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Supplemental Data

SIRT1 Redistribution on Chromatin Promotes Genomic Stability but Alters Gene Expression during Aging

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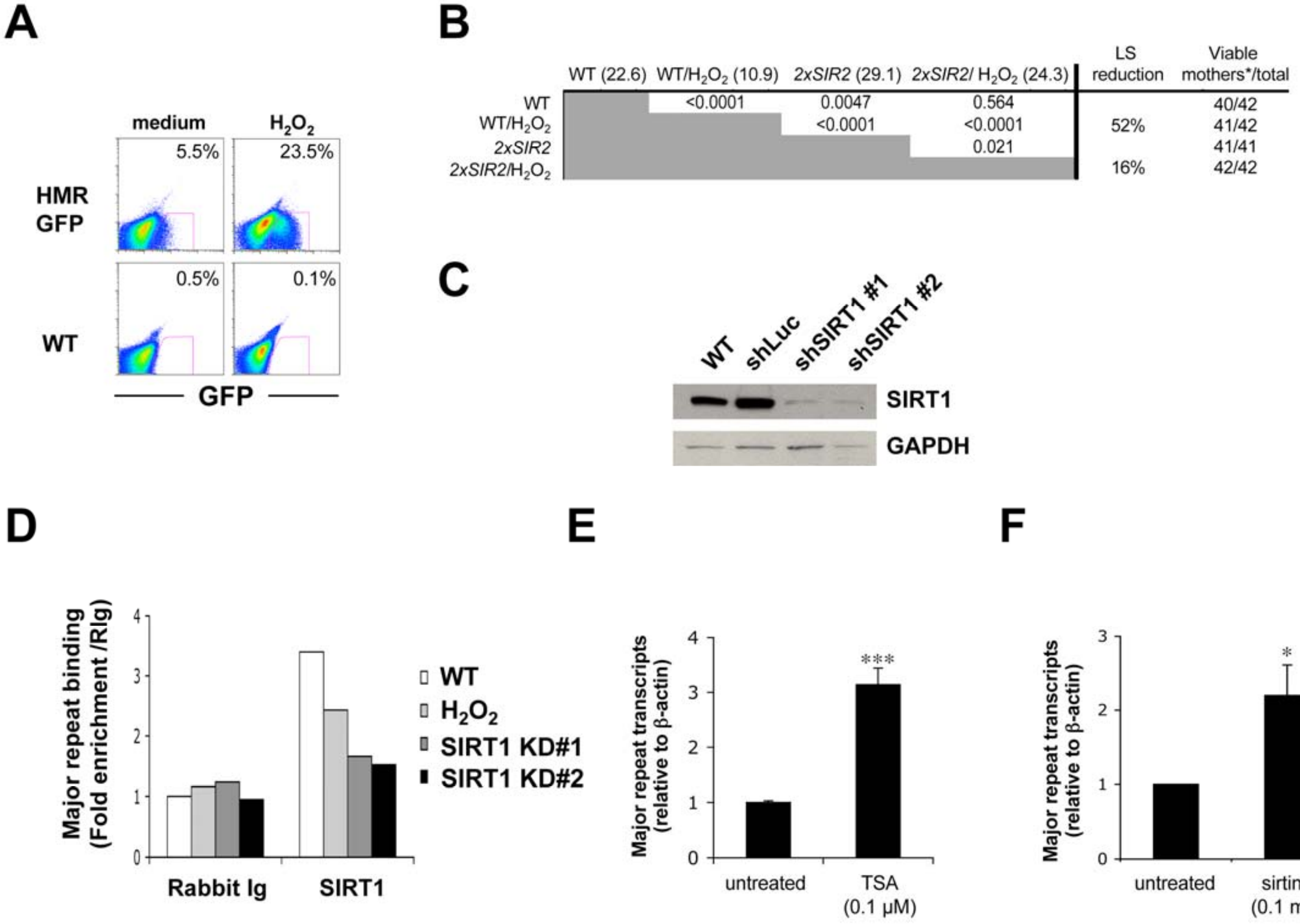

	WT (22.6)	WT/H_2O_2 (10.9)	*2xSIR2* (29.1)	*2xSIR2*/ H_2O_2 (24.3)	LS reduction	Viable mothers*/total
WT		<0.0001	0.0047	0.564		40/42
WT/H_2O_2			<0.0001	<0.0001	52%	41/42
2xSIR2				0.021		41/41
2xSIR2/H_2O_2					16%	42/42

Figure S1. (A) FACS analysis of loss of mating type silencing using *HMR::GFP* or isogenic control yeast cells. Cells were left untreated or treated with H_2O_2. The fraction of GFP^+ cells is indicated. (B) P values and mean replicative lifespans for the experiments in Figure 1C, the viability of yeast mother cells was not affected by H_2O_2. * Number of mother cells that have undergone at least 1 division. (C) Western blot analysis of SIRT1 knock-down in two independently derived stable, polyclonal ES cell populations. A stably integrated luciferase-specific hairpin served as scrambled control (shLuc). (D) Quantitative PCR (q-PCR) analysis of ChIP experiments using a SIRT1-specific antibody or rabbit control Ig. Stable SIRT1 knock-down ES cell lines and wild-type ES cells that were left untreated or treated with H_2O_2 for 1h were subjected to ChIP followed by q-PCR analysis for major satellite repeat DNA. (E, F) q-RT-PCR analysis of major satellite repeat transcripts in response to TSA treatment (0.1 µM, 16-24 h) or sirtinol treatment (100 µM, 16-24h). Data are represented as mean +/- SEM.

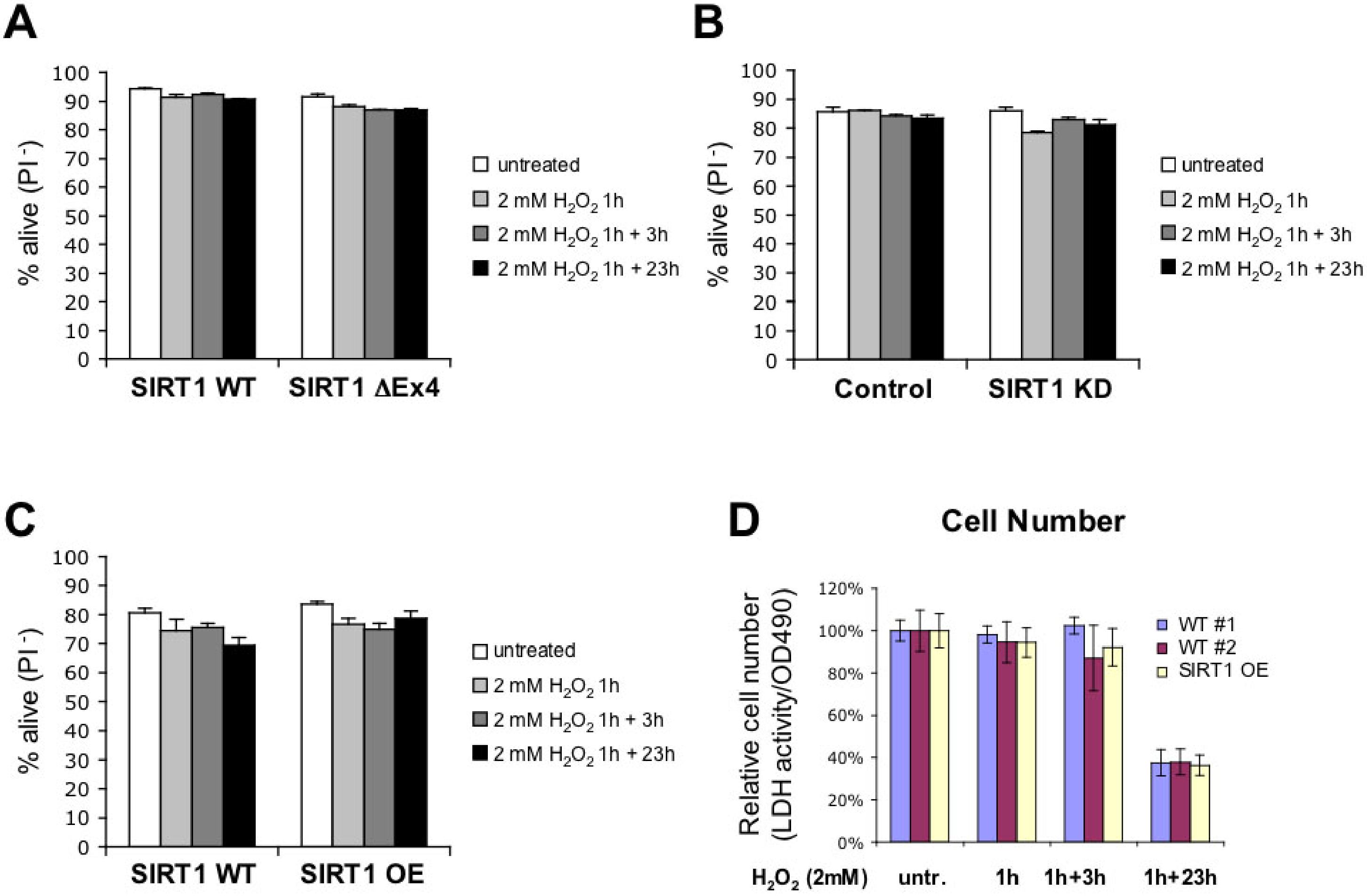

Figure S2. Cell survival of SIRT1 overexpressing or deficient ES cells in response to H_2O_2. (A-C). Fraction of live cells as determined by propidium iodide exclusion (PI^-) in response to a 1h treatment with 2 mM H_2O_2. Analysis was performed at the indicated time-points, SIRT1 KO (ΔEx4) cells (A), SIRT1 knock-down (KD) cells (B) and SIRT1 overexpressing (OE) cells (C) were compared to their respective unmanipulated controls (WT). (D) Number of viable WT and SIRT1 overexpressing cells after indicated H_2O_2 treatments. Viable cells were assessed by measuring LDH activity using the CytoTox 96 non-radioactive Cytotoxicity Assay (Promega) following the manufacturer's instructions. Relative cell numbers were determined as the percentage of LDH activity compared to untreated controls.

