by RNA-Seq in GA-13315 treated A549 cells, compared to vehicle control treated cells.

Gene symbol	Name	Fold change	P-value	FDR	AD1	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
ARC	Activity-regulated cytoskeleton-associated protein	4.895620787	0.00224	0.064286	0.33316	0.24466	0.23862	1.35009	1.02905	1.7833047
BNC1	Basonuclin 1	4.411512542	0.00022	0.0142903	0.22211	0.48932	0.11931	1.05007	1.20056	1.5089501
MAMDC2	MAM domain containing 2	3.894372317	0.00051	0.0236741	0.33316	0.24466	0.35793	1.5001	1.02905	1.2345955
FAM196B	Family with sequence similarity 196, member B	3.60403021	5.53E-05	0.0054277	0.66632	0.61165	0.71586	2.85019	2.40112	2.0576592
PCDHAI	Protocadherin alpha 1	3.36988654	0.00038	0.0200297	0.44421	0.73397	0.23862	1.35009	1.71509	1.7833047
CPA4	Carboxypeptidase A4	3.186487982	8.43E-08	3.04E-05	3.99793	3.18056	3.93721	10.5007	12.1771	12.757487
PLA2G4C	Phospholipase A2, group IV/C (cytosolic, calcium-independent)	2.780653954	0.00274	0.0722871	0.66632	0.97863	0.71586	2.70018	1.37207	2.4691911
CHRNA3	Cholinergic receptor, nicotinic, alpha 3 (neuronal)	2.702435167	0.00066	0.0285947	0.55527	0.48932	0.95448	1.95013	1.71509	1.7833047
CYP1A1	Cytochrome P450, family 1, subfamily A, polypeptide 1	2.623402886	0.00092	0.03549	0.55527	0.8563	0.71586	1.95013	1.71509	1.920482
RNF212	Ring finger protein 212	2.573772792	0.00055	0.0249576	0.66632	0.73397	1.43171	2.10014	3.08715	2.1948365
PTCHD4	Patched domain containing 4	2.548864485	0.0203	0.2276879	0.44421	0	0.95448	1.05007	1.37207	1.2345955
SH3BP5-AS1	SH3BP5 antisense RNA 1	2.491711392	0.00291	0.0746163	0.33316	0.8563	1.07379	1.65011	2.22961	1.7833047
MPZL3	Myelin protein zero-like 3	2.457513319	0.01755	0.208263	0.22211	1.10096	0.47724	0.60004	2.0581	1.7833047
PLA2G4B	Phospholipase A2, group IVB (cytosolic)	2.455264269	0.01729	0.2069721	1.4437	0	0.71586	2.40016	1.54358	1.5089501
ZHX1-C8orf76	ZHX1-C8orf76 readthrough	2.393790351	0.02446	0.2513213	0.77738	0.24466	1.67033	3.45023	1.37207	1.6461274
TNFRSF10C	Tumor necrosis factor receptor superfamily, member 10c, decoy without an intracellular domain	2.377597438	0.01545	0.1957085	0.88843	0.24466	0.59655	1.5001	1.02905	1.6461274
SLC52A1	Solute carrier family 52 (riboflavin transporter), member 1	2.36054652	0.00036	0.0194277	0.77738	1.46795	1.3124	2.85019	3.25866	2.3320138
RAP2C-AS1	RAP2C antisense RNA 1	2.333595317	0.02048	0.2285335	0.77738	0.24466	0.35793	1.20008	1.02905	1.0974183
SCHIP1	Schwannomin interacting protein 1	2.302232415	0.0039	0.0911472	2.11002	1.22329	1.55102	3.0002	6.0028	2.4691911
GJB2	Gap junction protein, beta 2, 26 kDa	2.291004549	0.00765	0.1372535	0.55527	1.22329	0.47724	1.80012	1.88659	1.5089501
DNAJC28	DnaJ (Hsp40) homolog, subfamily C, member 28	2.283687831	0.00959	0.1566619	0.66632	0.48932	1.07379	1.80012	1.37207	1.920482
TRIM67	Tripartite motif containing 67	2.194791464	0.0026	0.0705097	1.77686	1.22329	1.07379	2.85019	3.9447	2.3320138
EME2	Essential meiotic structure-specific endonuclease subunit 2	2.134930158	0.01077	0.1635644	0.55527	1.34562	1.90895	1.80012	3.60168	2.7435457
LOC101927181	NA	2.078453753	0.00205	0.0611657	1.33264	0.8563	1.43171	2.70018	2.57263	2.3320138

Table SII. Continued.

