SUPPLEMENTARY MATERIALS AND METHODS:

Generation of conditional Ada3 knockout targeting construct-To generate a conditional targeting construct, we examined the genomic structure of the mouse Ada3 gene. According to the NCBI mouse genome resources (Build 32.1), mouse Ada3 gene is located on chromosome 6, is composed of 9 exons and spans approximately 11kb. We flanked exons 2 to 4 with loxP sequences so that these exons can be removed from the chromosome using Cre-dependent recombination. Exons 2 to 4 were targeted based on the following considerations. Targeting of these three exons will lead to deletion of 188 amino acids amounting to about 43% of protein coding sequence and the transcript from the remaining exons is unlikely to lead to a functional protein product. Limiting the gene manipulation to exons 2 to 4 also minimized potential effects on promoter/enhancer elements of neighboring genes (**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=Graphics&list_uids=70601**). We used a probe from Ada3 genomic region to screen a BAC library (RPCI-22 (129S6/SvEvTac) (Children's Hospital Oakland Research Institute, bacpac.chori.org) and identified a clone that had the required genomic region of Ada3 locus to generate a targeting construct. LoxP sites were introduced using a recombineering technique, as previously described (1).

Generation of Ada3 gene-targeted mice and isolation of mouse embryos and PCR genotyping-A duplex-PCR based strategy was developed to distinguish between the wild-type and Ada3 mutant alleles. The primers are as follows: a, 5'-CGGGAGGGGGAGCTCTATGAATCCTGATCTAT-3'; b, 5'-TCAACATAATTTCTCTGTATAACAACTCTGGC-3'; c, 5'- CAATATGACTAACTACATCTCTGG-3' (Supplementary Figure S1A). A 470-bp fragment indicates the presence of the wild type allele, whereas a 703-bp fragment is amplified from the mutated allele. For analysis of post implantation embryos, *Ada3*$^{+/-}$ females were sacrificed at various time points (see Table 1) after being mated to *Ada3*$^{+/-}$ males. Embryos were dissected from the uteri and washed in phosphate-buffered saline (PBS), and DNA was isolated after proteinase K (Roche) digestion. Genotyping was performed by a duplex PCR using the duplex-PCR mentioned above. For blastocyst isolation, plugged *Ada3*$^{+/-}$ females were euthanized at 3.5 dpc, and their uteri were dissected and flushed with DMEM. Blastocysts were either directly genotyped or seeded singly onto 24-well plates and cultured in complete DMEM at 37°C with 5% CO_2. After 4 days, the medium was changed, and after 7 days in culture, blastocyst DNA was isolated and subjected to genotyping PCR

Generation of Ada3 monoclonal antibody and Immunoblotting-Full length human Ada3 cDNA was cloned into pGEX 6P1 bacterial expression vector (that contain N-terminal GST tag followed by a precision protein). The recombinant protein (hAda3) was purified from a large scale culture of BL21 *E. coli* using Glutathione Sepharose 4B beads (Pharmacia). GST tag was cleaved using Precision protease and purified hAda3 was used as an antigen to produce monoclonal antibodies at the Monoclonal Antibody Core Facility, Lurie Cancer Center, Northwestern University, Chicago. The clones were screened by i) western blotting using 293T cell lysates as an endogenous Ada3 and using flag-tagged Ada3 overexpressing 293T cell lysates and also by ii) immunoprecipitation of endogenous or exogenous Ada3 from 293T cell lysates (data not shown). A few well reacting antibodies were selected among which the clone 5C9/C8 was used for subsequent experiments. Clone 5C9/C8 recognized a single band of estimated size in western blotting and immunoprecipitation. This clone was used for immunoblotting experiments conducted in the paper. Other primary antibodies used to perform immunoblotting were Rb (554136, Pharmingen); Cyclin A (sc-596), Cyclin E (sc-481), Cyclin D1 (sc-20044), Cdk2 (sc-6248), Cdk4 (sc-260), Cdk6 (sc-53638), p27 (sc-1641), p21 (sc-6246), p16 (sc-1661), p300 (sc-585), PCAF (sc-15124) and Hsc-70 (sc-7298) (Santa Cruz Biotechnology, Santa Cruz, CA); c-myc (1472-1, Epitomics); H2B-K5 (07-382), H2B (05-1352), H3 (06-755), H3-K9 (07-352), H3-K56 (07-677) and H4 (05-858) (Millipore); histone Ab sampler kit (H2A-K5, H2A, H2B-K5, H3-K9, H4-K8) (9933, Cell Signaling) and β-actin (A5441, Sigma).

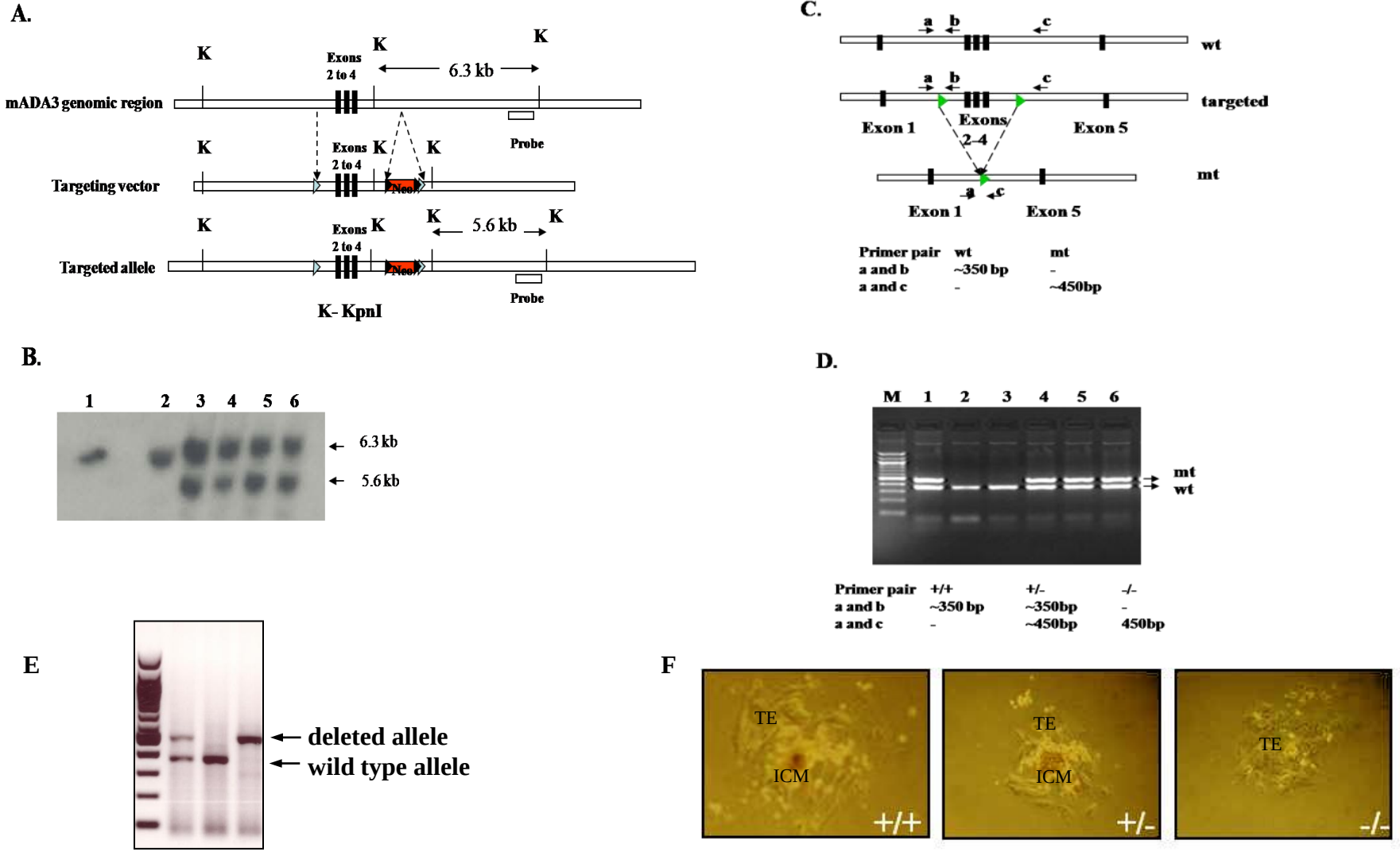
Generation of recombinant baculoviruses and Ada3-His expression using Bac-to-Bac® Expression System-Ada3 coding sequence was PCR amplified to contain 6X Histidine tag in the C-terminus and cloned into (SalI and NotI Sites) of pFastBac™ donor plasmid and

the recombinant baculovirus expressing Ada3-His protein was produced following manufacturer's instructions. Sf21 cells infected with recombinant baculovirus were lysed and the Ada3-His protein was purified using Ni-NTA column.