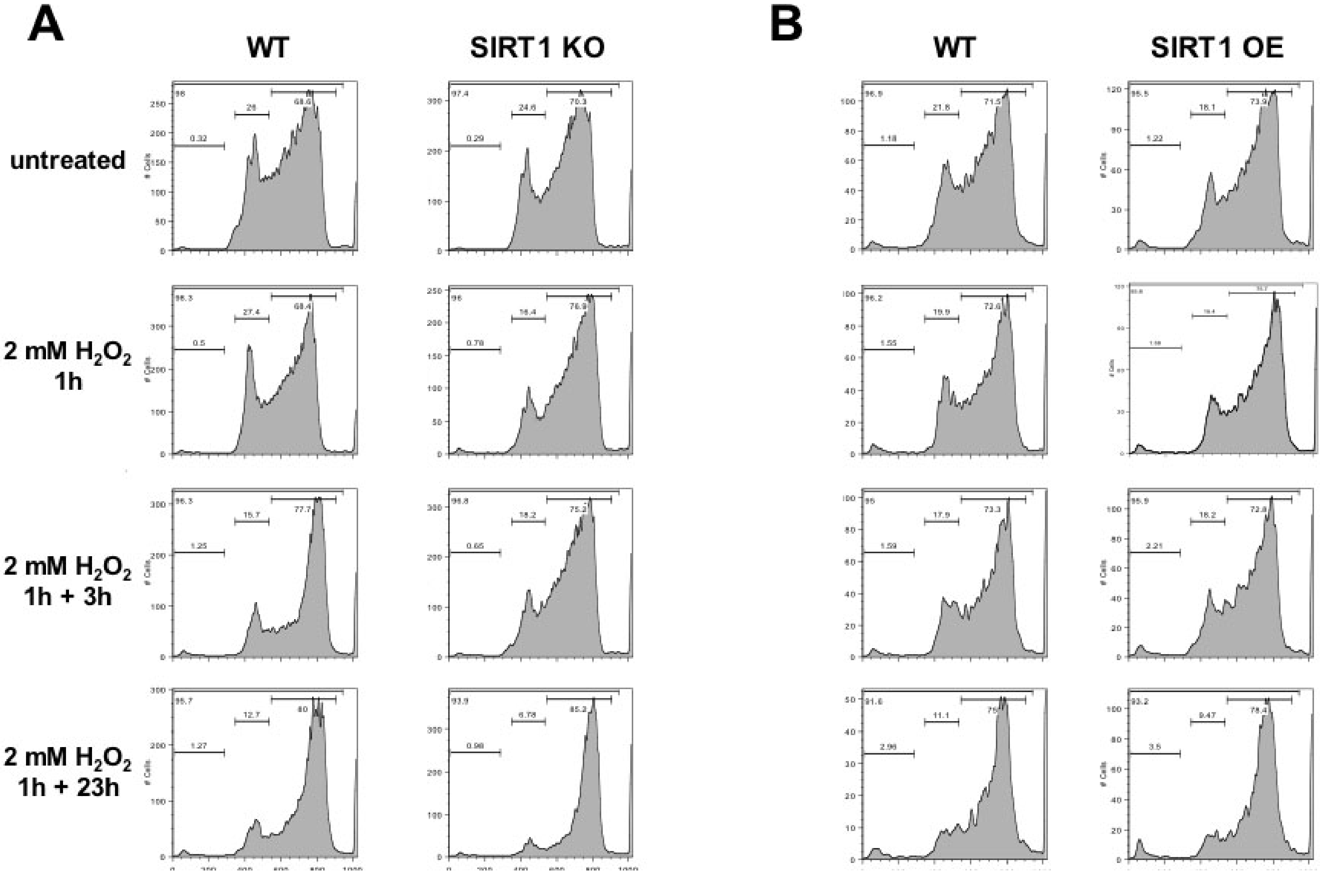

Figure S3. Cell cycle analysis of SIRT1 deficient (A) or overexpressing ES cells (B) in response to H_2O_2. DNA content was measured by PI staining of ethanol-fixed, Tween-permeabilized cells at the indicated time-points after a 1h H_2O_2 treatment.

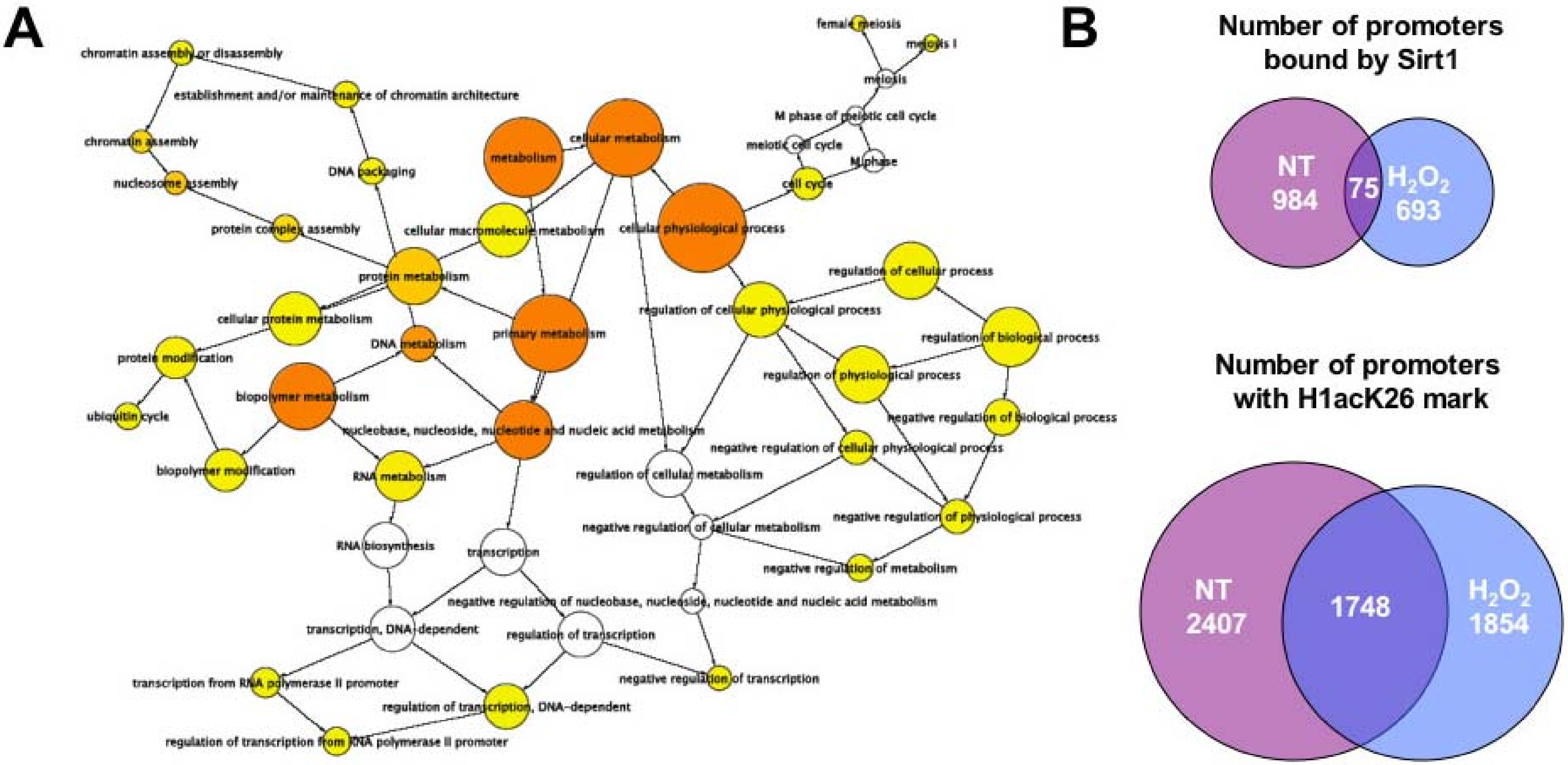

Figure S4. (A) Gene ontology (GO) cluster analysis of SIRT1 target genes based on GO gene function. SIRT1-associated promoters (*FDR < 0.1*) were clustered using BiNGO analysis. Colored nodes represent groups that are significantly over-represented, the color intensity reflects the level of significance (increasing from yellow to orange). (B) Venn diagram of SIRT1 associated Nimblegen probe sets (top) and H1AcK26 associated probe sets (bottom) before (red) and after H_2O_2 treatment (blue). Shown are SIRT1-enriched probe sets with an *FDR < 0.1*, numbers indicate how many probe sets can be found in the respective subsets.