Gene symbol	Name	Fold change	P-value	FDR	AD1	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
KLRG2	Killer cell lectin-like receptor subfamily G, member 2	2.069880601	0.04759	0.3438947	0.44421	1.10096	0.71586	1.05007	1.54358	2.0576592
ANKRD20A5P	Ankyrin repeat domain 20 family, member A5, pseudogene	2.062053202	0.01241	0.1747908	0.66632	0.8563	1.1931	1.95013	1.71509	1.920482
ITGAM	Integrin, alpha M (complement component 3 receptor 3 subunit)	2.060500708	0.00796	0.1412262	1.77686	0.73397	1.3124	2.10014	3.9447	2.0576592
ARMCX4	Armadillo repeat containing, X-linked 4	2.018234028	0.01313	0.1794567	2.11002	1.34562	0.59655	2.85019	2.0581	3.2922548
LOC102723769	NA	2.017657723	0.00738	0.1347353	0.99948	2.32425	1.3124	3.45023	1.88659	3.8409639
NRG4	Neuregulin 4	1.992424527	0.02283	0.2425992	0.66632	0.8563	0.59655	1.35009	1.37207	1.5089501
BCHE	Butyrylcholinesterase	1.975983516	0.01213	0.1732844	1.88791	0.73397	1.3124	3.45023	2.0581	2.3320138
DNAH1	Dynein, axonemal, heavy chain 1	1.96485697	0.01455	0.188828	2.3213	1.10096	1.3124	3.90026	1.54358	3.8409639
TPIP2	Triosephosphate isomerase 1 pseudogene 2	1.953574668	0.00939	0.1550827	0.99948	1.10096	0.83517	1.95013	1.71509	2.0576592
WDR63	WD repeat domain 63	1.950116311	0.02174	0.2366571	1.99897	1.22329	1.43171	3.0002	4.63073	1.6461274
C15orf48	Chromosome 15 open reading frame 48	1.924483771	0.00612	0.1216587	2.77634	2.20192	3.22136	5.55037	6.34582	3.9781412
XDH	Xanthine dehydrogenase	1.904436046	0.00406	0.0927433	1.4437	2.0796	1.67033	3.45023	3.25866	3.1550775
GSTO2	Glutathione S-transferase omega 2	1.901610045	0.01338	0.1811604	1.33264	1.34562	1.1931	1.80012	2.0581	3.4294321
CPE	Carboxypeptidase E	1.894239909	2.38E-05	0.0028318	5.21952	4.03686	4.05652	8.55057	9.43297	7.4075733
FBXO15	F-box protein 15	1.8749325	0.04186	0.3274236	0.77738	0.97863	1.78964	1.05007	2.40112	3.1550775
PCDHAC1	Protocadherin alpha subfamily C, 1	1.853111833	0.01235	0.1747337	2.33213	4.40385	2.14757	7.95053	3.43017	4.9383822
TSGA10	Testis specific, 10	1.843929851	0.03597	0.3052035	0.66632	0.97863	1.67033	1.35009	2.74414	2.0576592
RNF144B	Ring finger protein 144B	1.843565083	0.03448	0.2992221	0.77738	0.97863	1.43171	1.80012	1.37207	2.6063684
MSTO2P	Misato family member 2, pseudogene	1.842077627	0.04503	0.3361414	1.77686	0.8563	1.67033	1.20008	4.1162	2.7435457
METTL12	Methyltransferase like 12	1.84110052	0.02782	0.2698593	1.33264	2.69124	2.02826	2.40016	4.45922	4.2524958
LOC100506860	NA	1.823034923	0.02877	0.274088	1.99897	1.83494	0.95448	2.40016	2.91565	3.4294321
ZNF471	Zinc finger protein 471	1.819398437	0.04026	0.3209389	0.99948	1.59028	1.1931	2.10014	1.20056	3.4294321
CRISPLD2	Cysteine-rich secretory protein LCCL domain containing 2	1.815133061	0.00057	0.0257982	7.4406	5.38248	7.75512	12.6008	13.3777	11.385714
LINC00472	Long intergenic non-protein coding RNA 472	1.813236012	0.00272	0.0720358	2.33213	2.81357	2.5055	4.20028	5.31676	4.389673
FGFBP1	Fibroblast growth factor binding protein 1	1.797178194	0.0114	0.1676771	1.55475	1.34562	2.38619	3.15021	2.40112	3.8409639
CBWD6	COBW domain containing 6	1.791163721	0.00206	0.0611657	3.44266	1.95727	3.45998	6.0004	4.97375	4.9383822

Table SII. Continued.

Gene symbol	Name	Fold change	P-value	FDR	AD1	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
AHRR	Aryl-hydrocarbon receptor repressor	1.787139323	0.00013	0.0092496	7.21849	4.03686	4.53376	9.15061	9.43297	9.7795871
PLEKHNI	Pleckstrin homology domain containing, family N member 1	1.771527307	0.00212	0.0622522	2.44318	2.0796	1.78964	3.90026	3.77319	3.5666093
GEMIN8P4	Gem (nuclear organelle) associated protein 8 pseudogene 4	1.740068795	0.0058	0.1174743	1.88791	2.0796	2.14757	4.20028	3.43017	3.0179002
CRABP2	Cellular retinoic acid binding protein 2	1.736174712	0.00058	0.0261199	4.66425	4.28152	5.13031	6.45043	8.74694	9.1908779
ZNF597	Zinc finger protein 597	1.732356481	0.02011	0.2262525	0.99948	1.46795	1.67033	2.10014	2.74414	2.3320138
KREMEN2	Kringle containing transmembrane protein 2	1.723364497	0.01743	0.2076014	2.44318	1.83494	1.07379	3.30022	3.60168	2.4691911
DGAT2	Diacylglycerol O-acyltransferase 2	1.71181325	0.03208	0.2900772	3.77582	2.56891	3.45998	6.0004	5.14526	5.6242686
TMEM27	Transmembrane protein 27	1.705668833	0.03929	0.3180132	2.44318	1.59028	1.67033	4.20028	2.0581	3.4294321
C1orf226	Chromosome 1 open reading frame 226	1.693755054	0.03763	0.3115401	1.99897	1.59028	1.07379	2.70018	3.43017	1.920482
ARAP2	ArfGAP with RhoGAP domain, ankyrin repeat and PH domain 2	1.681405274	0.04319	0.3317092	1.6658	0.97863	1.55102	2.10014	2.0581	2.8807229
DSC3	Desmocollin 3	1.661332423	0.00478	0.1033257	2.8874	3.54754	3.93721	7.5005	5.14526	4.5268503
AOX1	Aldehyde oxidase 1	1.661286851	0.00104	0.0382852	4.99741	3.66987	4.29514	6.75045	5.83129	8.7793461
ZNF483	Zinc finger protein 483	1.641106576	0.04376	0.3330515	1.4437	1.34562	2.5055	3.30022	3.08715	2.3320138
RRAD	Ras-related associated with diabetes	1.632698384	0.00257	0.0699725	7.55165	5.50481	6.80064	9.90066	12.0056	10.562651
NFKB2	Nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100)	1.630125756	0.00034	0.0187939	37.4251	30.5823	32.6908	49.5033	56.4263	57.751636
ZNF782	Zinc finger protein 782	1.629551296	0.01386	0.1841457	2.99845	3.54754	2.26688	6.0004	5.14526	3.2922548
APLF	Aprataxin and PNKP like factor	1.628669555	0.01075	0.1634863	3.1095	2.56891	2.98274	6.30042	4.1162	3.7037866
SLC25A42	Solute carrier family 25, member 42	1.625981552	0.03294	0.2922674	1.55475	1.95727	1.43171	2.25015	2.57263	3.1550775
ANKRD1	Ankyrin repeat domain 1 (cardiac muscle)	1.624915703	0.00049	0.02334051	7.4406	7.58441	6.68133	13.9509	10.805	10.425473
CDKN1A	Cyclin-dependent kinase inhibitor 1A (p21, Cip1)	1.620366541	1.49E-10	1.66E-07	104.501	103.246	113.583	176.862	171.68	170.23701
LINC00910	Long intergenic non-protein coding RNA 910	1.612822314	0.04728	0.3434686	1.55475	2.32425	1.3124	3.75025	2.40112	2.1948365
CYFIP2	Cytoplasmic FMR1 interacting protein 2	1.610610649	7.92E-12	1.17E-08	51.3068	54.6811	58.1037	84.1556	94.3297	85.049915
NAPII2	Nucleosome assembly protein 1-like 2	1.590350577	0.01558	0.1960489	3.33161	2.69124	2.38619	5.55037	4.80224	3.1550775