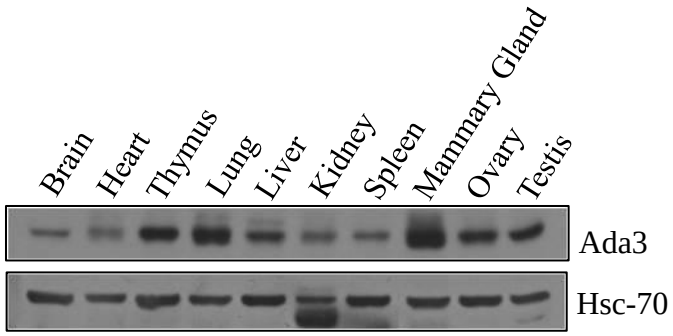
HAT assay-HAT assays were carried out in buffer containing 50 mM Tris HCl pH 8.0, 50 mM KCl, 5% glycerol, 0.1 mM EDTA, 1mM DTT, 10mM sodium butyrate, [^{3}H] Acetyl Coenzyme-A (Perkin-Elmer) and 1mM PMSF at 30°C using core histones or histone H3 alone as a substrate. Recombinant p300 catalytic domain was purchased from Active Motif. Purified core histones from chicken erthyrocytes were purchased from Upstate and purified. Histone H3 from calf thymus was purchased from Roche. Briefly, 10ng of p300 catalytic domain was incubated with varying concentrations of purified baculoviral Ada3 and either 1 ug of core histones or 1 ug of Histone H3 in HAT buffer for 15 min. The products were subjected to SDS-PAGE, transferred to PVDF membranes, and autoradiographed. The PVDF membranes were sprayed with EN^{3}HANCE spray (Perkin Elmer) to enhance the signals from tritium prior to autoradiography.

Microarray analyses-Three days after infecting *Ada3*$^{FL/FL}$ MEFs with Ctrl and Cre Adenoviruses, total RNA was isolated using the TRIzol reagent. Biotin labeled cRNA was generated from 200 ng of total RNA using the Ambion WT Expression Kit (Ambion) per manufacturer's instructions. Hybridization, scanning of the chip and initial scaling was performed as previously described (2); except that Affymetrix GeneChip Mouse Genome 430 2.0 Array was used for cRNA hybridization. Intensities were imported into Affymetrix Expression console software using Robust Multi-chip Averaging (RMA) background correction and fold-change differences between samples were determined. Microarray analysis was performed using duplicate samples and the values represent average of the two independent experiments.

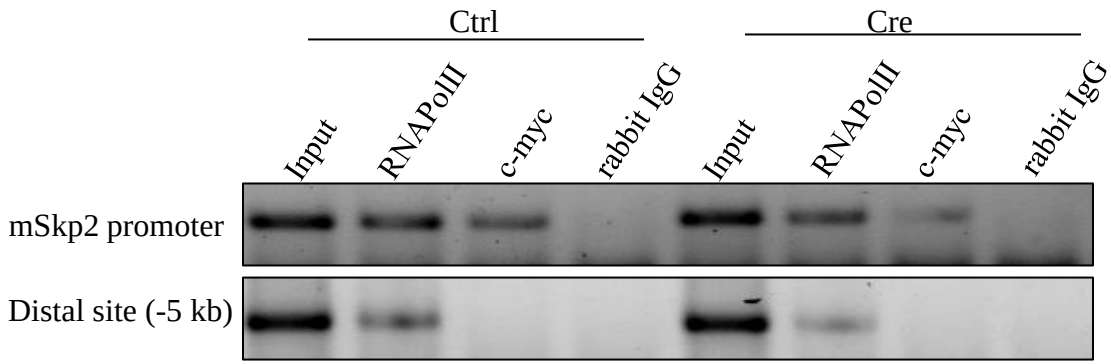
Time Lapse Microscopy-24 h after control and Cre adenovirus infection, *Ada3*$^{FL/FL}$ MEFs were plated in 6 well plates at 30% confluency. One day after plating, cells were placed on a robotized stage of an Olympus IX81 DSU Spinning Disk confocal microscope equipped with a chamber maintained at 37^o C with 5% CO_2. Movies were acquired over 24 h (10 min intervals) using Hamamatsu ORCA-ERG camera and automated acquisition software (Slidebook Software) at 10x magnification.



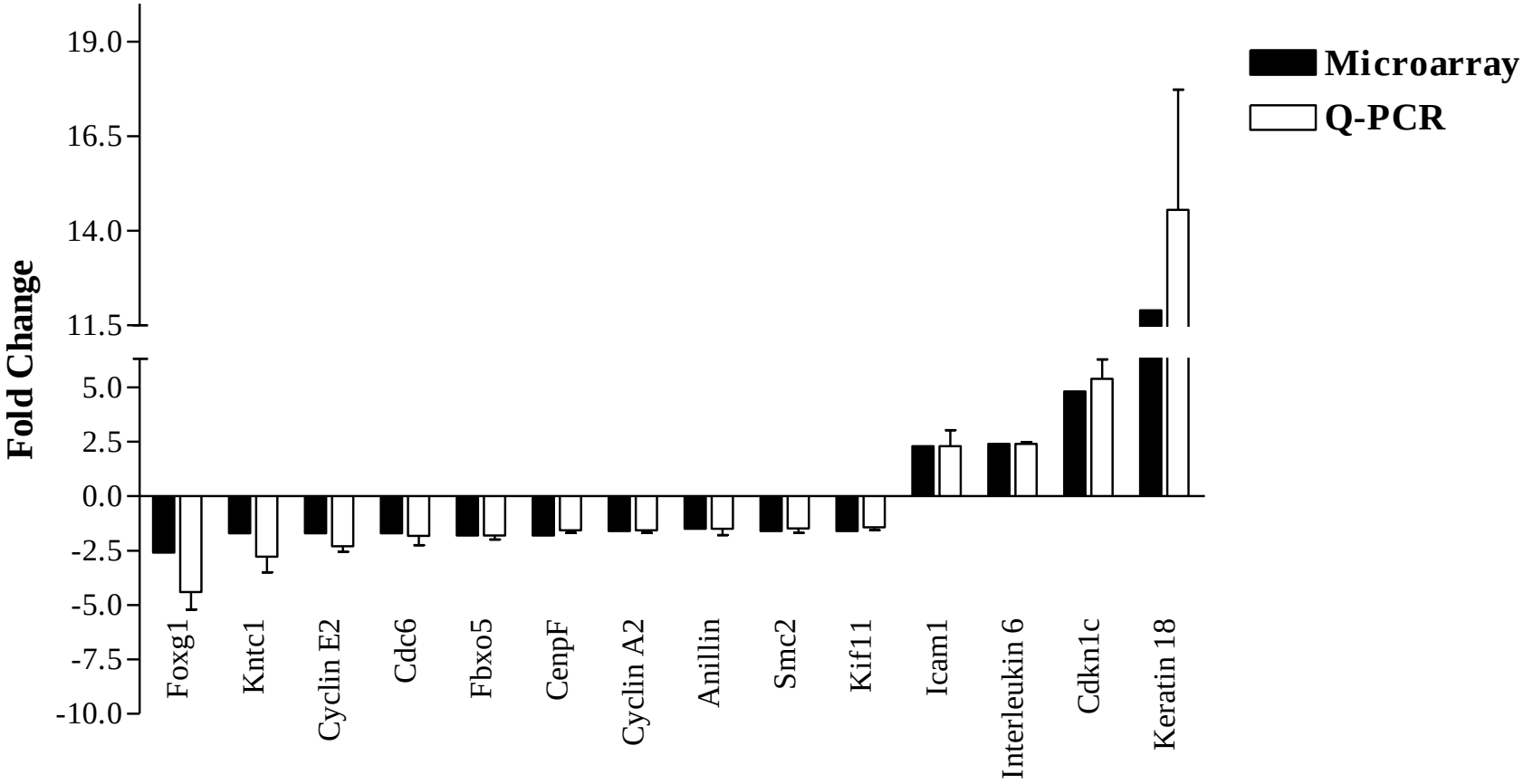
Supplementary Figure S1. **Targeting of *mAda3* locus and PCR genotyping strategy.** (A) Schematic representation of the targeting strategy used to disrupt *mAda3*. (B) Southern blotting of DNA from ES cell clones digested with KpnI and probed with *Ada3* locus specific probe; lanes 3-6 represent positive clones; lanes 1 and 2 represent wild type. (C) PCR strategy to screen for the deleted allele. (D) A representative gel picture showing genotyping of a litter from *Ada3*$^{+/-}$ intercross. (E) Blastocysts isolated from 3.5 day post coitus from *Ada3*$^{+/-}$ females mated with *Ada3*$^{+/-}$ males were cultured in DMEM with 10% fetal calf serum for 7 days and the cells recovered from blastocyst outgrowth were subjected to genotyping PCR. A representative gel image showing PCR results of blasocyst outgrowths. (F) Representative microscopic images showing each of the three Ada3 genotype blastocysts. ICM, inner cell mass; TE, trophectoderm



Supplementary Figure S2. Analysis of Ada3 protein levels in mouse tissues. Protein lysates obtained from various tissues of an adult wild type mouse were subjected to immunoblotting to determine the expression levels of Ada3 protein.