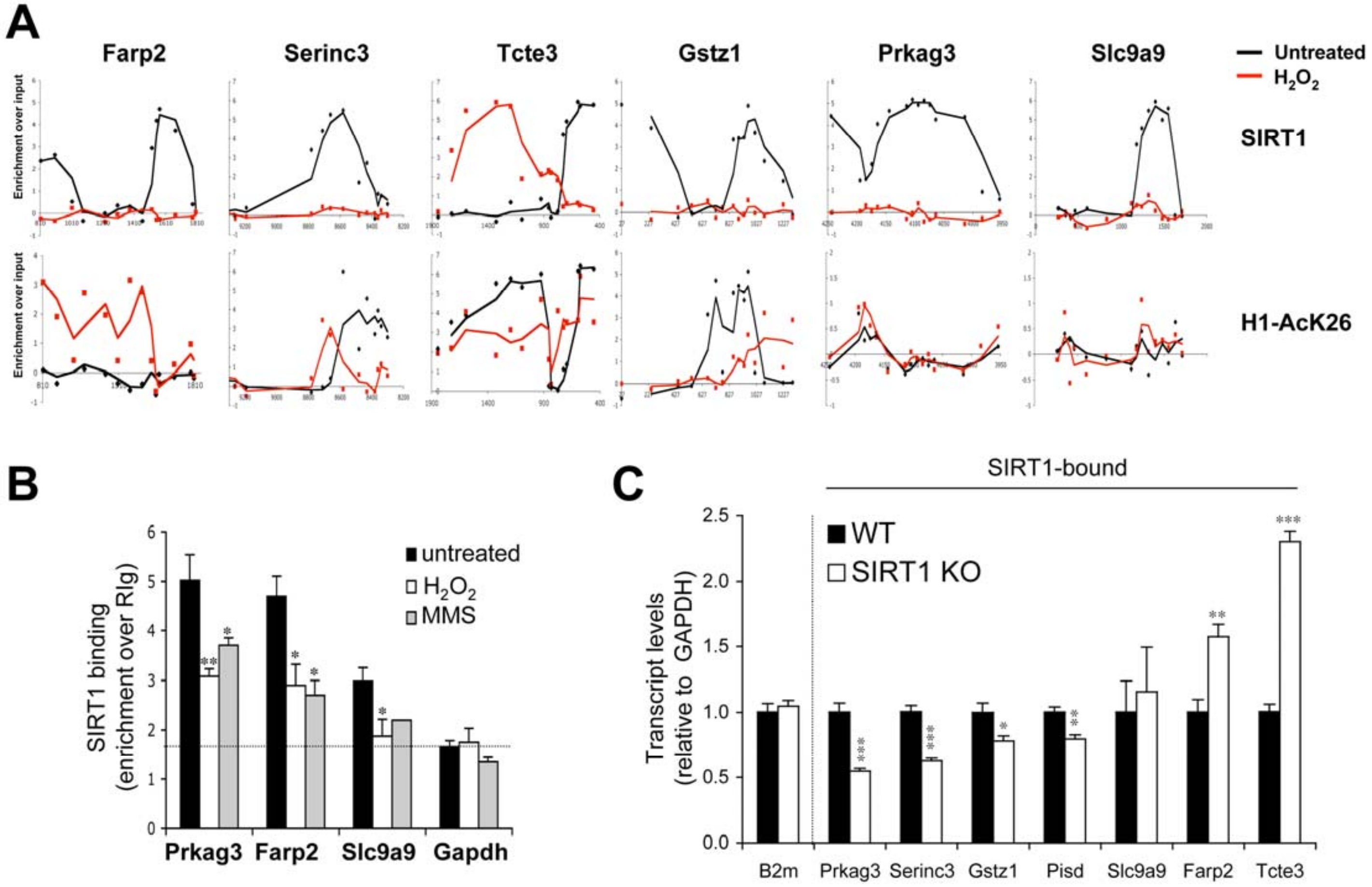

Figure S5. (A) SIRT1 and H1AcK26 binding profiles at promoters of SIRT1 target genes that are upregulated in response to H_2O_2 treatment and contain at least one 50mer probe with a H1AcK26 signal $\geq 1\log_2$. (B) Validation of SIRT1 association with selected target promoters. ES cells were either left untreated or treated with 2 mM H_2O_2 or 1 mM MMS for 1 h, subjected to ChIP for SIRT1 or a rabbit control Ig, followed by q-PCR analysis of promoters of the indicated genes. Fold enrichment was calculated based on the average background signal obtained with rabbit Ig alone for each promoter. Data are represented as mean +/- SEM. GAPDH served as a control locus. P values are based on student's one-tailed t-test. (C) q-PCR gene expression analysis of SIRT1 target genes from Figure 3 in WT or SIRT1 ΔEx4 (KO) ES cells. All samples were normalized to GAPDH, b2m is shown as a control.

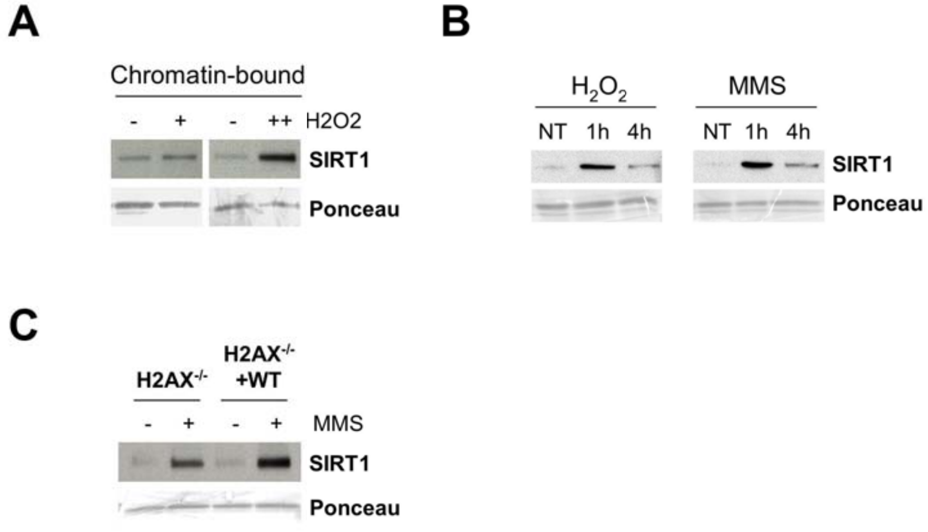

Figure S6. (A-C) Western blot analyses of chromatin-bound SIRT1 protein. (A) SIRT1 recruitment increases with increasing doses of H_2O_2. (B) SIRT1 recruitment to chromatin is transient. Cells were treated with H_2O_2 (2 mM) or MMS (2 mM) for 1 h, followed by a 3 h recovery in medium (4 h). (C) SIRT1 recruitment upon MMS-treatment is reduced in H2AX-deficient (H2AX$^{-/-}$) ES cells compared to H2AX$^{-/-}$ cells reconstituted with WT H2AX. Ponceau staining for histones is shown as loading control.