Table SII. Continued.

Gene symbol	Name	Fold change	P-value	FDR	ADI	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
NFE2L3	Nuclear factor, erythroid 2-like 3	1.588028086	0.00062	0.027397	17.8796	22.5086	21.1178	34.8023	37.0458	25.652152
ZNF468	Zinc finger protein 468	1.572978854	0.03686	0.3084912	2.77634	3.30289	1.78964	4.35029	3.25866	4.6640276
FAS	Fas cell surface death receptor	1.566192801	6.08E-05	0.0057055	23.8765	22.8755	18.9702	35.1023	34.9877	32.648193
ZNF286B	Zinc finger protein 286B	1.560708186	0.03245	0.2909888	2.11002	1.59028	2.5055	3.90026	2.74414	3.0179002
GOLGA6L5P	Golgin A6 family-like 5, pseudogene	1.559669556	0.02047	0.2285335	4.5532	2.69124	2.98274	6.30042	4.28771	5.349914
ZNF85B	Zinc finger protein 585B	1.554057151	1.36E-05	0.0018713	11.5496	12.3552	10.6185	15.001	20.4095	18.244579
ANKRD2	Ankyrin repeat domain 2 (stretch responsive muscle)	1.55156466	0.04672	0.3412571	3.88688	2.44658	3.8179	5.70038	4.97375	5.0755595
MCOLN2	Mucolipin 2	1.544595695	0.02296	0.2433915	2.11002	2.56891	2.5055	4.5003	2.91565	3.5666093
ANKRD20A12P	Ankyrin repeat domain 20 family, member A12, pseudogene	1.53870674	0.00835	0.145226	6.77427	6.60577	5.96548	11.8508	10.119	7.8191051
ALDH1A3	Aldehyde dehydrogenase 1 family, member A3	1.535192553	0.00067	0.0288443	23.4323	25.1998	25.2936	40.0527	34.8162	38.135285
RRP7B	NA	1.533993945	0.01521	0.1941024	2.99845	3.54754	3.93721	4.35029	4.97375	6.5845096
ZNF432	Zinc finger protein 432	1.530145771	0.01183	0.1710126	3.88688	4.89317	3.10205	6.30042	4.97375	6.7216868
FOSL1	FOS-like antigen 1	1.528349293	0.01285	0.1772416	18.7681	16.0251	22.5495	27.6018	32.9296	26.886747
BIRC3	Baculoviral IAP repeat containing 3	1.528010464	0.00132	0.0458977	28.4297	28.625	21.9529	35.7024	42.1911	42.524958
MYPN	Myopalladin	1.527030897	0.00282	0.0736702	6.10795	5.13782	6.08478	8.10054	9.77599	8.6421688
REPS2	RALBP1 associated Eps domain containing 2	1.525024598	0.04816	0.3451425	2.66529	2.81357	2.74412	2.55017	5.83129	4.2524958
ZKSCAN3	Zinc finger with KRAB and SCAN domains 3	1.520575197	0.02421	0.2497912	3.88688	4.89317	2.02826	4.95033	6.0028	5.4870913
ZNF329	Zinc finger protein 329	1.517321746	0.00041	0.0211769	5.88584	6.97276	6.20409	9.90066	8.91844	9.8767643
ZNF841	Zinc finger protein 841	1.511225202	0.00835	0.145226	4.5532	4.03686	3.57929	5.55037	7.20336	5.7614459
HENMT1	HEN1 methyltransferase homolog 1 (Arabidopsis)	1.510336689	0.0004	0.0209419	6.66322	7.95139	7.63581	11.5508	9.77599	11.934424
LINC00342	Long intergenic non-protein coding RNA 342	1.504034509	0.02781	0.2698593	3.88688	3.18056	2.98274	6.90046	3.77319	4.389673
ABHD8	Abhydrolase domain containing 8	-1.50025148	0.0027	0.0716197	9.1064	9.29701	12.7661	7.05047	5.14526	8.230637
NR4A1	Nuclear receptor subfamily 4, group A, member 1	-1.501325062	6.68E-07	0.0001746	27.9855	26.0561	27.3219	17.5512	18.8659	17.695869
ZNF467	Zinc finger protein 467	-1.503852715	0.0106	0.1629032	5.33058	4.89317	4.89169	3.0002	3.77319	3.2922548
SAMD11	Sterile alpha motif domain containing 11	-1.505125541	1.91E-06	0.0003974	49.641	50.6443	52.7348	34.0523	35.8453	31.550775

Table SII. Continued.