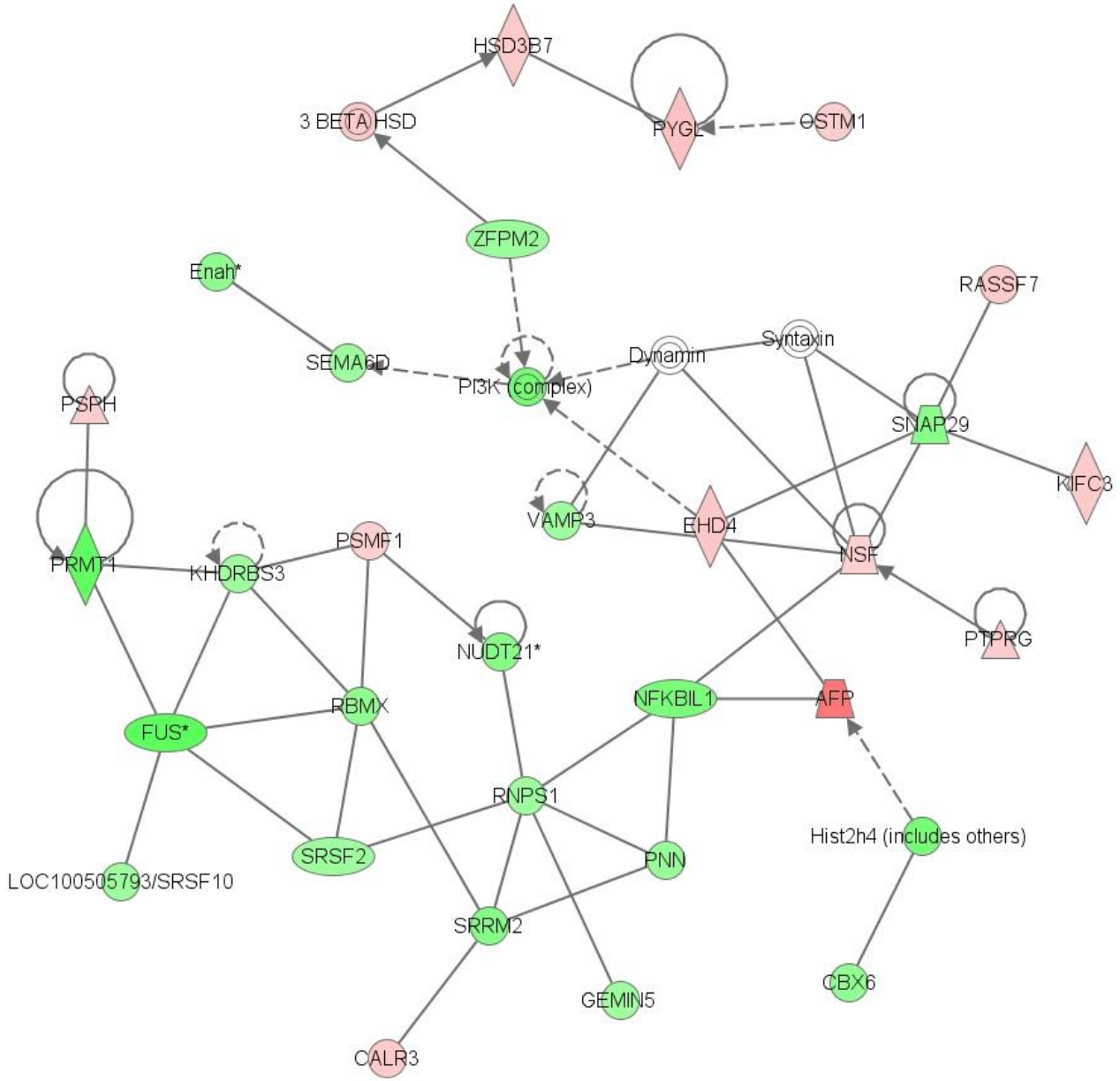
Supplementary Figure S3. Skp2 promoter occupancy by c-myc is reduced upon deletion of Ada3. Chromatin fragments from asynchronous control (Ctrl) and Cre *Ada3*$^{FL/FL}$ MEFs cells were immunoprecipitated with anti c-myc antibody. The immunoprecipitated DNA was analyzed by PCR, using mouse Skp2 promoter specific primers. Primers amplifying a region that is 5 kb upstream of the mouse Skp2 promoter were used as a negative control.



Supplementary Figure S4. Validation of microarray analysis by q-RT-PCR. Microarray data from Ctrl and Cre infected MEFs was verified by qRT-PCR by picking several deregulated genes from microarray. Error bars indicate mean ± S.E. from three independent experiments.

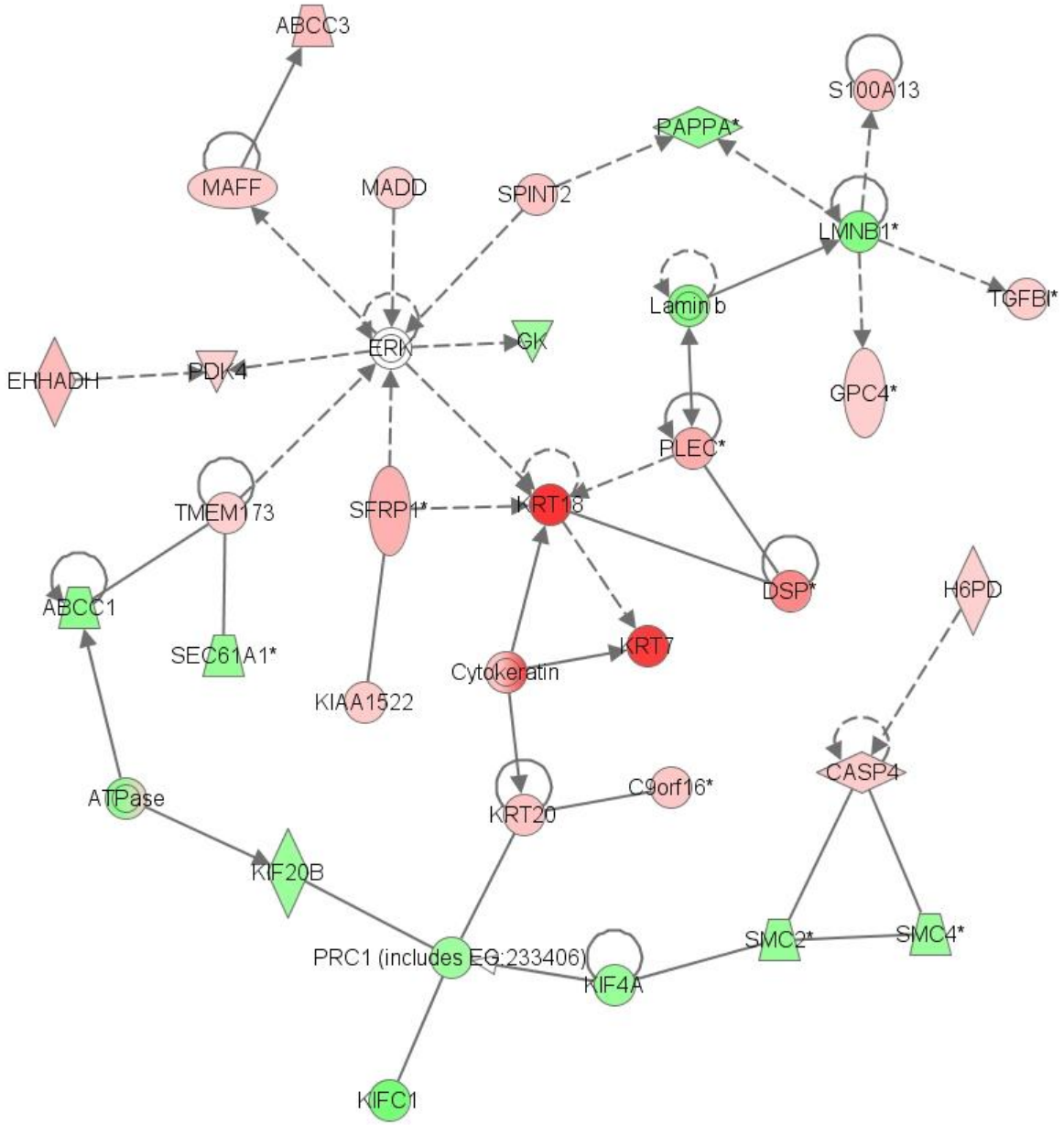
A

Network 1: RNA Post-Transcriptional Modification, Cellular Assembly and Organization, Gastrointestinal Disease