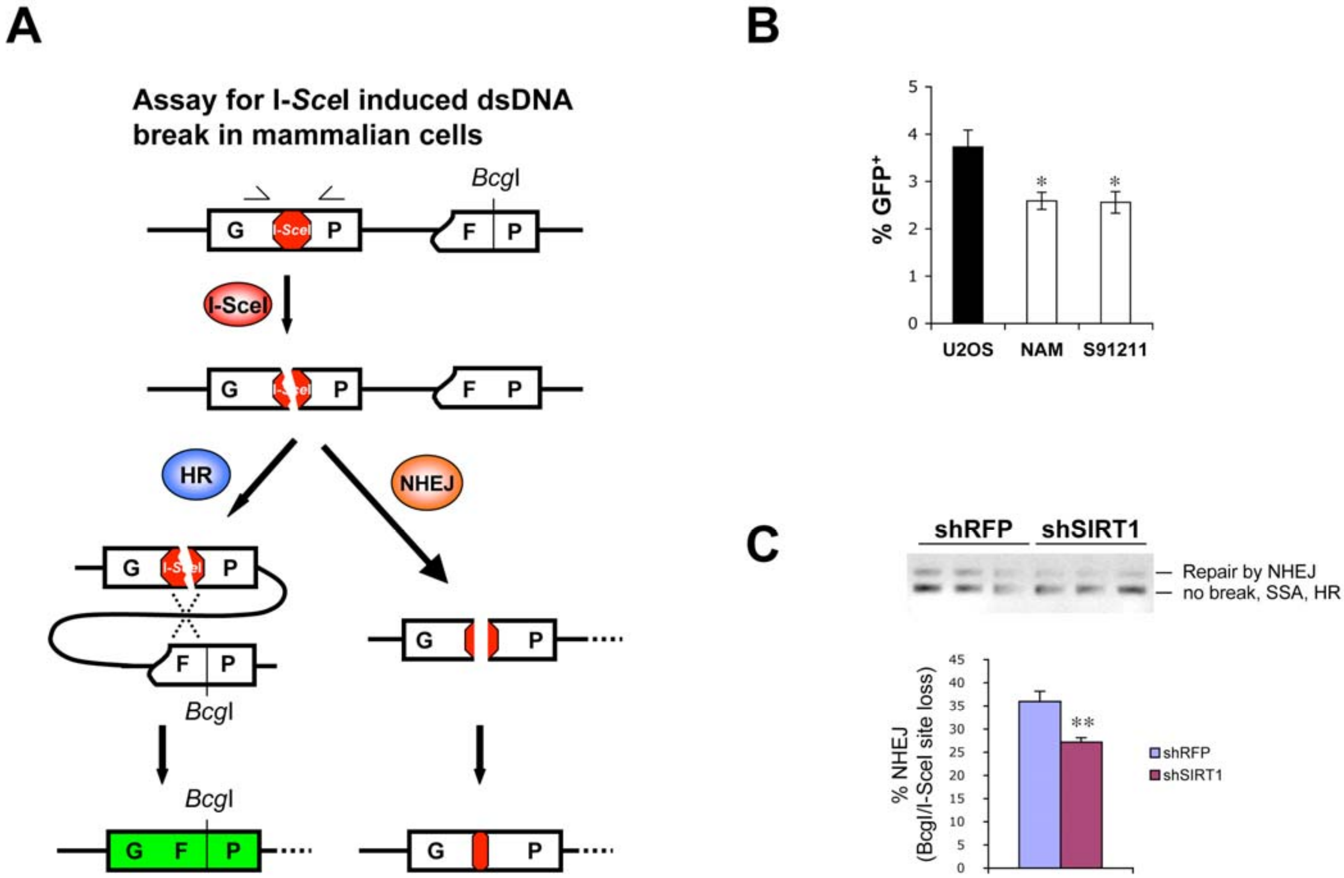

Figure S7. (A) Schematic illustrating I-*Sce*I mediated DSB induction and repair using the *DRGFP* transgene. This transgene consists of a GFP encoding cDNA that has an endogenous *Bcg*I restriction site replaced by an I-*Sce*I restriction site, and is, thereby, rendered non-functional. Transfection with an I-*Sce*I encoding plasmid (pCBASce) induces a DSB at the I-*Sce*I site. An incomplete *GFP* sequence (FP) is located downstream and can serve as a donor for intra-chromosomal homologous recombination (HR), one way of repairing the I-*Sce*I mediated DSB. Repair by HR restores a functional GFP cDNA including the endogenous *Bcg*I site and can be detected by FACS. Non-homologous end-joining (NHEJ) results in the imprecise fusion of the broken ends, causing a loss of the I-*Sce*I site but no restoration of *GFP* or the *Bcg*I site. Repair by NHEJ can be estimated by PCR amplification of the *GFP* gene (primers are indicated, see Table S5) and subsequent restriction digest with *Bcg*I and I-*Sce*I. The fraction of PCR products that are insensitive to either I-*Sce*I or *Bcg*I digestion reflects the NHEJ frequency (Weinstock et al., 2006). (B) HR efficiency in *DRGFP* transgenic U2OS cells exposed to the sirtuin inhibitors NAM or S91211. Cells were treated with 10 mM NAM or 50 µM S91211 starting 2 h prior to transfection with either pCBASce or pCAGGS-Ds-red. Recombination was measured 48 h later by measuring the fraction of GFP^+ cells. Ds-red was used to determine transfection efficiency. The ratio of GFP^+ to Ds-red^+ cells is graphed for untreated (closed bar) and NAM or S91211 treated cells (open bars). Experiments were done in triplicate, data are represented as mean +/- SEM. (C) NHEJ analysis of *DRGFP* transgenic U2OS cells stably knocked-down for either RFP (scrambled control) or SIRT1 (Figure 5). PCR products were digested with I-*Sce*I and *Bcg*I and separated by gel electrophoresis. The undigested PCR product (top band) reflects

DNA repaired by NHEJ, the bottom band results from digestion with *Bcg*I or I-*Sce*I and reflects unrepaired DNA as well as DNA repaired by HR or single-strand annealing (SSA). Band intensities were quantified using ImageJ. The ratio of top to bottom band adjusted for the band size (in bp) represents the frequency of repair by NHEJ, data are represented as mean +/- SEM.