Gene symbol	Name	Fold change	P-value	FDR	ADI	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
PALMD	Palmdelphin	-1.505127699	0.00187	0.0586975	9.1064	9.17468	11.3344	5.25035	7.37487	6.9960414
RARA-AS1	RARA antisense RNA 1	-1.507091176	0.01506	0.1927993	4.88636	4.40385	5.60755	3.90026	2.40112	3.4294321
IGFBP3	Insulin-like growth factor binding protein 3	-1.510813298	0.00434	0.0965693	354.705	297.26	396.108	233.866	228.964	228.12582
CCNB3	Cyclin B3	-1.515194319	0.03482	0.3002008	3.22056	4.15919	4.17583	1.95013	2.22961	3.2922548
C1R	Complement component 1, r subcomponent	-1.517644944	6.27E-06	0.0010079	43.8662	46.1181	50.3486	29.252	33.9587	29.081584
SLC26A10	Solute carrier family 26, member 10	-1.519349656	0.03046	0.2821222	3.44266	3.05823	3.22136	1.95013	2.40112	2.0576592
IL32	Interleukin 32	-1.52213744	0.00899	0.1523312	7.10743	5.01549	7.5165	4.20028	3.9447	4.6640276
TM4SF4	Transmembrane 4 L six family member 4	-1.524545795	0.0017	0.0550962	10.9943	13.3339	12.6468	8.25055	8.0609	7.8191051
ZSCAN31	Zinc finger and SCAN domain containing 31	-1.524725253	0.02377	0.2490641	3.55372	4.52618	3.8179	2.25015	2.91565	2.6063684
TREX1	Three prime repair exonuclease 1	-1.527860327	0.00137	0.0473153	7.4406	7.95139	7.87443	4.80032	4.45922	5.7614459
DACT2	Dishevelled-binding antagonist of beta-catenin 2	-1.537262167	0.03757	0.3113866	4.10899	2.69124	3.93721	1.80012	2.40112	2.7435457
TNS1	Tensin 1	-1.537365667	0.00087	0.0342586	20.5449	18.3494	17.1806	12.4508	13.0346	10.974183
HSD17B14	Hydroxysteroid (17-beta) dehydrogenase 14	-1.537917784	0.00404	0.0925303	7.88481	8.93003	12.8854	6.0004	7.54638	5.7614459
S100P	S100 calcium binding protein P	-1.539211916	0.00841	0.1457754	14.548	14.0679	23.8619	9.0006	13.0346	11.934424
PLEKHG4B	Pleckstrin homology domain containing, family G (with RhoGef domain) member 4B	-1.539543618	0.04732	0.3435004	2.55423	3.05823	3.34067	2.70018	1.54358	1.5089501
HECA	hdc homolog, cell cycle regulator	-1.54959842	0.00468	0.1015865	7.88481	9.54167	7.39719	7.05047	4.63073	4.2524958
PTPNM3	PTPNM family member 3	-1.549757401	0.00078	0.0317002	7.4406	7.21742	7.75512	4.80032	4.28771	5.2127367
RNASE4	Ribonuclease, RNase A family, 4	-1.554861839	0.01282	0.1772416	28.0966	34.3745	37.1053	22.6515	21.0955	20.027883
MDK	Midkine (neurite growth-promoting factor 2)	-1.556198651	3.94E-06	0.0007003	19.2123	18.594	22.3109	13.9509	11.4911	12.894665
RND1	Rho family GTPase 1	-1.556996534	4.79E-05	0.0048059	23.9876	28.0134	23.6233	17.1011	16.9793	14.403615
FAM110B	Family with sequence similarity 110, member B	-1.557070996	0.01853	0.2156808	3.44266	3.54754	3.45998	1.95013	2.0581	2.6063684
NEK8	NIMA-related kinase 8	-1.557197658	0.0071	0.1322865	6.77427	5.38248	4.89169	3.30022	4.1162	3.5666093
IGFLR1	IGF-like family receptor 1	-1.564941809	0.00067	0.0286155	8.55113	7.70674	8.47097	6.30042	3.9447	5.349914
FGB	Fibrinogen beta chain	-1.567158258	0.01418	0.1857971	21.3223	24.4658	28.3957	15.151	16.6363	15.363856

Table SII. Continued.