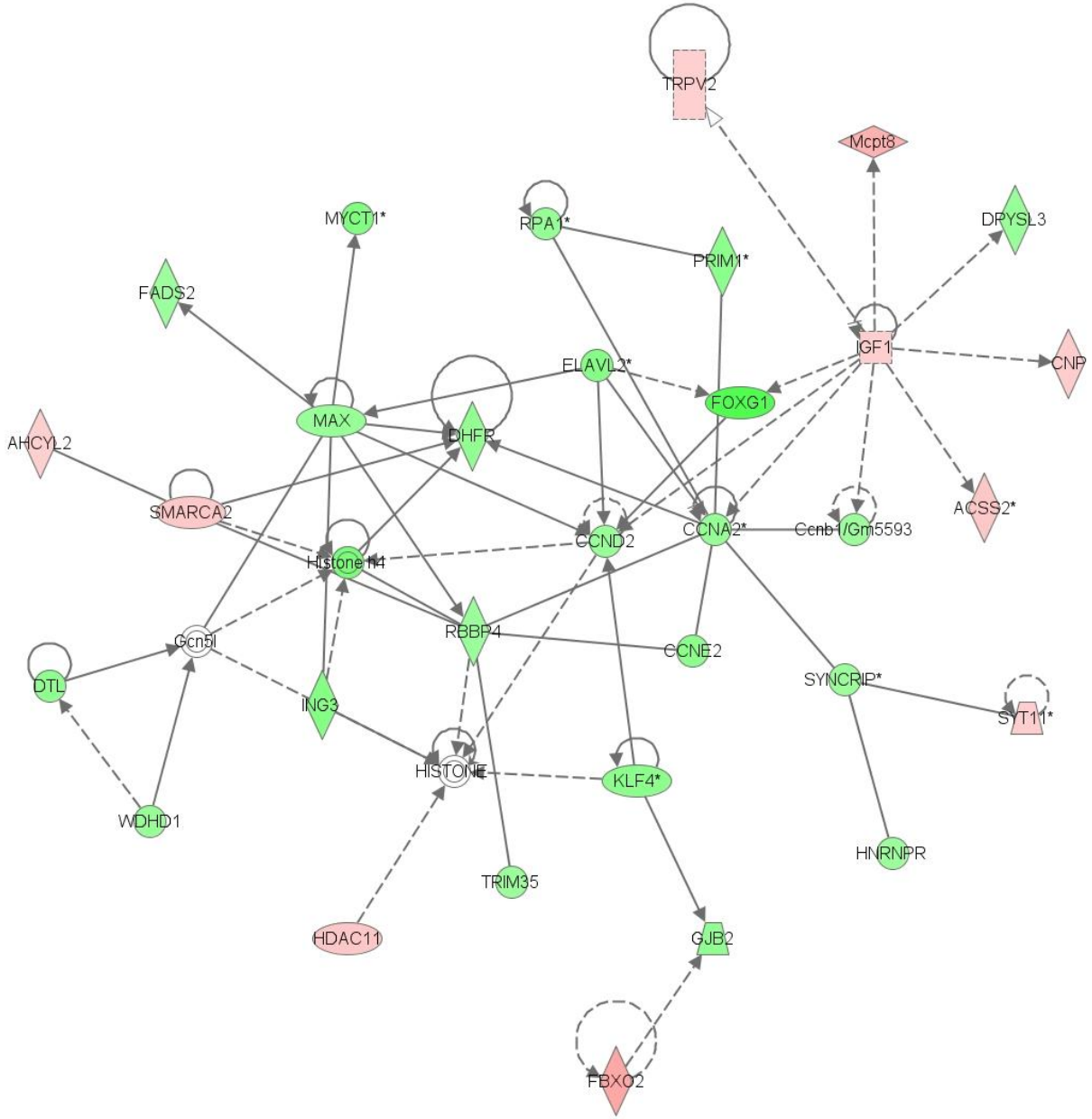
B

Network 2: Cellular Function and Maintenance, Molecular Transport, Cell Death



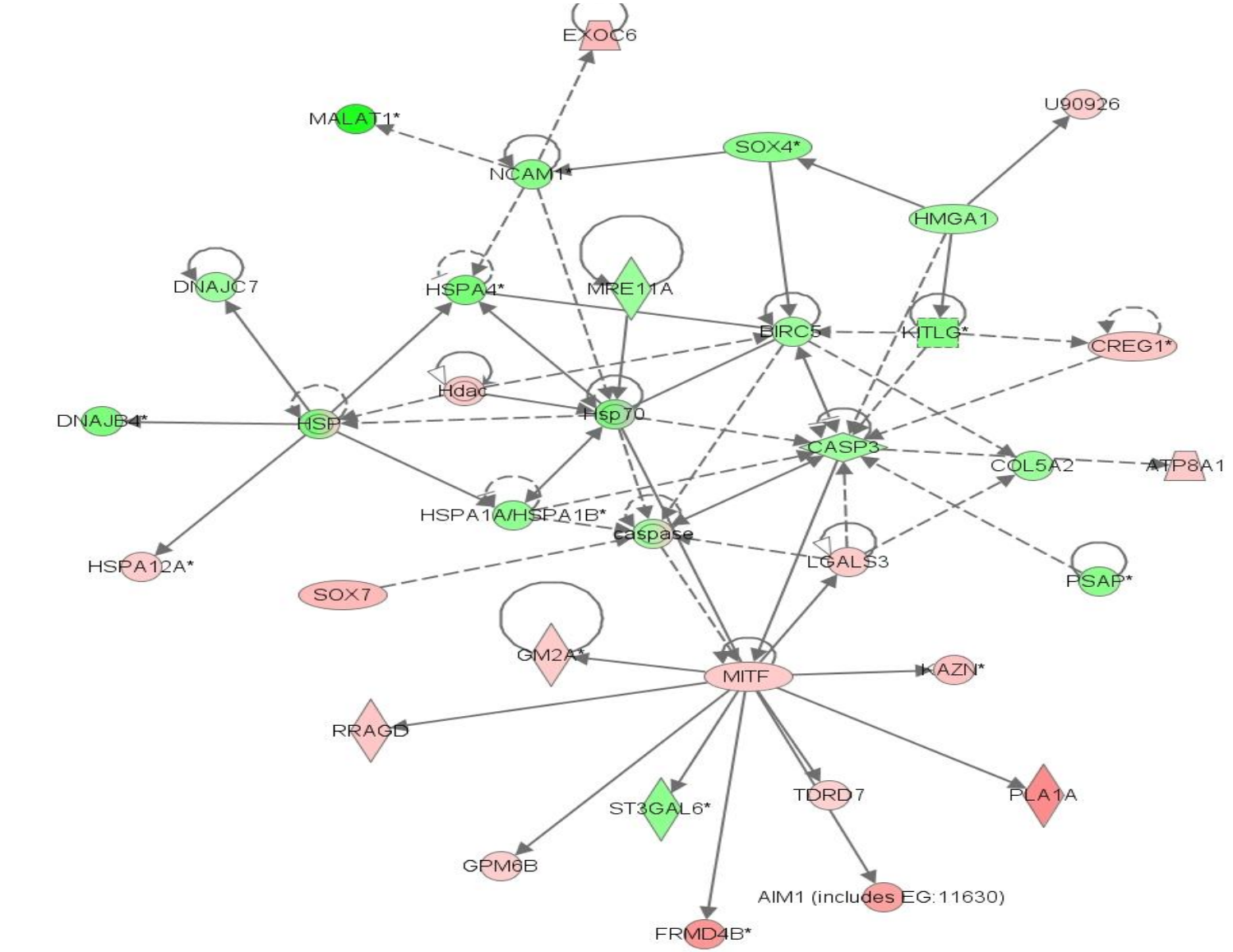
C

Network 3: Cell Cycle, Endocrine System Development and Function, Cancer



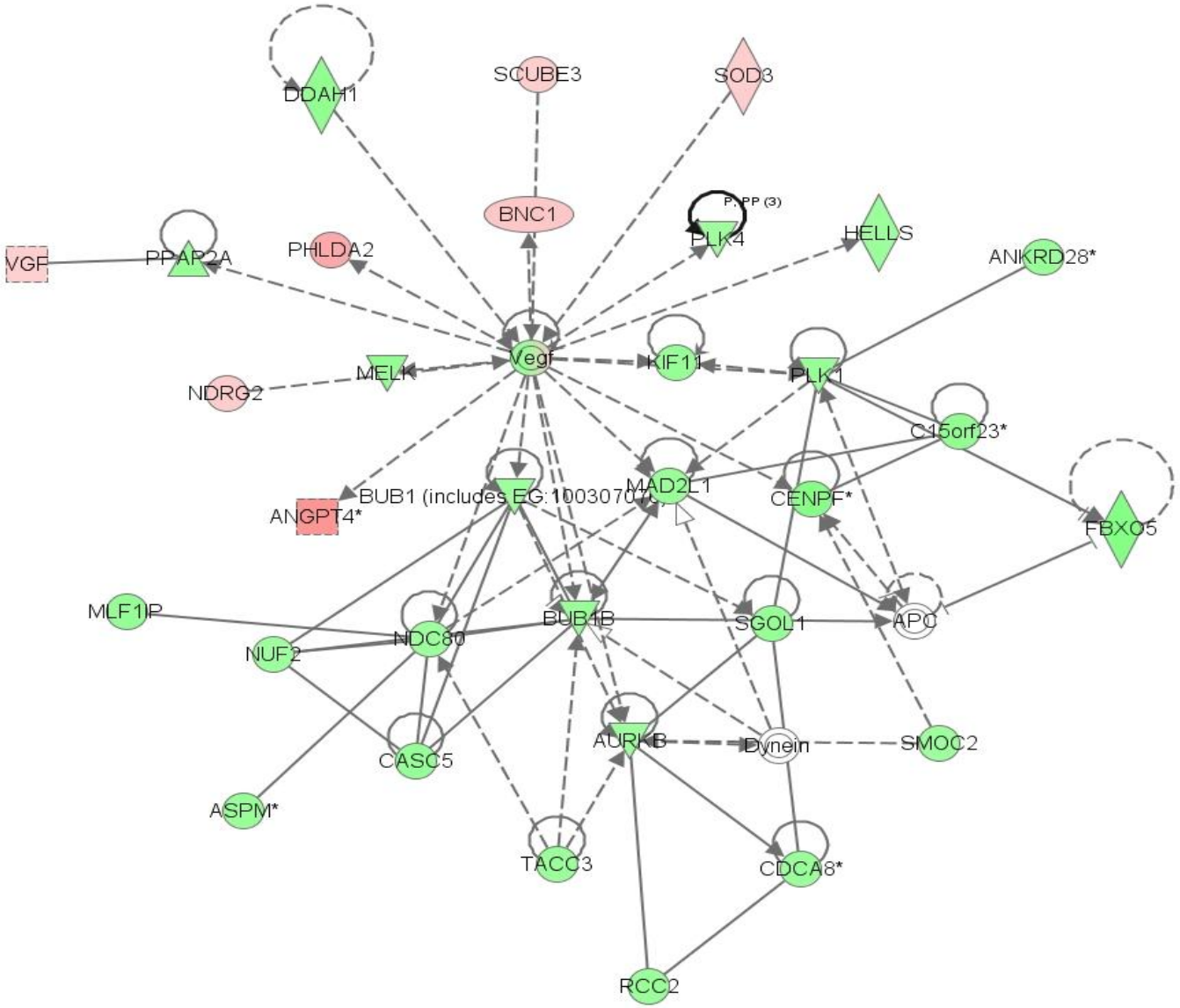
D

Network 4: Lipid Metabolism, Small Molecule Biochemistry, Cell Death

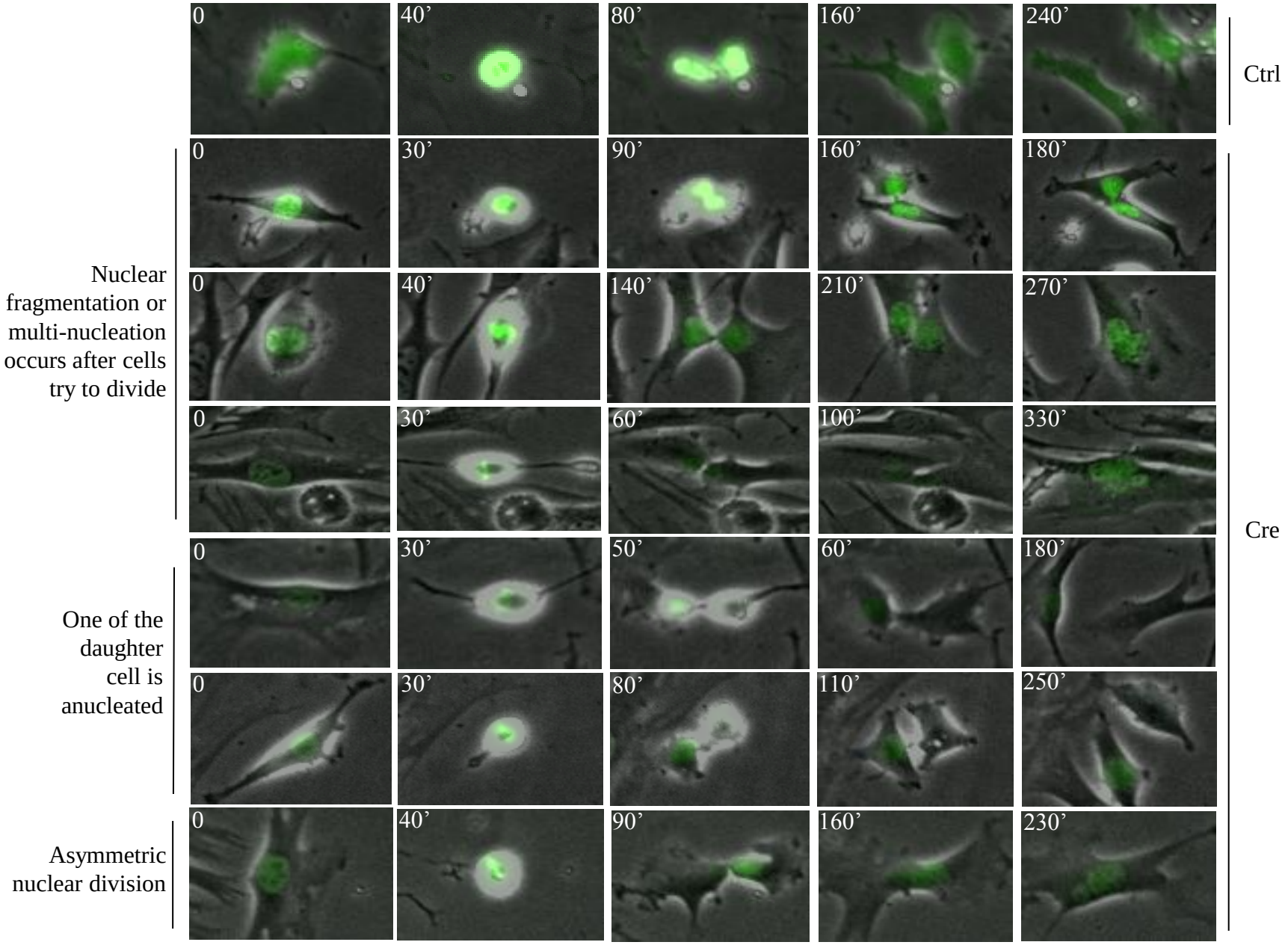


E

Network 5: Cell Cycle, Cellular Assembly and Organization, DNA Replication, Recombination, and Repair



Supplementary Figure S5. Ingenuity Pathway Analysis. (A-E) Top 5 networks affected upon Ada3 deletion as obtained by Ingenuity pathway analysis. All the genes that were induced or downregulated at least 1.5 fold were used for the analysis



Supplementary Figure S6. Abnormal cell division of Ada3 deleted cells. Representative time lapse images of *Ada3*$^{FL/FL}$ cells after 2 days of infection with control (Ctrl) or Cre adenovirus captured over 24 hours period. Note that cells infected with control virus express eGFP in both cytoplasm and nucleus whereas expression of eGFP in Cre infected cells is restricted to the nucleus. Figures in the upper left hand corner of each image indicate minutes.

Supplemental Table S1: Deregulated genes in Ada3-deleted cells

Gene Symbol	Representative Public ID	Fold change
Downregulated genes		
Hmox1	NM_010442	5.4
Cdkn2a	NM_009877	4.5
Gsta1 /// Gsta2	NM_008182	4.3
Malat1	AW012617	3.9
Ptprz1	BC002298	3.4
Ptprz1	BC002298	3.2
LOC639633 /// Npm3 /// Npm3-ps1	BB811478	2.7
Foxg1	NM_008241	2.6