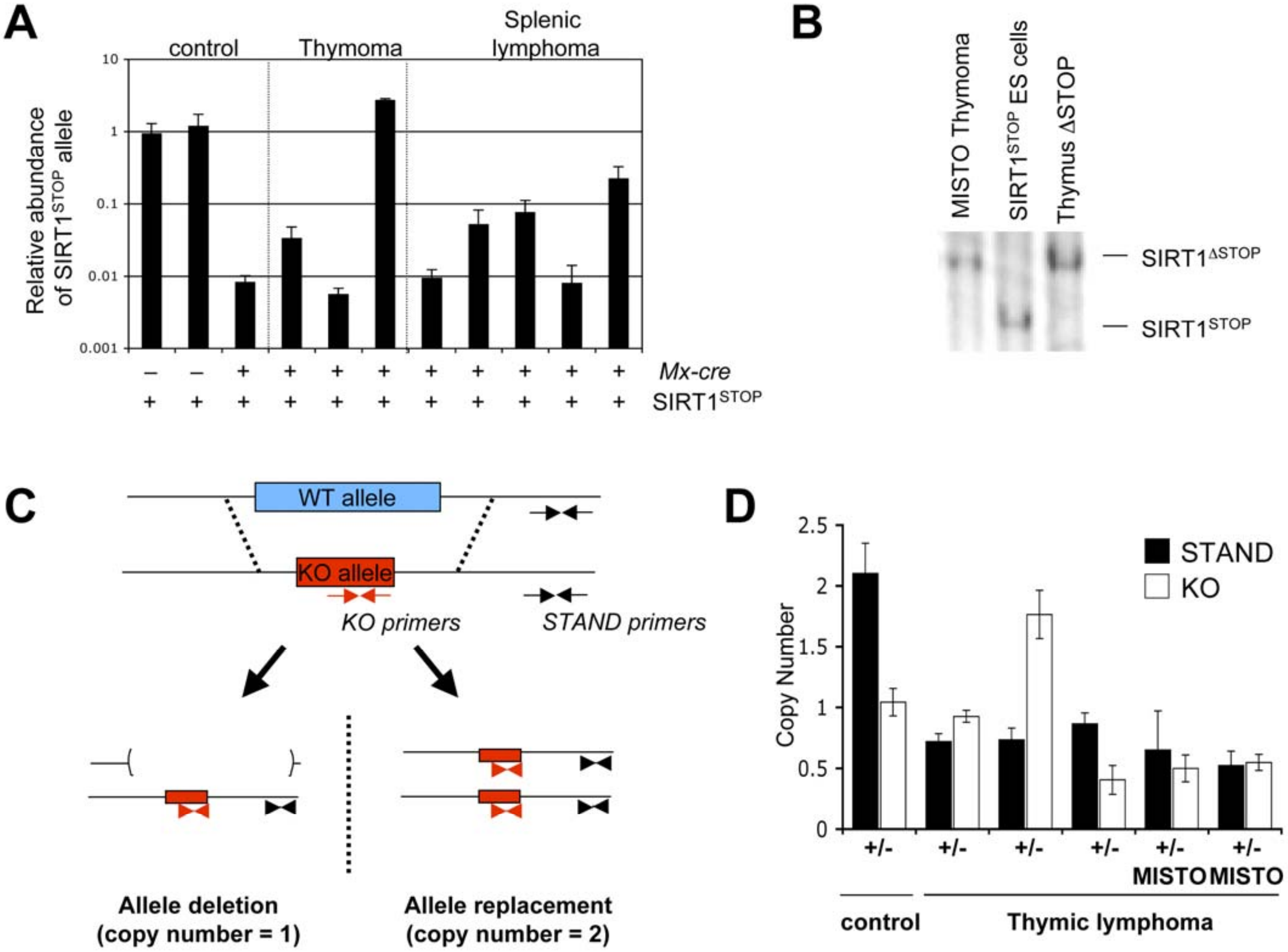

Figure S8. (A and B) Efficiency of Cre-mediated deletion in MISTO mice. (A) Genomic DNA from the indicated tumor tissues was subjected to q-PCR analysis of the $SIRT1^{STOP}$ locus and three control loci (ube2i promoter, gapdh promoter and SIRT1 exon 4). The ratio of $SIRT1^{STOP}$ to control in tissue lacking the *Mx-cre* transgene was set as 1. Shown is average and S.D. of $SIRT1^{STOP}$ abundance. One MISTO-transgenic thymic lymphoma showed no signs of deletion and was excluded from the analysis. (B) Southern blot analysis of tumor and control DNAs using a $SIRT1^{STOP}$ specific radio-labeled probe. (C and D) LOH at the *p53* locus in thymic lymphomas from irradiated $p53^{+/-}$ mice. (C) LOH at the *p53* locus can occur through allele deletion (left) or allele replacement by gene conversion (right). q-PCR analysis can be utilized to detect these events by amplifying either a DNA segment specific for the *p53*-deficient allele (KO, red), or an adjacent control segment present in both the WT and the KO allele (STAND, black). (D) q-PCR analysis of LOH at the *p53* locus. DNA from five thymic lymphomas obtained from irradiated control ($p53^{+/-}$) or experimental (MISTO; $p53^{+/-}$) mice was analyzed using primers indicated in (C), PCR products were normalized to a set of four control genes (Ldk, PrkCD, G22, CD28) to determine the copy number for each allele using a known $p53^{+/-}$ sample as reference. Data are represented as mean +/- SEM. All tumors showed loss of one STAND copy but not the KO copy, indicative of *p53* LOH by allele deletion. One tumor showed an increase in KO copy number, possibly due to a duplication event involving the KO allele. Primer sequences are available upon request.

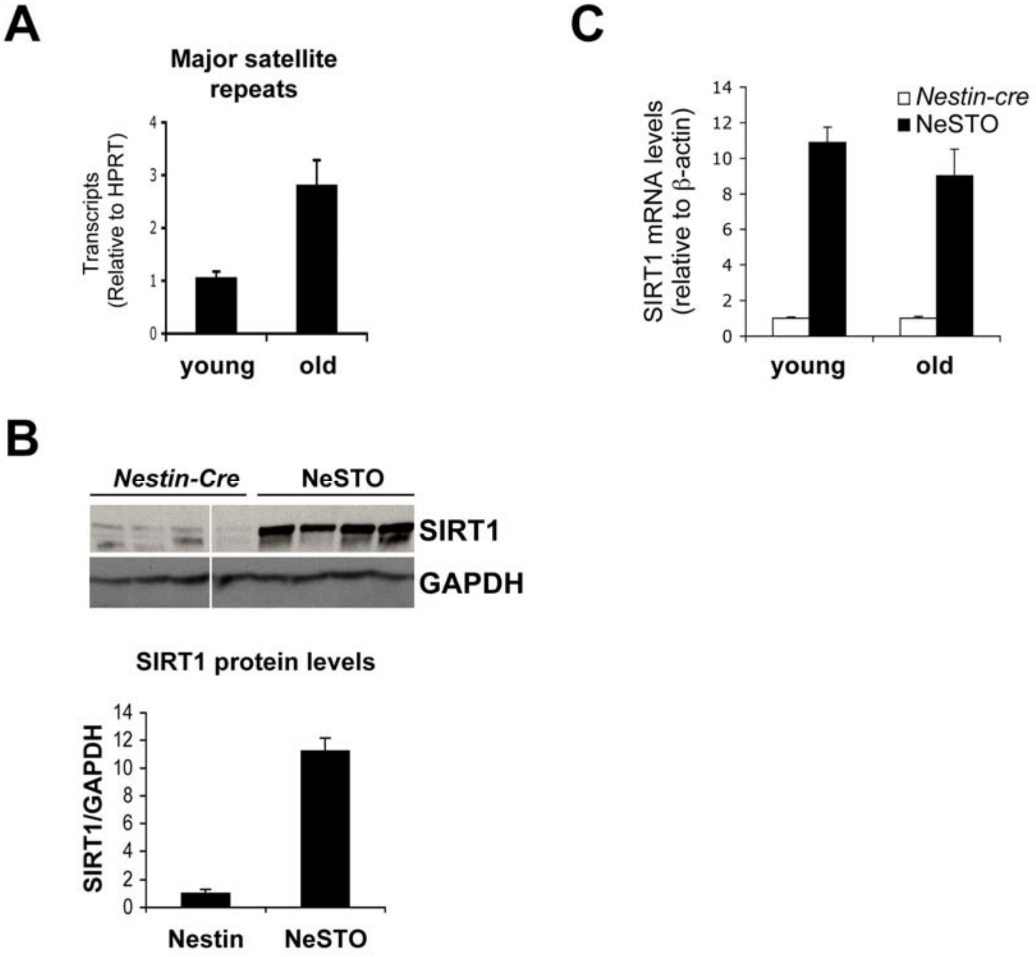

Figure S9. (A) Age-dependent increase in major satellite repeat transcripts in mice. RNA from young (2 months, n = 6) and old (24 months, n = 6) mouse cortices was subjected to q-RT-PCR. Samples were normalized to HPRT. (B) and (C) SIRT1 protein (B) and mRNA expression (C) in NeSTO mice and *Nestin-cre* littermate controls. Expression of SIRT1 in NeSTO mice was generally 9-13-fold higher than in *Nestin-cre* littermate controls, although there was a subset of mice with very high expression (20-fold or greater), which was not considered for further analysis. Data are represented as mean +/- SEM, analyzing young (8-10 months) animals (C) and old (18-19 months) animals (B and C).

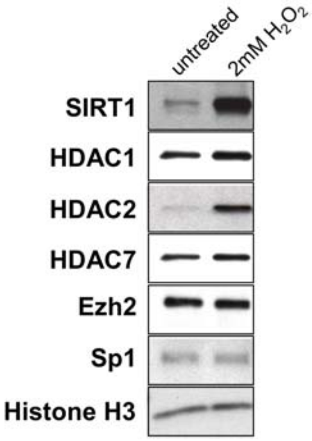

Figure S10. Western blot analysis of SIRT1 and indicated control proteins in the chromatin-bound protein fraction of ES cells that were either left untreated or treated with H_2O_2 for 1 h. Antibodies against HDAC1, HDAC2 and HDAC7 were from Santa Cruz, anti-Ezh2 from BD Biosciences. The antibody against Spe1 was kindly provided by Dr. G. Gill.

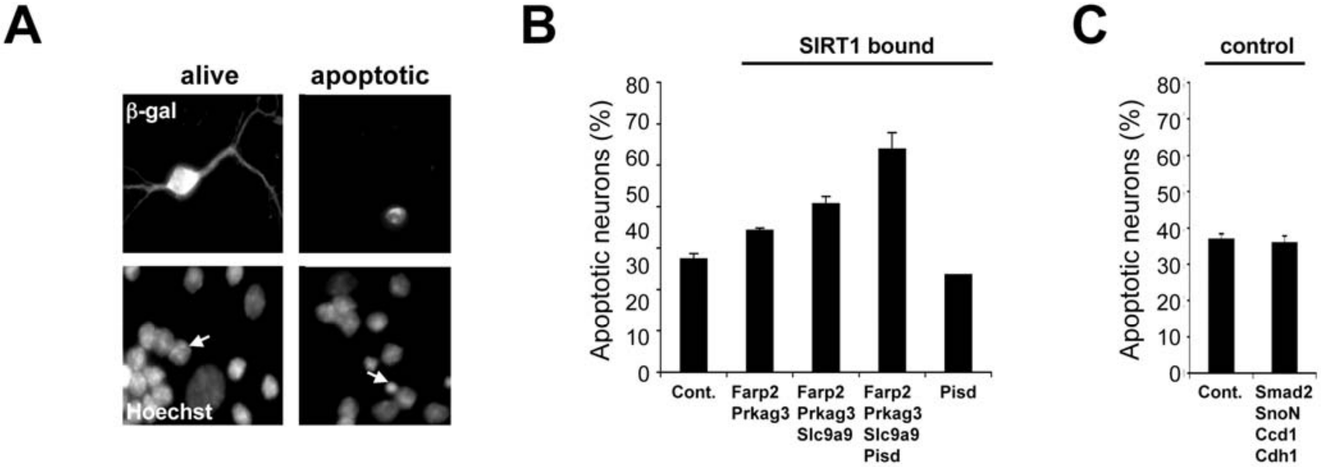

Figure S11. (A) Apoptosis of cerebellar granule neurons. Cerebellar granule neurons were prepared from isolated cerebella of P6 Long-Evans rat pups and were transfected 48 h after plating with a modified calcium phosphate method (Becker and Bonni, 2006). Cells were fixed 72 h thereafter and stained for β-gal and Hoechst. Expression vectors (pCMV-SPORT6) for mFarp2, hPrkag3, mPisd and hSlc9a9 were from Open Biosystems. pβ-Gal, pCMV5, pCMV5-hCdh1, pCMV5-hSmad2 and pCMV5-hSnoN were from A. Bonni, pCMV5-hCcd1 was a gift from S.-C. Lin (Hong Kong University of Science and Technology). Disintegration of neuronal processes and nuclear condensation indicated apoptosis of β-gal$^+$ cells, representative live and apoptotic neurons are shown. (B and C) Analysis of apoptosis upon ectopic overexpression of the indicated genes in primary rat neurons. (B) Cerebellar granule neurons were transfected with a pCMV-SPORT6 empty vector (2 µg), the indicated combinations of expression vectors for the SIRT1-associated genes prkag3, slc9a9, pisd and farp2 (0.5 µg each), or 2 µg of the pisd expression vector. (C) Granule neurons were transfected with a pCMV5 empty control vector (2 µg) or a combination of the indicated non-SIRT1-associated genes (0.5 µg each). Data are represented as mean +/- SEM.