Gene symbol	Name	Fold change	P-value	FDR	AD1	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
UTS2B	Urotensin 2B	-1.567550072	0.01594	0.1981172	4.77531	4.28152	4.77238	2.70018	2.74414	3.2922548
ETS2	v-ets avian erythroblastosis virus E26 oncogene homolog 2	-1.57029571	8.49E-15	1.62E-11	109.943	117.681	118.355	72.0048	69.6325	77.505165
TM4SF20	Transmembrane 4 L six family member 20	-1.57111399	0.00033	0.0182159	57.6368	51.8676	56.9106	37.6525	35.8453	32.099484
PDK1	Pyruvate dehydrogenase kinase, isozyme 1	-1.573402897	0.00858	0.1477052	13.1043	7.70674	11.3344	7.80052	6.86034	5.7614459
MT1X	Metallothionein 1X	-1.573862892	9.54E-05	0.0076151	27.4303	26.5454	34.4804	19.3513	16.1218	20.302238
CDKN2D	Cyclin-dependent kinase inhibitor 2D (p19, inhibits CDK4)	-1.576508704	0.04374	0.3330515	2.8874	2.20192	3.8179	1.80012	2.0581	1.7833047
PCDHA5	Protocadherin alpha 5	-1.577175889	0.03953	0.3186393	3.55372	3.91453	3.57929	2.25015	2.0581	2.6063684
LDLRAD4	Low density lipoprotein receptor class A domain containing 4	-1.577327426	0.01033	0.1611284	5.77479	5.99413	5.72686	4.05027	2.91565	3.9781412
SALL1	Spalt-like transcription factor 1	-1.577539773	0.02939	0.2765207	3.22056	3.54754	2.62481	1.5001	2.22961	2.1948365
CACNA1D	Calcium channel, voltage-dependent, L type, alpha 1D subunit	-1.5786995	0.00636	0.1246838	7.4406	5.99413	7.39719	5.40036	3.25866	4.389673
HNF4A	Hepatocyte nuclear factor 4, alpha	-1.583472908	2.74E-06	0.0005211	64.3001	58.1063	62.5182	38.1025	39.6185	38.683994
CAMSAP3	Calmodulin regulated spectrin-associated protein family, member 3	-1.586559818	0.00125	0.0441081	7.88481	10.765	10.022	4.95033	4.97375	7.8191051
CHMP1B2P	Charged multivesicular body protein 1B2, pseudogene	-1.586938056	0.04425	0.3334613	2.8874	2.9359	2.14757	1.80012	1.20056	1.920482
DCDC5	Doublecortin domain containing 5	-1.594118603	0.00063	0.0278565	15.9917	15.7805	16.1068	9.75065	10.462	9.7395871
IL18BP	Interleukin 18 binding protein	-1.5956581881	0.02802	0.270838	2.66529	3.91453	3.22136	2.10014	2.22961	1.7833047
ZNF789	Zinc finger protein 789	-1.599285837	0.039	0.3177362	2.8874	3.18056	4.77238	2.10014	3.08715	1.6461274
RBMI4-RBM4	RBM14-RBM4 readthrough	-1.601822017	0.00241	0.067736	8.21797	8.31838	8.70959	3.75025	6.86034	5.2127367
MST1R	Macrophage stimulating 1 receptor	-1.608022687	0.00011	0.0082657	11.6606	10.5203	9.54476	6.30042	5.83129	7.4075733
FOS	FBJ murine osteosarcoma viral oncogene homolog	-1.608504168	0.00399	0.0920107	21.2112	18.8387	17.8964	10.9507	13.2062	11.797246
HHIP-AS1	HHIP antisense RNA 1	-1.613655549	0.04638	0.3400766	2.66529	3.18056	2.98274	1.65011	1.20056	2.4691911
LIPT2	Lipoyl(octanoyl) transferase 2 (putative)	-1.61712485	0.02247	0.240541	2.55423	3.42522	3.45998	1.95013	2.40112	1.5089501
IGFBP1	Insulin-like growth factor binding protein 1	-1.619505552	9.38E-05	0.0075479	20.767	15.5358	21.9529	12.0008	11.1481	12.62031
ENO3	Enolase 3 (beta, muscle)	-1.623722618	2.87E-06	0.0005325	20.5449	20.429	24.1005	14.551	11.1481	13.992083
HSP90AA1	Heat shock 70 kDa protein 1-like	-1.624775682	0.02397	0.249735	3.44266	2.9359	2.5055	2.10014	1.20056	2.0576592

Table SII. Continued.