Stmn2	BM115022	2.6
Mex3b	BG072837	2.5
Fus	AF224264	2.5
Vcan	BM251152	2.4
Fam171a2	BB452429	2.4
Cd80	X60958	2.4
Prmt1	AK020120	2.4
3110039M20Rik	AW494150	2.4
Rian	AK017440	2.3
Ptk7	AK018379	2.3
Psma3	C77757	2.3
LOC100047441 /// Msl1	AW495537	2.3
Zc3h7b	BM125518	2.3
Gpr124	NM_054044	2.3
Dok1	BC013066	2.2
Rtn4	NM_024226	2.2
Vip	AK018599	2.2
Pik3r1	M60651	2.1
Mmp14	BB535404	2.1
Plec1	BM232239	2.1
Mgp	NM_008597	2.1
Rad18	AK012795	2.1
2310076G05Rik	BB197581	2.1
Fgf13	AF020737	2.1
Setd5	BI739725	2.1
Nrk	AK012873	2.1
Gja1	M63801	2.1
Mycl1	BG064871	2.1
Tcfec	NM_031198	2.1
Prl8a9	AF158744	2.1

Hspa4	BE912771	2.1
6030442H21Rik	AK020062	2.1
Stxbp6	BC024598	2.1
Col11a1	NM_007729	2.0
Kifc1 /// LOC100044746	NM_016761	2.0
Plau	NM_008873	2.0
2210411K19Rik	BI694945	2.0
Gas7	AI506234	2.0
Cdc42ep3	BB012489	2.0
Rab5c	BC023027	2.0
Dhrs3	NM_011303	2.0
Pip5k1a	BC003763	2.0
A630033H20Rik	BB034567	2.0
Nfkbil1	NM_010909	2.0
Cdc42ep3	BB012489	2.0
Cd34	NM_133654	2.0
Arpc3	BC013618	2.0
Col11a1	NM_007729	2.0
Dnajb4	AK006478	2.0
LOC100047441 /// Msl1	AW495537	2.0
Epha3	AV226618	2.0
Cxcr7	BC015254	2.0
D330050I23Rik	BE303700	2.0
Grb14	NM_016719	2.0
Plau	NM_008873	1.9
D17H6S56E-5	NM_033075	1.9
D17H6S56E-5	NM_033075	1.9
Pik3r1	BB426164	1.9
Lce1h	NM_026335	1.9
Kitl	BB815530	1.9
Adra2a	BB262415	1.9
Sema3a	NM_009152	1.9
C530008M17Rik	BB493717	1.9
S1pr1	BB133079	1.9
Atp2b1	BI080417	1.9
Adamts6	BB227648	1.9
Thoc3	BE335845	1.9
Myct1	AI642973	1.9
Arl2bp	NM_024191	1.9
Stmn2	BM115022	1.9
Kitl	BB815530	1.9
Epha7	BC026153	1.9
Tmem35	NM_026239	1.9