Table S1. List of genes in overrepresented gene ontology groups. 574 annotated genes were identified amongst SIRT1-associated promoters (*FDR < 0.01*) out of 15850 whole annotations. Selected: number of SIRT1-associated promoters per GO group, total: all genes per GO group. *: Benjamini-Hochberg FDR correction.

<table>
<tr><th>GO-ID</th><th>p-value</th><th>corr . p-value*</th><th>selected</th><th>total</th><th>Description</th><th>Genes in test set</th></tr>
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<tr><td>43170</td><td>3.46E-13</td><td>1.64E-10</td><td>316</td><td>6398</td><td>macromolecule metabolism</td><td>CDK6|APOE|HIST1H2BM|FBXL14|ETF1|TSSK3|PLAGL2|HIST1H2BP|HYOU1|RPO1-1|EIF1|TARS|MCPT1|TUBB3|RBM4|2610031L17RIK|SIL1|BRD8|CDC40|PJA1|MAST2|GYS1|MAST1|ILF3|PTPRK|MSC|PCSK1N|RG9MTD2|GM711|MYT1L|TSHZ3|ERCC2|CBX2|GLT8D1|HIST1H3D|FBXO6B|CAPZA1|EIF5|TRERF1|USP3|PRKAR1A|HIST2H3C2|PRUNE|HNRPF|WBSCR18|BRWD1|BIRC1C|CRKRS|PRSS15|MCPT2|SRRM2|RG9MTD1|UBE2E3|PDK3|HIST1H3C|UBE2D3|ADRA1D|SPCS1|ZFP263|C2TA|SRRM1|HIST1H3E|PHF10|POMT2|TEP1|HIST1H3F|SNRPE|USP43|MECP2|HIST2H3C1|DCAMKL2|UBB|IRX3|D11BWG0434E|PIAS2|NPR2|ESPL1|CHD4|IRX6|ORC1L|PIAS3|NOL5A|NLN|STAMBP|GLIS2|POFUT1|FEM1A|VAX1|SPIN|MBD4|EDG2|C77668|INVS|SMARCAL1|EPHB2|TWIST2|EBF2|MRPL14|CDK7|1700030G11RIK|ZBTB1|WASF1|PRMT5|SMARCA5|ZBTB37|UHMK1|AMFR|TIMM8A1|PRPF31|METAP2|PLD2|HOXD8|PGPEP1|HECW1|RPS5|GANC|LRPAP1|TCERG1|RFC2|PLAT|SERTAD2|CAPZA2|FBXO38|PAPOLG|ADPRH|SIM1|TDG|WRNIP1|MGAT3|GGN|SNRPB2|BACE2|MID1IP1|LHX6|NOTCH2|GALNT3|D11ERTD730E|CTCF|BTK|DCLRE1B|UBQLN4|9130017K11RIK|OAS2|PCSK4|CD9|4732466D17RIK|NDUFAF1|4930429M06RIK|PSMA7|ROR2|PHKA2|UBE2T|HIST2H2AA1|ADAM23|C1RL|STC1|3230401I01RIK|HIST1H1B|CNDP2|DPH5|ZFP715|SPO11|EIF3S4|KLF3|OPN3|ZFHX1A|REX2|RNASEH2A|CLASP1|CDC16|D7WSU128E|UBTD1|BRCC3|A730008L03RIK|4930432O21RIK|CUTL1|SS18L1|CSNK1G1|B3GALT6|PRKCBP1|TGIF2|GIYD2|MAL|SLA2|WWTR1|HEMK1|MRPL17|CCNE2|2610305D13RIK|MMS19L|FBXO44|RLF|RUVBL2|PIGQ|RPL36|ZFP397|4933424A20RIK|PHF6|PSMB5|CDX4|RPS12|RWDD4A|TM4SF4|MCPT4|U2AF2|EIF3S3|GAG|X83328|NCOA2|TBX2|PHF15|BCL6B|FBXL21|DDX54|PRPF18|OXCT2A|TBX3|SUZ12|GSPT2|MAGI1|UGP2|UBE2M|9030624G23RIK|PARS2|HIST2H2AA2|TSC22D4|D1ERTD161E|OASL1|THRAP5|NR2F2|MLH3|RXRB|FHIT|E2F7|RPS27A|FOSL1|DRAP1|MRPL37|PCOLN3|A630042L21RIK|RBMXRT|HIST1H3B|FANCC|GYK|RBAK|MEN1|C330022B21RIK|C2|FAH|SGIP1|HLCS|PIGT|SMAD1|ZFP580|TXNL4B|SF3B2|D5ERTD593E|RHOX5|GYLTL1B|E2F6|FKBP7|TARSL2|KLHL12|STK38L|ELF1|NKX2-6|C1R|SECISBP2|SYCP1|WBP4|ZFP579|E2F8|RELB|CTNNA1|BC012278|</td></tr>
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<tr><td></td><td></td><td></td><td></td><td></td><td></td><td>HIST1H3A|ZDHHC7|RHOX4E|VARS2|HIST1H3G|RPS28|MYNN|GAPDHS|DUSP3|HIST1H3I|UBE3B|CUL4A|CDC25C|ADAMTS2|BAG5|FOXJ3|2400003N08RIK|NFE2L2|USP27X|PTPRG|HIST1H3H|CEBPB|1700016G05RIK|PRKAG3|PPP1R12B|RPA3|B3GNT6|RHOX4A|DBF4|CDC7|TRAK1|HS2ST1|ATF7|PPP1CA|CLN8|ATG9A|APOA1|HIST2H3B|RPS21|DDB2|LDLR</td></tr>
<tr><td>44238</td><td>1.97E-12</td><td>7.00E-10</td><td>347</td><td>7320</td><td>primary metabolism</td><td>CDK6|APOE|HIST1H2BM|FBXL14|ETF1|TSSK3|PLAGL2|HIST1H2BP|HYOU1|RPO1-1|EIF1|TARS|MCPT1|TUBB3|KYNU|PLA2G1B|RBM4|PIK3C2A|2610031L17RIK|SIL1|FDPS|BRD8|CDC40|PJA1|MAST2|GYS1|MAST1|ILF3|PTPRK|MSC|PCSK1N|RG9MTD2|ATP6V1E1|MYT1L|GM711|TSHZ3|ERCC2|CBX2|GLT8D1|HIST1H3D|FBXO6B|EIF5|CAPZA1|TRERF1|USP3|PRKAR1A|HIST2H3C2|PRUNE|HNRPF|WBSCR18|BRWD1|BIRC1C|CRKRS|PRSS15|MCPT2|SRRM2|RG9MTD1|UBE2E3|PDK3|HIST1H3C|UBE2D3|ADRA1D|SPCS1|ZFP263|SLC27A3|C2TA|SRRM1|HIST1H3E|PHF10|POMT2|TEP1|HIST1H3F|SNRPE|USP43|MECP2|HIST2H3C1|DCAMKL2|UBB|PITPNC1|IRX3|H2-KE6|D11BWG0434E|PIAS2|NPR2|ESPL1|CHD4|IRX6|ORC1L|PIAS3|NOL5A|NLN|STAMBP|POFUT1|GLIS2|FEM1A|VAX1|SPIN|MBD4|EDG2|C77668|INVS|PPP1R1B|SMARCAL1|EPHB2|TWIST2|EBF2|MRPL14|CDK7|1700030G11RIK|WASF1|ZBTB1|PRMT5|NPPC|SMARCA5|ZBTB37|UHMK1|ATP8B3|AMFR|TIMM8A1|PRPF31|PPAT|METAP2|PLD2|HPCA|HOXD8|PGPEP1|RPS5|HECW1|GANC|STARD3|COMT|LRPAP1|TCERG1|RFC2|PLAT|SERTAD2|CAPZA2|FBXO38|PAPOLG|WRNIP1|TDG|ADPRH|SIM1|MGAT3|GGN|SNRPB2|BACE2|MID1IP1|LHX6|NOTCH2|GALNT3|D11ERTD730E|CTCF|BTK|DCLRE1B|UBQLN4|GUCY1B2|9130017K11RIK|OAS2|PCSK4|CD9|4732466D17RIK|NDUFAF1|4930429M06RIK|PSMA7|ROR2|PHKA2|ADSS|UBE2T|HIST2H2AA1|ADAM23|C1RL|STC1|PIP5K2B|3230401I01RIK|HIST1H1B|CNDP2|SPO11|ZFP715|DPH5|EIF3S4|KLF3|OPN3|ITGB8|ZFHX1A|REX2|RNASEH2A|CLASP1|CDC16|D7WSU128E|UBTD1|BRCC3|A730008L03RIK|4930432O21RIK|CUTL1|SS18L1|CSNK1G1|B3GALT6|PRKCBP1|NEB|TGIF2|GIYD2|MAL|SLA2|WWTR1|HEMK1|MRPL17|CCNE2|2610305D13RIK|MMS19L|FBXO44|RLF|RUVBL2|PIGQ|RPL36|ZFP397|PCYT1A|COPG2|4933424A20RIK|PHF6|PSMB5|CDX4|POLR2H|RPS12|RWDD4A|TM4SF4|MCPT4|U2AF2|EIF3S3|GAG|X83328|NCOA2|TBX2|PHF15|BCL6B|FBXL21|DDX54|PRPF18|OXCT2A|GSTZ1|TBX3|SUZ12|GSPT2|MAGI1|UGP2|UBE2M|9030624G23RIK|PARS2|HIST2H2AA2|TSC22D4|D1ERTD161E|OASL1|THRAP5|NR2F2|MLH3|RXRB|ASNS|FHIT|E2F7|RPS27A|FOSL1|DDAH2|DRAP1|IDI1|ELOVL2|MRPL37|PCOLN3|A630042L21RIK|RBMXRT|HIST1H3B|FANCC|GYK|RBAK|MEN1|C330022B21RIK|C2|FAH|SGIP1|HLCS|PIGT|SMAD1|ZFP580|TXNL4B|SF3B2|D5ERTD593E|RHOX5|GYLTL1B|E2F6|FKBP7|TARSL2|KLHL12|STK38L|ELF1|NKX2-6|C1R|SECISBP2|SYCP1|WBP4|OAZ1|ZFP579|E2F8|RELB|CTNNA1|BC012278|HIST1H3A|ZDHHC7|RHOX4E|PISD|VARS2|HIST1H3G|RPS28|MYNN|GAPDHS|DUSP3|HIST1H3I|UBE3B|CUL4A|CDC25C|ADAMTS2|BAG5|FOXJ3|2400003N08RIK|NFE2L2|USP27X|PTPRG|HIST1H3H|CEBPB|1700016G05RIK|PRKAG3|PPP1R12B|RPA3|B3GNT6|RHOX4A|DBF4|CDC7|TRAK1|HS2ST1|ATF7|PPP1CA|CLN8|ATG9A|APOA1|HIST2H3B|RPS21|PRKAB2|DDB2|LDLR</td></tr>