Gene symbol	Name	Fold change	P-value	FDR	AD1	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
H19	H19, imprinted maternally expressed transcript (non-protein coding)	-1.632448521	0.00209	0.0614848	26.4308	21.1629	18.0157	10.8007	12.8631	16.324097
HDAC5	Histone deacetylase 5	-1.637416184	0.00016	0.0114671	10.9943	9.17468	11.931	5.85039	6.34582	7.270396
MTSS1	Metastasis suppressor 1	-1.640016148	0.00206	0.0611657	6.66322	7.33975	5.24962	4.35029	3.77319	3.5666093
LINC01279	Long intergenic non-protein coding RNA 1279	-1.646368277	8.96E-05	0.0073344	19.1012	16.0251	17.5385	9.45063	14.5782	8.230637
MAP3K7CL	MAP3K7 C-terminal like	-1.646423343	0.04359	0.3327291	3.33161	2.81357	3.22136	1.65011	2.74414	1.3717728
FGA	Fibrinogen alpha chain	-1.651985104	0.00382	0.0899893	32.9829	32.5395	33.8839	19.8013	16.9793	23.045783
OTUD1	OTU deubiquitinase 1	-1.657434805	0.01065	0.163077	5.77479	6.60577	6.91995	5.55037	3.60168	2.4691911
GNG4	Guanine nucleotide binding protein (G protein), gamma 4	-1.665252004	6.04E-08	2.52E-05	21.5444	20.062	22.5495	11.2508	13.8922	13.306196
B3GNT3	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 3	-1.665733978	0.00146	0.0493183	7.4406	8.31838	8.70959	4.20028	5.83129	4.6640276
RRN3P3	RRN3 homolog, RNA polymerase I transcription factor pseudogene 3	-1.665862897	0.03382	0.296552	4.5532	3.66987	1.90895	2.40016	1.88659	1.7833047
TPPP3	Tubulin polymerization-promoting protein family member 3	-1.671406748	3.03E-06	0.0005541	36.2035	34.3745	39.9687	17.8512	24.3542	23.73167
EPHA4	EPH receptor A4	-1.671773199	0.00155	0.0513286	6.55217	5.50481	6.08478	3.30022	4.97375	2.7435457
MEX3B	Mex-3 RNA binding family member B	-1.672477607	0.0006	0.0268189	9.21745	6.97276	7.27788	5.25035	5.48827	3.4294321
VASH2	Vasohibin 2	-1.673283288	0.00053	0.0247193	7.6627	10.2756	7.63581	4.80032	5.48827	4.9383822
FST	Follistatin	-1.677779786	0.0003	0.0172272	8.10692	9.54167	9.30614	5.55037	6.0028	4.5268503
TSHZ3	Teashirt zinc finger homeobox 3	-1.678877103	0.00077	0.0317002	6.77427	7.33975	10.2606	4.95033	4.97375	4.5268503
SCG2	Secretogranin II	-1.686351041	0.01556	0.1960489	3.33161	2.81357	4.17583	2.40016	2.22961	1.5089501
TFR2	Transferrin receptor 2	-1.687060313	0.03582	0.3044785	3.55372	2.0796	4.65307	2.25015	1.88659	1.920482
NTRK3	Neurotrophic tyrosine kinase, receptor, type 3	-1.694208995	2.08E-07	6.31E-05	89.1761	95.6614	93.7773	57.9039	50.252	55.556799
SLC3A1	Solute carrier family 3 (amino acid transporter heavy chain), member 1	-1.694673835	0.03734	0.3104771	2.44318	1.83494	1.90895	1.35009	0.85754	1.3717728
BMP6	Bone morphogenetic protein 6	-1.69961553	5.50E-05	0.0054277	11.7717	14.4348	14.1978	8.40056	7.37487	7.8191051
JUNB	Jun B proto-oncogene	-1.705400162	1.35E-16	3.59E-13	63.5227	72.0519	66.2168	39.9027	37.5604	40.192944
UNC5CL	Unc-5 family C-terminal like	-1.721470405	0.01823	0.2136816	2.44318	4.03686	3.57929	2.55017	1.88659	1.3717728
GAS6	Growth arrest-specific 6	-1.729052638	1.48E-06	0.0003227	15.1033	11.4989	12.7661	8.55057	6.86034	7.270396
BAAT	Bile acid CoA:amino acid N-acyltransferase	-1.72925001	2.05E-08	1.05E-05	39.2019	35.1085	34.1225	23.2516	20.0665	19.20482

Table SII. Continued.

Gene symbol	Name	Fold change	P-value	FDR	AD1	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
LOC101928062	NA	-1.759974878	0.0432	0.3317092	1.88791	1.71261	1.78964	0.45003	1.37207	1.2345955
LOC101927621	NA	-1.761982974	0.02896	0.2747047	1.77686	2.56891	2.14757	0.90006	1.20056	1.5089501
FXYD2	FXYD domain containing ion transport regulator 2	-1.763052614	0.0044	0.0974612	13.5485	7.82906	14.0785	6.15041	7.03185	6.8588641
SLCO1B1	Solute carrier organic anion transporter family, member 1B1	-1.770355018	0.04216	0.3285111	1.99897	1.59028	2.38619	1.5001	1.20056	0.6858864
FGG	Fibrinogen gamma chain	-1.772318038	0.01448	0.1882712	20.5449	17.4931	25.2936	11.2508	15.0928	9.3280552
LCN2	Lipocalin 2	-1.775143672	0.0097	0.1575668	2.8874	4.40385	4.17583	1.35009	2.91565	2.1948365
GBP2	Guanylate binding protein 2, interferon-inducible	-1.799820038	0.03934	0.3180132	1.33264	1.71261	1.67033	1.05007	0.85754	0.6858864
MRAP2	Melanocortin 2 receptor accessory protein 2	-1.809937005	0.03044	0.2820988	2.44318	2.20192	3.34067	0.75005	1.37207	2.1948365
EPHB3	EPH receptor B3	-1.810222933	0.03289	0.2922674	2.22107	2.0796	2.02826	0.90006	0.68603	1.7833047
CASKIN1	CASK interacting protein 1	-1.819587672	0.03936	0.3180132	1.99897	2.69124	2.26688	0.60004	1.37207	1.7833047
COL3A1	Collagen, type III, alpha 1	-1.832931321	5.03E-05	0.0050024	9.32851	7.46208	7.39719	4.35029	3.77319	4.9383822
NR4A2	Nuclear receptor subfamily 4, group A, member 2	-1.837798745	0.00734	0.1343844	2.55423	3.7922	3.22136	1.05007	1.71509	2.3320138
GPR98	NA	-1.840921336	0.04881	0.3475531	2.11002	1.83494	1.43171	1.20008	1.20056	0.5487091
ZNF674-AS1	ZNF674 antisense RNA 1 (head to head)	-1.84797447	0.00269	0.0716197	4.44215	5.74947	4.29514	1.35009	3.9447	2.6063684
BCL11B	B-cell CLL/lymphoma 11B (zinc finger protein)	-1.866695202	0.00285	0.0739926	4.99741	3.91453	3.57929	2.70018	1.88659	2.0576592
LAIR1	Leukocyte-associated immunoglobulin-like receptor 1	-1.873039808	0.00283	0.0736702	3.33161	3.91453	5.011	2.70018	1.02905	2.6063684
PLG	Plasminogen	-1.874254798	0.01823	0.2136816	2.22107	3.05823	2.26688	1.20008	2.22961	0.6858864
MTMR7	Myotubularin related protein 7	-1.874487713	0.03782	0.312702	2.8874	2.69124	1.3124	1.65011	1.20056	0.8230637
ANG	Angiogenin, ribonuclease, RNase A family, 5	-1.890088396	0.00149	0.0500648	10.5501	11.6213	13.2434	5.25035	4.28771	8.9165234
ABI3BP	ABI family, member 3 (NESH) binding protein	-1.892270228	0.00695	0.1307576	3.77582	5.13782	2.86343	1.35009	1.71509	3.0179002
F2	Coagulation factor II (thrombin)	-1.899125276	0.00974	0.1578659	2.66529	3.30289	4.41445	1.05007	1.37207	2.8807229
PRKCG	Protein kinase C, gamma	-1.903185385	0.02679	0.2664098	1.77686	2.9359	1.43171	1.35009	0.85754	0.960241
MYOCD	Myoardin	-1.929293951	3.51E-08	1.67E-05	22.2107	20.9183	17.0613	10.5007	10.462	10.151119