Cd80	AK019867	1.9
2210411K19Rik /// Rpl41	BI694945	1.9
Stom	AF093620	1.9
Slfn9	BI647893	1.9
Blnk	AF068182	1.9
Ptchd1	BB271066	1.9
Samd4	BF319665	1.9
Lpar4	AW493905	1.9
Lmnb1	AA270173	1.9
Aldh1a1	NM_013467	1.9
4921513D23Rik	AV254721	1.9
C130021I20Rik	AW209204	1.9
Rnf25	NM_021313	1.8
Itgbl1	BC020152	1.8
Dbc1	AB060589	1.8
Hmgb3	NM_008253	1.8
Fbxo5	AK011820	1.8
Rlf	BF020283	1.8
Jun	NM_010591	1.8
Unc5c	NM_009472	1.8
LOC100046744 /// Srrm2	BQ176063	1.8
Tnfrsf11b	AB013898	1.8
5430416N02Rik	AW112059	1.8
Arl2bp	AK006418	1.8
Slc20a2	BG144370	1.8
Elavl2	BB105998	1.8
Gap43	BB622036	1.8
Cenpf	BE848253	1.8
Ing3	BB020556	1.8
Nudt21	BG070110	1.8
Edil3	BB377340	1.8
Slc8a1	BB313689	1.8
Hipk2	AF170301	1.8
Maoa	AW986246	1.8
OTTMUSG00000015563	AK013448	1.8
9830001H06Rik	BB093445	1.8
Arf6	BI248938	1.8
Dhcr24	BG295389	1.8
Alg8	BM249614	1.8
Snap29	BF682880	1.8
Fam110c	NM_027828	1.8
Lpar4	BB417145	1.8
Ncam1	BM201198	1.8

Lpar4	BB297502	1.8
Tbx20	AK020409	1.8
Myct1	W34301	1.8
Npy1r	NM_010934	1.8
Sprr2k	NM_011477	1.7
Klf4	BG069413	1.7
Cenpf	BB667318	1.7
Gpr149	BB126999	1.7
D430042O09Rik	BB486367	1.7
Galntl4	AV238718	1.7
Prim1	J04620	1.7
Mcm7	NM_008568	1.7
A4galt	BG064632	1.7
Hcn1	NM_010408	1.7
Macc1	BB007136	1.7
Dnajb4	BC017161	1.7
Maoa	AV356118	1.7
Mirhg1	AK017164	1.7
Pip5k1a	BB822856	1.7
OTTMUSG00000015563	AK013448	1.7
Vcan	BM251152	1.7
Sox4	AI428101	1.7
Nes	AK012622	1.7
Psap	BM212050	1.7
Prpf19	BC004070	1.7
Ccne2	AF091432	1.7
Galnt2	AF348968	1.7
Sema3d	BB499147	1.7
Cspg4	BB377873	1.7
BC020402	BB029175	1.7
Kitl	M64262	1.7
Vcan	NM_019389	1.7
Itga4	BB205589	1.7
Sesn2	AV308638	1.7
Enah	AV329519	1.7
Metrn	BE947704	1.7
Sdpr	AV064339	1.7
Pola1	NM_008892	1.7
OTTMUSG00000015563 /// Ppp1r14c	AK013448	1.7
Lasp1	BC010840	1.7
Dusp10	NM_022019	1.7
Fam110c	NM_027828	1.7
St3gal6	NM_018784	1.7

Elavl2	BB105998	1.7
Npnt	AA223007	1.7
Aff2	BB342212	1.7
Abcc1	NM_008576	1.7
Cspg4	BB377873	1.7
Serpinb1b	AF426025	1.7
Brd2	BI155271	1.7
Dtl	AV308327	1.7
Sema3a	NM_009152	1.7
Sprr1a	NM_009264	1.7
Rbmx	NM_011252	1.7
Nrn1	AK003046	1.7
Swap70	AK019882	1.7
4930402H24Rik	BQ173880	1.7
9130008F23Rik	BB763680	1.7
Utp6	BC025074	1.7
Kif22	BC003427	1.7
Cdc6	NM_011799	1.7
LOC627626	BB111245	1.7
D530037H12Rik	BG066910	1.7
C330027C09Rik	AU018569	1.7
Gjb2	AV239646	1.7
100040182 /// 677010 /// EG433003 /// EG619883 /// EG625281 /// EG664969 /// Rpl30	BB283415	1.7
Hspa1b	M12573	1.7
Gabra4	BB430205	1.7
Gja1	BB142324	1.7
Chtf18	BM233289	1.7
Cbx6	BC019942	1.7
Rab40c	AF422144	1.7
Kntc1	AW536884	1.7
2610002D18Rik	AK011279	1.7
2010300F17Rik	AK008491	1.7
2810055G20Rik	AK021336	1.6
D0H4S114	D45203	1.6
Sdc1	BI788645	1.6
Col10a1	NM_009925	1.6
Haus6	BB794620	1.6
Areg	NM_009704	1.6
Cd80	D16220	1.6
Sdpr	BE197945	1.6
Arl5a	BB811124	1.6
Rpl12	BG807990	1.6

Fam134c	BC016089	1.6
Zdhhc21	BI900142	1.6
Klf4	BG069413	1.6
Gja1	BB039269	1.6
Ddah1	BE283964	1.6
D0H4S114	BB369191	1.6
D2Ertd750e	AU019491	1.6
Nfib	BB092799	1.6
Psap	BM212050	1.6
Ung	BC004037	1.6
Melk	NM_010790	1.6
Col1a2	BB150460	1.6
Hspa1b	M12573	1.6
Fam65b	BM242294	1.6
Erf	BB453531	1.6
Slc7a11	BB453858	1.6
Dhfr	NM_010049	1.6
Pcdh18	BM218630	1.6
Aldh1a7	NM_011921	1.6
C77370	AW495307	1.6
Baz1b	BB253608	1.6
2810026P18Rik	AK012825	1.6
Tcf19	BC004617	1.6
Galnt2	BG064057	1.6
Ywhag	NM_018871	1.6
Uhrf1	BB702754	1.6
Tmem121	AF488729	1.6
Nrcam	BB202655	1.6
Nufip2	AV112972	1.6
Sh3kbp1	AK007283	1.6
Pappa	AF439513	1.6
Uhrf1	BB702754	1.6
Sec61a1	BC003707	1.6
Tcf20	AW552808	1.6
Mcm7	NM_008568	1.6
Prim1	J04620	1.6
Gja1	M63801	1.6
Mfap3l	AV280494	1.6
100042515 /// EG545555 /// EG546331 /// EG665056 /// ENSMUSG00000060128 /// Hmg1l1 /// Hmgb1 /// LOC100045972 /// LOC100046019 /// LOC637733	AV127023	1.6
Cck	NM_031161	1.6
Mtm1	BG976607	1.6

Foxp2	BM964154	1.6
Tmtc2	AK018506	1.6
Dpp8	BM939621	1.6
Mlf1ip	BB667813	1.6
Myh10	BQ176159	1.6
Fam131b	AW490145	1.6
D2Ertd750e	AK012148	1.6
Foxp2	AV322952	1.6
Kif11	BB827235	1.6
Ccna2	X75483	1.6
Gpr149	BB075339	1.6
Inhba	NM_008380	1.6
OTTMUSG00000015351	BB830168	1.6
Slc40a1	AF226613	1.6
Nes	AI413223	1.6
Zcchc5	BQ126004	1.6
Orc1l	BC015073	1.6
Ncam1	BB698413	1.6
Diras2	BM114282	1.6
Nmt2	AV167182	1.6
Sh3kbp1	AK018032	1.6
Hoxb7 /// Hoxb8	X13721	1.6
Dnm3os	BB542096	1.6
Rrm1	BB758819	1.6
Swap70	AV024531	1.6
Smc2	BI684556	1.6
Itga5	AW544851	1.6
Lmnb1	AA270173	1.6
Megf10	AK013855	1.6
Sgol1	BB410537	1.6
Flrt2	BB817332	1.6
Gorab	BB183144	1.6
Pcdh9	BB244656	1.6
Nmt2	AI503912	1.6
Npnt	AA223007	1.6
Kdm4a	AA415022	1.6
100039963 /// Sema3a	NM_009152	1.6
Hoxb9	AA386586	1.6
Kif22	BC003427	1.6
Flnb	BB667380	1.6
Casc5	BB818947	1.6
Pappa	BB635017	1.6
Kif2c	BB104669	1.6