<tr><td>44237</td><td>8.17E-12</td><td>2.33E-09</td><td>354</td><td>7581</td><td>cellular metabolism</td><td>CDK6|APOE|HIST1H2BM|FBXL14|ETF1|TSSK3|PLAGL2|HIST1H2BP|HYOU1|RPO1-1|EIF1|TARS|MCPT1|TUBB3|KYNU|PLA2G1B|RBM4|PIK3C2A|2610031L17RIK|SIL1|FDPS|BRD8|CDC40|PJA1|MAST2|GYS1|MAST1|ILF3|PTPRK|MSC|PCSK1N|RG9MTD2|ATP6V1E1|MYT1L|GM711|TSHZ3|ERCC2|CBX2|GLT8D1|HIST1H3D|FBXO6B|EIF5|CAPZA1|TRERF1|USP3|PRKAR1A|HIST2H3C2|HNRPF|WBSCR18|BRWD1|BIRC1C|CRKRS|PRSS15|MCPT2|SRRM2|RG9MTD1|UBE2E3|PDK3|HIST1H3C|UBE2D3|ADRA1D|SPCS1|ZFP263|SLC27A3|C2TA|SRRM1|HIST1H3E|TEP1|PHF10|POMT2|HIST1H3F|SNRPE|USP43|MECP2|HIST2H3C1|DCAMKL2|UBB|PITPNC1|IRX3|H2-KE6|D11BWG0434E|PIAS2|NPR2|ESPL1|CHD4|IRX6|ORC1L|PIAS3|NOL5A|NLN|STAMBP|POFUT1|GLIS2|FEM1A|VAX1|SPIN|MBD4|EDG2|C77668|INVS|PPP1R1B|SMARCAL1|EPHB2|TWIST2|EBF2|MRPL14|CDK7|1700030G11RIK|WASF1|ZBTB1|PRMT5|NPPC|SMARCA5|ZBTB37|UHMK1|ATP8B3|AMFR|TIMM8A1|CYP3A25|PRPF31|PPAT|METAP2|PLD2|HPCA|HOXD8|PGPEP1|RPS5|HECW1|GANC|STARD3|COMT|LRPAP1|TCERG1|RFC2|PLAT|SERTAD2|CAPZA2|FBXO38|PAPOLG|WRNIP1|TDG|ADPRH|SIM1|MGAT3|SNRPB2|BACE2|MID1IP1|COX7A2|LHX6|OXCT2B|NOTCH2|D11ERTD730E|CTCF|BTK|DCLRE1B|UBQLN4|GUCY1B2|9130017K11RIK|OAS2|PCSK4|4732466D17RIK|NDUFAF1|4930429M</td></tr>
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<table>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td>06RIK|PSMA7|ROR2|PHKA2|ADSS|UBE2T|HIST2H2AA1|ADAM23|C1RL|STC1|PIP5K2B|3230401I01RIK|HIST1H1B|CNDP2|SPO11|ZFP715|DPH5|EIF3S4|KLF3|OPN3|PRDX1|ZFP277|ITGB8|ZFHX1A|MC1R|REX2|RNASEH2A|CLASP1|CDC16|D7WSU128E|UBTD1|BRCC3|MCHR1|A730008L03RIK|4930432O21RIK|CUTL1|SS18L1|CSNK1G1|B3GALT6|PRKCBP1|NEB|2810410C14RIK|TGIF2|GIYD2|MAL|SLA2|WWTR1|HEMK1|MRPL17|CCNE2|2610305D13RIK|MMS19L|FBXO44|RLF|RUVBL2|PIGQ|RPL36|ZFP397|PCYT1A|COPG2|4933424A20RIK|PHF6|PSMB5|CDX4|POLR2H|RPS12|RWDD4A|TM4SF4|MCPT4|U2AF2|EIF3S3|GAG|X83328|NCOA2|TBX2|PHF15|BCL6B|FBXL21|DDX54|MUG1|PRPF18|OXCT2A|GSTZ1|TBX3|SUZ12|GSPT2|UGP2|UBE2M|9030624G23RIK|PARS2|HIST2H2AA2|TSC22D4|D1ERTD161E|OASL1|CYP4A12|THRAP5|NR2F2|MLH3|RXRB|ASNS|FHIT|E2F7|RPS27A|FOSL1|DDAH2|DRAP1|IDI1|SLC37A2|ELOVL2|MRPL37|PCOLN3|A630042L21RIK|RBMXRT|HIST1H3B|FANCC|GYK|RBAK|MEN1|C330022B21RIK|C2|FAH|SGIP1|HLCS|PIGT|SMAD1|ZFP580|TXNL4B|SF3B2|RHOX5|GYLTL1B|E2F6|FKBP7|TARSL2|KLHL12|STK38L|ELF1|NKX2-6|C1R|SECISBP2|SYCP1|WBP4|OAZ1|ZFP579|E2F8|RELB|BC012278|HIST1H3A|ZDHHC7|RHOX4E|PISD|VARS2|HIST1H3G|RPS28|MYNN|GAPDHS|NDUFA7|DUSP3|HIST1H3I|UBE3B|CUL4A|CDC25C|ADAMTS2|BAG5|FOXJ3|2400003N08RIK|NFE2L2|USP27X|PTPRG|HIST1H3H|CEBPB|1700016G05RIK|PRKAG3|PPP1R12B|PRDX2|RPA3|B3GNT6|RHOX4A|DBF4|CDC7|TRAK1|HS2ST1|ATF7|PPP1CA|CLN8|ATG9A|APOA1|HIST2H3B|RPS21|PRKAB2|DDB2|LDLR|TXNRD2</td></tr>
<tr><td>8152</td><td>2.00E-10</td><td>4.74E-08</td><td>367</td><td>8104</td><td>metabolism</td><td>CDK6|APOE|HIST1H2BM|FBXL14|ETF1|TSSK3|PLAGL2|HIST1H2BP|HYOU1|RPO1-1|EIF1|TARS|MCPT1|TUBB3|KYNU|PLA2G1B|RBM4|PIK3C2A|2610031L17RIK|SIL1|FDPS|BRD8|CDC40|PJA1|MAST2|GYS1|MAST1|ILF3|PTPRK|MSC|PCSK1N|RG9MTD2|ATP6V1E1|MYT1L|GM711|TSHZ3|ERCC2|CBX2|GLT8D1|HIST1H3D|FBXO6B|EIF5|CAPZA1|TRERF1|USP3|PRKAR1A|HIST2H3C2|PRUNE|HNRPF|WBSCR18|BRWD1|BIRC1C|PRSS15|CRKRS|MCPT2|SRRM2|RG9MTD1|UBE2E3|PDK3|HIST1H3C|UBE2D3|ADRA1D|SPCS1|ZFP263|HSDL2|SLC27A3|C2TA|SRRM1|HIST1H3E|TEP1|POMT2|PHF10|HIST1H3F|SNRPE|USP43|MECP2|HIST2H3C1|DCAMKL2|UBB|PITPNC1|ALDH7A1|IRX3|H2-KE6|NPL|D11BWG0434E|PIAS2|NPR2|ESPL1|CHD4|IRX6|ORC1L|PIAS3|NOL5A|NLN|STAMBP|POFUT1|GLIS2|FEM1A|VAX1|SPIN|MBD4|EDG2|C77668|INVS|PPP1R1B|SMARCAL1|EPHB2|TWIST2|EBF2|MRPL14|CDK7|1700030G11RIK|WASF1|ZBTB1|PRMT5|NPPC|SMARCA5|ZBTB37|UHMK1|ATP8B3|AMFR|TIMM8A1|CYP3A25|PRPF31|PPAT|METAP2|PLD2|HPCA|HOXD8|PGPEP1|RPS5|HECW1|GANC|STARD3|COMT|LRPAP1|TCERG1|RFC2|PLAT|SERTAD2|CAPZA2|FBXO38|PAPOLG|WRNIP1|TDG|ADPRH|SIM1|MGAT3|GGN|SNRPB2|BACE2|MID1IP1|COX7A2|LHX6|OXCT2B|NOTCH2|GALNT3|D11ERTD730E|CTCF|BTK|DCLRE1B|UBQLN4|GUCY1B2|9130017K11RIK|OAS2|PCSK4|CD9|4732466D17RIK|NDUFAF1|4930429M06RIK|PSMA7|ROR2|PHKA2|ADSS|UBE2T|HIST2H2AA1|ADAM23|C1RL|STC1|PIP5K2B|3230401I01RIK|HIST1H1B|CNDP2|SPO11|ZFP715|DPH5|EIF3S4|KLF3|OPN3|PRDX1|ZFP277|ITGB8|ZFHX1A|MC1R|REX2|RNASEH2A|CLASP1|CDC16|D7WSU128E|UBTD1|BRCC3|MCHR1|A730008L03RIK|BC052066|4930432O21RIK|CUTL1|SS18L1|CSNK1G1|B3GALT6|PRKCBP1|NEB|2810410C14RIK|TGIF2|GIYD2|MAL|SLA2|WWTR1|HEMK1|MRPL17|CCNE2|2610305D13RIK|MMS19L|FBXO44|RLF|RUVBL2|PIGQ|RPL36|ZFP397|PCYT1A|COPG2|4933424A20RIK|PHF6|PSMB5|CDX4|POLR2H|RPS12|RWDD4A|TM4SF4|AF397014|MCPT4|U2AF2|EIF3S3|GAG|X83328|NCOA2|TBX2|PHF15|BCL6B|FBXL21|DDX54|MUG1|PRPF18|OXCT2A|GSTZ1|TBX3|SUZ12|GSPT2|MAGI1|UGP2|UBE2M|9030624G23RIK|PARS2|HIST2H2AA2|TSC22D4|D1ERTD161E|OASL1|CYP4A12|THRAP5|NR2F2|MLH3|RXRB|ASNS|FHIT|E2F7|RPS27A|FOSL1|DDAH2|DRAP1|IDI1|SLC37A2|ELOVL2|MRPL37|PCOLN3|A630042L21RIK|RBMXRT|HIST1H3B|FANCC|GYK|RBAK|MEN1|C330022B21RIK|C2|FAH|SGIP1|HLCS|PIGT|SMAD1|ZFP580|TXNL4B|SF3B2|D5ERTD593E|RHOX5|GYLTL1B|E2F6|FKBP7|TARSL2|KLHL12|STK38L|ELF1|NKX2-6|C1R|SECISBP2|SYCP1|WBP4|OAZ1|ZFP579|E2F8|RELB|CTNNA1|BC012278|HIST1H3A|ZDHHC7|RHOX4E|PISD|VARS2|HIST1H3G|RPS28|MYNN|GAPDHS|NDUFA7|DUSP3|HIST1H3I|UBE3B|CUL4A|CDC25C|ADAMTS2|BAG5|FOXJ3|2400003N08RIK|NFE2L2|USP27X|PTPRG|HIST1H3H|CEBPB|1700016G05RIK|PRKAG3|PPP1R12B|PRDX2|RPA3|B3GNT6|RHOX4A|DBF4|CDC7|TRAK1|HS2ST1|ATF7|PPP1CA|SMPDL3A|CLN8|ATG9A|APOA1|HIST2H3B|RPS21|PRKAB2|DDB2|LDLR|TXNRD2</td></tr>
</table>