Table SII. Continued.

Gene symbol	Name	Fold change	P-value	FDR	AD1	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
FRAT1	Frequently rearranged in advanced T-cell lymphomas 1	-1.945807296	0.00129	0.0452709	3.44266	5.13782	3.69859	2.10014	2.74414	1.5089501
MGAT3	Mannosyl (beta-1,4)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase	-1.950444042	0.00099	0.037243	4.33109	4.03686	3.57929	1.80012	2.91565	1.5089501
FRRS1	Ferric-chelate reductase 1	-1.956458279	0.00549	0.1126554	3.22056	4.28152	5.48824	1.05007	3.43017	2.1948365
LRRC24	Leucine rich repeat containing 24	-1.95678578	0.01226	0.1742846	2.11002	2.69124	4.17583	1.20008	1.37207	1.920482
EGR1	Early growth response 1	-1.960045921	0.00352	0.084482	5.9969	3.66987	6.20409	2.70018	2.91565	2.4691911
DEGS2	Delta(4)-desaturase, sphingolipid 2	-1.960046663	0.0421	0.3285111	1.55475	1.59028	1.07379	0.45003	0.85754	0.8230637
MYL9	Myosin, light chain 9, regulatory	-1.97835078	8.71E-08	3.06E-05	11.8827	11.6213	11.4537	5.25035	6.17431	6.1729777
VAX1	Ventral anterior homeobox 1	-2.002689357	0.01997	0.2255566	1.99897	2.20192	1.3124	0.75005	0.68603	1.2345955
CD274	CD274 molecule	-2.00726291	0.00204	0.0611657	2.77634	2.81357	3.34067	1.35009	1.88659	1.2345955
MSMP	Microseminoprotein, prostate associated	-2.019594437	0.0235	0.2473248	2.22107	2.32425	1.3124	1.35009	0.51453	0.960241
MMP14	Matrix metallopeptidase 14 (membrane-inserted)	-2.032149637	0.00537	0.1105657	4.22004	2.9359	2.38619	1.35009	1.20056	2.0576592
PRR22	Proline rich 22	-2.040823897	0.01364	0.1824337	1.99897	1.46795	2.14757	0.45003	0.85754	1.3717728
COL1A1	Collagen, type I, alpha 1	-2.071937911	2.40E-09	2.13E-06	64.189	40.0016	41.2811	22.5015	22.6391	24.829088
LINC01271	Long intergenic non-protein coding RNA 1271	-2.076694922	0.02109	0.2322828	2.66529	2.56891	1.78964	0.30002	1.71509	1.3717728
FSBP	Fibrinogen silencer binding protein	-2.088057696	0.00012	0.008672	9.66167	6.97276	9.18683	3.30022	4.80224	4.2524958
TLE6	Transducin-like enhancer of split 6	-2.088484152	0.00838	0.1454804	1.88791	3.30289	1.90895	1.5001	1.20056	0.6858864
LOC100130705	NA	-2.105940315	0.02531	0.2576507	1.33264	1.10096	1.78964	0.75005	0.68603	0.5487091
KRT4	Keratin 4, type II	-2.122715036	0.0011	0.0398502	4.22004	3.18056	3.93721	1.20008	2.0581	2.0576592
NOG	Noggin	-2.13510553	0.03657	0.3077433	1.11054	1.46795	2.02826	0.45003	0.68603	0.960241
TENM2	Teneurin transmembrane protein 2	-2.149681097	0.02021	0.2268746	1.77686	2.20192	1.3124	1.35009	0.51453	0.5487091
PTPRB	Protein tyrosine phosphatase, receptor type, B	-2.151228609	0.04406	0.3334613	2.11002	1.10096	1.78964	0.60004	1.20056	0.5487091
RPL21	Ribosomal protein L21	-2.166932484	0.00088	0.0342992	31.2061	69.2383	82.4429	20.4014	34.9877	28.670052
CRYAB	Crystallin, alpha B	-2.172882122	0.01804	0.211952	2.11002	1.10096	1.43171	0.45003	0.68603	0.960241
EBF4	Early B-cell factor 4	-2.185969936	3.12E-05	0.0036241	4.77531	4.28152	4.29514	1.80012	2.40112	1.920482
MTIF	Metallothionein 1F	-2.190948314	0.00656	0.1266567	2.99845	1.46795	3.93721	1.80012	1.20056	0.8230637
ANKS4B	Ankyrin repeat and sterile alpha motif domain containing 4B	-2.200370939	0.01247	0.1754934	1.55475	2.44658	2.14757	0.75005	1.37207	0.6858864
SPAG4	Sperm associated antigen 4	-2.226403951	0.01922	0.2205792	3.1095	1.59028	2.14757	1.5001	1.02905	0.5487091

Table SII. Continued.