Trib2	BB354684	1.6
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Lmo4	NM_010723	1.6
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Pdgfc	NM_019971	1.6
Cdt1	AF477481	1.6
C77370	C77386	1.6
Rai14	BB308974	1.6
Herc3	AK017531	1.6
Hspa4	BB541289	1.6
100040123 /// EG383032 /// EG665772 /// Rps17	AA030209	1.6
Ptprd	BB075247	1.6
Flrt2	AW555664	1.6
Gja1	AV330726	1.6
Serpinb1a	AF426024	1.6
Wdhd1	C77437	1.6
Mcm7	BB407228	1.6
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Dis3	BM232345	1.6
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Stom	AF093620	1.6
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Foxp1	BG962849	1.5
Col6a3	AF064749	1.5
Mtm1	BG976607	1.5
Bub1b	AU045529	1.5
Aspm	NM_009791	1.5
Hmgb1	BF166000	1.5
Foxp1	BG962849	1.5
Tnfrsf11b	AB013898	1.5
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Hipk2	AF208292	1.5
Anln	BI690018	1.5
Ppap2a	NM_008903	1.5
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Zwilch	BC027435	1.5
Mki67	X82786	1.5
Mad2l1	NM_019499	1.5
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Dpysl3	AV161550	1.5
Uty	BB742957	1.5
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Fus	AF224264	1.5
Zfpm2	NM_011766	1.5
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Rad51ap1	BC003738	1.5
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Gins2	AW488914	1.5
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Usp1	BC018179	1.5
Rgs16	U72881	1.5
Foxs1	BB040642	1.5
Rbbp4	BF011461	1.5
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St3gal6	NM_018784	1.5

Chaf1b	BC013532	1.5
Kcnk2	NM_010607	1.5
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6430598A04Rik	BB387298	1.5
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Ncapg	BB702347	1.5
Alcam	U95030	1.5
Tead2	D50563	1.5
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Mcm7	BB464359	1.5
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Ccdc68	AV378320	1.5
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Kif20b	BB200034	1.5
Malat1	AW012617	1.5
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Ddit4	AK017926	1.5
Loxl3	NM_013586	1.5
Tacc3	NM_011524	1.5
Cct4	AV103196	1.5
Tk1	NM_009387	1.5
2700078E11Rik	BB137173	1.5
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Ar	AV232123	1.5
Hells	NM_008234	1.5
E2f8	BM247465	1.5
Pcdh9	BQ177394	1.5
Syncrip	BG920261	1.5
Rg9mtd2	BG063557	1.5
Tnik	AI117633	1.5
Calu	BB120190	1.5
Hnrnpr	BB822465	1.5
Arih2	NM_011790	1.5
Ccnb1	AU015121	1.5
Enah	BQ044016	1.5
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Asph	AF289490	1.5
Ahctf1	BM247201	1.5
Adam15	BC009132	1.5
Fscn1	NM_007984	1.5
Flrt2	BG075699	1.5
Rad54l	AV310220	1.5
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Cdca3	BI081061	1.5
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Ttll12	BB481662	1.5
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Nuf2	AK010351	1.5
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Ogn	BB542051	1.5
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Bbx	BF319769	1.5
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Arl15	BB445175	1.5
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Rabgap1	BM223600	1.5
Mre11a	NM_018736	1.5
Ctdsp2 /// ENSMUSG00000040540	BB294133	1.5
Gja1	BB043407	1.5
Osr1	NM_011859	1.5
Rad51ap1	BC003738	1.5

Syncrip	BG920261	1.5
Ankrd28	BG066840	1.5
Chek1	BB298208	1.5
Sh3kbp1	BB766215	1.5
Aspm	BB648052	1.5
Trim59	AK012269	1.5
Nrp1	AK011144	1.5
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1810032O08Rik	BM502805	1.5
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Fusip1	NM_010178	1.5
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Lman1	BE981934	1.5
Alcam	U95030	1.5
Plxdc2	AK017369	1.5
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Kpna6	BC004833	1.5
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Socs2	NM_007706	1.5
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Srebf2	BM123132	1.5

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Rtn4	BG072267	1.5
Aurkb	BC003261	1.5
Dpy19l1	BM119324	1.5
Lsm2	AF204156	1.5
Ppp3r1	NM_024459	1.5
EG383815 /// EG547267 /// EG668041 /// LOC677113 /// Rps24	BM119287	1.5
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Vamp3	NM_009498	1.5
Plk4	AI385771	1.5
Sprr2h	NM_011474	1.5
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Pde4b	BM246564	1.5
Wee1	NM_009516	1.5
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Smoc2	AK006809	1.5
Ccna2	X75483	1.5
Hmga1	NM_016660	1.5
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Krt18	NM_010664	11.9
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Crym	NM_016669	7.2
Aard	AV256613	6.5
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Clu /// LOC100046120	AV152288	5.7
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Ifi44	BB329808	5.2
Cdkn1c	NM_009876	4.8
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Afp	NM_007423	4.3
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Trim30	AF220015	4.1
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Ifit1	NM_008331	3.9
Tgtp /// Tgtp2	NM_011579	3.9
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Clu /// LOC100046120	NM_013492	3.7
Pla1a	NM_134102	3.6
Lyz1	AV066625	3.6
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Abhd3	NM_134130	3.6
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Xaf1	BB645745	3.5
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Synpo2l	BB322227	3.5
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Iigp1	BM239828	3.5
Rtp4	BC024872	3.4
Cmpk2	AK004595	3.4
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Trim63	BG817292	3.2
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Tnfsf9	NM_009404	3.2
Igtp	NM_018738	3.2
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F5	NM_007976	2.8
Clip4	BM217861	2.8
Kng1	NM_023125	2.8
Rgs4	NM_009062	2.8
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Cd38	BB256012	2.6
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Rsad2	BB741897	2.5
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Vnn1	NM_011704	2.5
Wdr40b	BB274776	2.5
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Acpp	BB008092	2.5
Gch1	BB698398	2.5
Liph	BB367422	2.5
Ifi205 /// Mnda	AI481797	2.5

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Il6	NM_031168	2.4
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Steap4	NM_054098	2.3
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Irf9	NM_008394	2.0
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Irf7	NM_016850	1.9
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Pygl	NM_133198	1.9

Arvcf	BE947943	1.9
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Aldh6a1	NM_134042	1.9
Cdkl2	NM_016912	1.9
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Slco2a1	AI606070	1.9
Pdlim4	NM_019417	1.9
Esrp2	BF124648	1.9
Adcy7	NM_007406	1.9
Plat	NM_008872	1.9
Parp12	BM227980	1.9
Adam8	NM_007403	1.9
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Galnt3	AK019995	1.9
Tspan9	AK020159	1.9
Bace2	BB558905	1.9
Herc5	AW208668	1.9
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Cxcr6	AF301018	1.9
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Serpinb9g	AF425083	1.9
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Selp	BB224329	1.9
Tmem51	BC003277	1.9
Trim54	NM_021447	1.9
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Tcp11l2	BM245221	1.9
Xdh	AV286265	1.9
Cd274	NM_021893	1.9
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Steap2	BB817972	1.9
Ildr2	BG067625	1.9
Radil	BB521978	1.9
C1r	NM_023143	1.9
Gbp6	BC010229	1.9
Arhgap18	BB667215	1.9
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Igfbp4	NM_010517	1.9
Aqp1	NM_007472	1.9
Ivl	AV009441	1.8
Upk1b	BB219662	1.8
Mtss1	BC024131	1.8
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Plcxd1	BB187908	1.8
Eif4e	BQ032226	1.8
Apcdd1	BB770932	1.8
Llgl2 /// LOC100047332	AY033650	1.8
Cand2	BM238658	1.8
Slco2a1	NM_033314	1.8
Boc	BB005556	1.8
Stard5	BI076697	1.8
Mmp3	NM_010809	1.8
Spint2	AV058358	1.8
Fuca2	BM054266	1.8
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Cib2	NM_019686	1.8
Fhod3	BG066491	1.8
Igf2	NM_010514	1.8
Serpini1	NM_009250	1.8
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Nmi	BC002019	1.8
Pfkfb4	BE136572	1.8
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Ptplad2	AV291250	1.8
Itih5	AV239969	1.8
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Sfmbt2	BM200222	1.8
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Prg4	NM_021400	1.8
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Lhx6	AB031040	1.8
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Phactr2	BE631955	1.8
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Scn3b	BE951842	1.8
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Sord	BI143942	1.8
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Svep1	NM_022814	1.8
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Lor	NM_008508	1.8
Rgs4	NM_009062	1.8
Larp6	NM_026235	1.8
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Ager	NM_007425	1.8
Pla2g16	BB404920	1.8
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Socs3	BB831725	1.8
Optn	BB770843	1.7
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Selp	M72332	1.7
Bnc1	U88064	1.7
Dgat2	AK002443	1.7
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1110008P14Rik	C79326	1.7
4930583H14Rik	NM_026358	1.7
Dach2	NM_033605	1.7
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Speg	NM_007463	1.7
Steap2	BB529332	1.7
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LOC100045567 /// Pnp1 /// Pnp2	AK008143	1.7
Vamp5	AK009266	1.7
Rnasel	BF714880	1.7
Cyld	AK013508	1.7
Ccl20	AF099052	1.7
Samd9l	BB145092	1.7
Rom1	NM_009073	1.7
Akr1c18	NM_134066	1.7
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Sema3e	AF034744	1.7
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Cxadr	BE824924	1.7
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Pnkd	NM_019999	1.7
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Ctnnal1	BQ031240	1.7
C1qtnf5 /// Mfrp	BC023068	1.7
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Glt8d4 /// LOC100048436	AV278332	1.7
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Eif2ak2	AV328340	1.7
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Acot11	AW060409	1.7
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Snhg11	BI731047	1.7
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Ch25h	NM_009890	1.7
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8430427H17Rik	AK018446	1.7
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Ptges	BB730139	1.7
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Speer3	NM_027650	1.7
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Apoe	AK019319	1.6
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Trf	AF440692	1.6
As3mt	AK009814	1.6
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Steap2	BE995447	1.6
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Speg	NM_007463	1.6
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Stard10	NM_019990	1.6
Tnfsf11	NM_011613	1.6
Cnp	BB251922	1.6

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Xkr8	AV273072	1.6
Cd40	NM_011611	1.6
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Stx11	BB767243	1.6
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Ptprg	AK017277	1.6
Dusp2	L11330	1.6
Slc9a3r1	BG066200	1.6
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Serping1	NM_009776	1.6
Obfc2a	BE457727	1.6
Ppfia3	BG962793	1.6
Cxcl2	NM_009140	1.6
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Fcgrt	NM_010189	1.6
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Pion	BB820613	1.5
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Ikbke	NM_019777	1.5
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Adar	AF291876	1.5

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Lipa	AI596237	1.5
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Camk2n2	AK013788	1.5
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Mtss1	AV024771	1.5
Enpp5	BC011294	1.5
Rsph1	NM_025290	1.5
H6pd	BC027358	1.5
Wrn	D86527	1.5
Efna1	D38146	1.5
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Entpd5	NM_007647	1.5
Akr1c13	NM_013778	1.5
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Dhrs11	BC022224	1.5

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Asah2	NM_018830	1.5
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Trpv2	NM_011706	1.5
Synpo	BB426294	1.5
Ereg	NM_007950	1.5
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Trim25	D63902	1.5
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Maob	BB549292	1.5
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Slfn8	BC024709	1.5
Ahcyl2	BG072404	1.5
Ern1	BG075179	1.5
Dtd1 /// LOC100048650	AI451865	1.5
Pon3	NM_008897	1.5
Slc41a3	BC011108	1.5
Cdadc1	BE200391	1.5
Tmem141	AW551717	1.5

Aldh5a1	BQ175320	1.5
Klc4	NM_029091	1.5
Ubxn2b	NM_026534	1.5
1110031I02Rik	NM_025402	1.5
Fkbp1b	NM_016863	1.5
Il13ra2	BC003723	1.5
Mkrn1	BE133749	1.5
Shb	BI408715	1.5
Abca3	AK007703	1.5
Pdk4	NM_013743	1.5
Syt11	BC025207	1.5
Dclk1	AW105916	1.5
Usp11	AI117611	1.5
Cacna1a	AB066608	1.5
Mpp5	AW258373	1.5
Psmb10	NM_013640	1.5
Rab15	NM_134050	1.5
Sgcb	AK014381	1.5
Mpzl3	BM246392	1.5
Ldhb	AV219418	1.5
Prkar1b	BB274009	1.5
Itga3	NM_013565	1.5
Fst	NM_008046	1.5
Ube2z	BB032870	1.5
A230050P20Rik	BB085904	1.5
Rnaset2a /// Rnaset2b	AV101824	1.5
Sf3b5	AU043053	1.5
Ebpl	BC027422	1.5
Cotl1	AI327078	1.5
Rhbdf2	BB005249	1.5
Commd9	BB264843	1.5
Spata13	AV271736	1.5
Gpc4	BB530689	1.5
Nsf	BB400581	1.5
9530058B02Rik	NM_026633	1.5
A930005H10Rik	BF318375	1.5
Fam105a	BM224662	1.5
Psmf1	BC012260	1.5
Ppp1r3c	BQ176864	1.5
Gmds	AI747296	1.5
Vav3	BC027242	1.5
Xlr3a /// Xlr3b /// Xlr3c	NM_011726	1.5
Ralgps2	AK008856	1.5

LOC100047530	BI735554	1.5
Igfbp6	NM_008344	1.5
Fdx1	D43690	1.5
Chchd6	BC011331	1.5
Fads3	BM235658	1.5
Gdf10	L42114	1.5
Tdrd7	BC025099	1.5
Fam102a	BC023470	1.5
Nudt6	BB043522	1.5
Stap2	BC026642	1.5
D730040F13Rik	AF031164	1.5
4933428G20Rik	BE988299	1.5
Aldoc	BC008184	1.5
Mmp23	NM_011985	1.5
Mkrn1	BQ176661	1.5
Retsat	BB775176	1.5

Supplementary Table S2: Top Biological Functions affected in Ada3 cells as obtained from ingenuity pathway analysis

Name	p-value	# Molecules
Diseases and Disorders		
Cancer	7.02E-27 - 4.66E-04	445
Dermatological Diseases and Conditions	2.53E-18 - 3.89E-04	105
Genetic Disorder	2.53E-18 - 4.66E-04	330
Gastrointestinal Disease	5.58E-18 - 4.66E-04	211
Inflammatory Response	7.65E-18 - 4.41E-04	222
Molecular and Cellular Functions		
Cell Death	1.76E-21 - 4.02E-04	359
Cellular Growth and Proliferation	1.40E-16 - 4.66E-04	389
Cellular Movement	2.48E-16 - 4.41E-04	229
Cellular Assembly and Organization	3.71E-11 - 4.27E-04	188
Cellular Function and Maintenance	3.71E-11 - 4.13E-04	174
Physiological System Development and Function		
Tissue Development	9.91E-16 - 4.27E-04	330
Organismal Survival	1.34E-12 - 5.77E-05	211
Hematological System Development and Function	2.69E-12 - 4.66E-04	224
Immune Cell Trafficking	2.69E-12 - 4.41E-04	120
Cardiovascular System Development and Function	3.03E-12 - 2.93E-04	144

Supplementary Table S3: Primers used for Real Time-qPCR

Oligo Name	Sequence 5' to 3'
p27 F	CAGAATCATAAGCCCCTGGA
p27 R	GGGGAACCGTCTGAAACATT
Skp2 F	TCCGAGCTGATCGGGTGTGCT
Skp2 R	TCGGAAGCTGCACATGCGCA
c-myc F	TGACCTAACTCGAGGAGGAGCTGGAATC
c-myc R	AAGTTTGAGGCAGTTAAAATTATGGCTGAAGC
β-actin F	GCGGACTGTTACTGAGCTGCGT
β-actin R	TGCTGTCGCCTTCACCGTTCC
Fbxo5 F	GGCACAATGAGTTCGTGGAGGTGG
Fbxo5 R	AGTTCCAGGCAAAGGACCCACT
Cenpf F	GTGGCAGCAGATCACAAAAGGTCA
Cenpf R	TCCCCACAGGCAGGCTCCTT
Cdc6 F	TGCCCAAAGAGGAGCGGCCT
Cdc6 R	AGAGGGGAAGGAACTTGGCCCC
Kntc1 F	CCCCTCAACGGTGCCCAGTG
Kntc1 R	GGCGCATGCCCAGTGTACTTGT
Kif11 F	CCAGCAAGGAGACCAGTCAGGACA
Kif11 R	TGGAGGTGTGAAGCGGCAGT
Cyclin A2 F	GAGCTGGCCTGAGTCATTGGCA
Cyclin A2 R	TGTTGGGCATGTTGTGGCGCT
Smc2 F	GGTGGTCAGAGGTCTCTAGTGGCT
Smc2 R	TCTTCCCAGCTTGACTCTGCGT
Anillin F	TGCCTGGCACCGAAGATGGTG
Anillin R	TGCAGAGAGCCAGTTCTTGGTGA
Cdkn1c-F	ACTGCTGCGGCCAATGCGAA
Cdkn1c-R	TGGGCTGCTCTACGCAACCATCT
Foxg1-F	TTCTAACACGGTGTGGAGTGTC
Foxg1-F	TTGTCAGGTTTGAATGAAATGG
Cyclin E2 F	AGGAATCAGCCCTTGCATTATC
Cyclin E2 R	CCCAGCTTAAATCTGGCAGAG
Keratin 18 F	CAAGTCTGCCGAAATCAGGGAC
Keratin 18 R	TCCAAGTTGATGTTCTGGTTTT
Icam1 F	TGTCAGCCACTGCCTTGGTA
Icam1 R	CAGGATCTGGTCCGCTAGCT

Interleukin-6 F	CACAGAGGATACCACTCCCAACA
Interleukin-6 R	TCCACGATTTCCCAGAGAACA

SUPPLEMENTARY REFERENCES

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