Gene symbol	Name	Fold change	P-value	FDR	AD1	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
NPTX1	Neuronal pentraxin I	-2.231436922	5.78E-47	7.70E-43	130.488	122.084	129.57	56.1037	56.5978	57.888813
SIDT1	SID1 transmembrane family, member 1	-2.234352381	0.04963	0.3495069	1.6658	2.44658	1.1931	0.75005	1.54358	0.1371773
SNTB1	Syntrophin, beta 1 (dystrophin-associated protein A1, 59 kDa, basic component 1)	-2.244434941	0.01393	0.184192	2.22107	3.54754	2.14757	0.90006	1.20056	1.3717728
SFRP5	Secreted frizzled-related protein 5	-2.253998948	0.00401	0.0924147	2.11002	1.59028	2.5055	0.90006	0.51453	1.2345955
SEPT5-GP1BB	NA	-2.266316713	0.0012	0.0425038	2.99845	2.0796	3.22136	1.35009	0.85754	1.3717728
CP	Ceruloplasmin (ferroxidase)	-2.269260559	0.00032	0.0180166	55.1937	45.0171	66.9326	24.7517	24.0112	24.554734
ASIC2	Acid sensing (proton gated) ion channel 2	-2.276481893	0.02231	0.2399662	1.22159	1.22329	1.43171	0.30002	0.68603	0.6858864
LOC100093631	NA	-2.321282658	6.44E-07	0.0001718	76.4049	63.2442	33.168	35.1023	20.0665	19.067642
PCSK4	Proprotein convertase subtilisin/kexin type 4	-2.335775789	0.01534	0.1951695	1.4437	1.59028	1.3124	0.15001	1.02905	0.6858864
MIR210HG	MIR210 host gene	-2.342697225	0.00977	0.1578919	3.22056	2.20192	2.74412	1.20008	0.68603	1.5089501
MBNL1-AS1	MBNL1 antisense RNA 1	-2.343089226	0.00948	0.1554006	1.77686	1.34562	1.55102	0.45003	0.51453	0.960241
NEB	Nebulin	-2.348399794	0.01391	0.184192	1.99897	1.71261	1.67033	0.60004	0.51453	1.0974183
CHRD12	Chordin-like 2	-2.353428269	0.00115	0.0411538	3.22056	2.56891	4.29514	1.35009	1.37207	1.5089501
SDS	Serine dehydratase	-2.361194975	0.00051	0.0236741	2.44318	2.56891	3.34067	1.35009	1.20056	0.960241
SSC5D	Scavenger receptor cysteine rich family, 5 domains	-2.366972498	0.00881	0.1504495	3.66477	2.69124	1.1931	0.90006	0.85754	1.3717728
PAQR6	Progesterin and adipoQ receptor family member VI	-2.376344402	0.00012	0.0090063	3.66477	3.91453	4.77238	1.5001	1.54358	2.0576592
CLV3	Clavesin 1	-2.456779726	0.00456	0.100139	1.77686	1.71261	1.43171	0.75005	0.51453	0.6858864
TAGLN	Transgelin	-2.47394612	2.61E-18	1.16E-14	26.6529	21.5299	24.2198	8.70058	8.74694	11.522892
CASC15	Cancer susceptibility candidate 15 (non-protein coding)	-2.551769394	0.00424	0.0951619	1.6658	2.9359	2.86343	1.65011	0.51453	0.6858864
PCDH10	Protocadherin 10	-2.598716548	0.00995	0.1585998	1.6658	1.71261	1.07379	0.60004	0.85754	0.2743546
IGFBP5	Insulin-like growth factor binding protein 5	-2.608845768	0.00222	0.0639028	43.533	8.07372	10.022	7.05047	7.71788	8.7793461
TOX3	TOX high mobility group box family member 3	-2.651944414	0.00253	0.0693256	1.99897	1.71261	1.1931	0.45003	0.68603	0.6858864
LPAR5	Lysophosphatidic acid receptor 5	-2.687286436	0.00689	0.1304139	1.6658	1.22329	1.67033	0	0.68603	0.960241
COL1A2	Collagen, type I, alpha 2	-2.784971607	0.00176	0.0557515	23.7655	4.28152	5.84617	4.95033	2.74414	4.389673

Table SII. Continued.

Gene symbol	Name	Fold change	P-value	FDR	AD1	AD2	AD3	AGA5-1	AGA5-2	AGA5-3
MEF2B	Myocyte enhancer factor 2B	-3.091863954	0.00198	0.0605891	1.88791	2.32425	1.55102	0.60004	0.68603	0.5487091
ENTPD2	Ectonucleoside triphosphate diphosphohydrolase 2	-3.113001185	5.39E-06	0.0009213	4.10899	4.03686	3.8179	1.05007	1.54358	1.2345955
CA9	Carbonic anhydrase IX	-3.284292015	0.00207	0.0611657	11.2164	5.50481	14.0785	3.45023	3.25866	2.6063684
LOC642423	NA	-3.914190738	0.00034	0.0186344	4.22004	2.44658	2.14757	0.60004	0	1.5089501
TMEFF1	Transmembrane protein with EGF-like and two follistatin-like domains 1	-11.37525213	1.22E-06	0.00002811	1.88791	2.81357	1.07379	0	0.51453	0