6139	1.49E-09	3.02E-07	186	3458	nucleobase, nucleoside, nucleotide and nucleic acid metabolism	ADSS|HIST2H2AA1|3230401I01RIK|HIST1H2BM|HIST1H1B|SPO11|ZFP715|KLF3|PLAGL2|HIST1H2BP|RPO1-1|ZFHX1A|REX2|RNASEH2A|TARS|A730008L03RIK|4930432O21RIK|KYNU|CUTL1|SS18L1|RBM4|PRKCBP1|2610031L17RIK|TGIF2|GIYD2|BRD8|MAL|SLA2|CDC40|WWTR1|HEMK1|ILF3|CCNE2|2610305D13RIK|MMS19L|MSC|RLF|RG9MTD2|ATP6V1E1|MYT1L|RUVBL2|TSHZ3|ERCC2|ZFP397|CBX2|HIST1H3D|PHF6|TRERF1|CDX4|POLR2H|U2AF2|PRKAR1A|HIST2H3C2|GAG|HNRPF|NCOA2|BRWD1|BIRC1C|TBX2|PHF15|BCL6B|DDX54|SRRM2|PRPF18|RG9MTD1|HIST1H3C|ADRA1D|TBX3|ZFP263|SUZ12|C2TA|UGP2|9030624G23RIK|PARS2|HIST2H2AA2|TSC22D4|D1ERTD161E|SRRM1|HIST1H3E|THRAP5|TEP1|PHF10|NR2F2|HIST1H3F|MLH3|SNRPE|RXRB|MECP2|HIST2H3C1|FHIT|E2F7|IRX3|FOSL1|DRAP1|PIAS2|NPR2|CHD4|IRX6|ORC1L|PIAS3|NOL5A|PCOLN3|POFUT1|GLIS2|A630042L21RIK|FEM1A|RBMXRT|HIST1H3B|VAX1|FANCC|RBAK|MEN1|SPIN|MBD4|EDG2|C77668|C330022B21RIK|INVS|FAH|PPP1R1B|SGIP1|SMARCAL1|TWIST2|EBF2|SMAD1|ZFP580|CDK7|TXNL4B|SF3B2|ZBTB1|RHOX5|PRMT5|E2F6|NPPC|SMARCA5|TARSL2|ZBTB37|ELF1|NKX2-6|PRPF31|SYCP1|WBP4|PPAT|ZFP579|E2F8|HOXD8|RELB|BC012278|HIST1H3A|RHOX4E|VARS2|HIST1H3G|MYNN|TCERG1|RFC2|HIST1H3I|CUL4A|SERTAD2|PAPOLG|WRNIP1|TDG|SIM1|FOXJ3|2400003N08RIK|NFE2L2|SNRPB2|HIST1H3H|CEBPB|LHX6|PPP1R12B|NOTCH2|D11ERTD730E|CTCF|DCLRE1B|RPA3|RHOX4A|DBF4|CDC7|TRAK1|GUCY1B2|ATF7|OAS2|HIST2H3B|4930429M06RIK|DDB2|ROR2
6259	1.84E-08	3.27E-06	57	716	DNA metabolism	HIST2H2AA1|HIST1H2BM|HIST1H1B|CHD4|ORC1L|SPO11|HIST1H3B|HIST1H2BP|FANCC|MEN1|RNASEH2A|MBD4|SMARCAL1|SGIP1|PRMT5|SMARCA5|GIYD2|BRD8|ELF1|SYCP1|HEMK1|CCNE2|MMS19L|RUVBL2|HIST1H3A|ERCC2|CBX2|HIST1H3D|HIST1H3G|RFC2|HIST1H3I|CUL4A|HIST2H3C2|GAG|BIRC1C|TDG|WRNIP1|2400003N08RIK|HIST1H3C|ADRA1D|SUZ12|HIST1H3H|HIST2H2AA2|CTCF|DCLRE1B|HIST1H3E|RPA3|DBF4|TEP1|CDC7|HIST1H3F|MLH3|HIST2H3C1|HIST2H3B|4930429M06RIK|FHIT|DDB2
6334	1.67E-06	2.65E-04	17	121	nucleosome assembly	HIST1H3H|HIST2H2AA1|HIST1H3D|HIST1H3G|HIST1H2BM|HIST1H1B|HIST2H2AA2|HIST1H3I|HIST1H3E|HIST2H3C2|HIST1H3F|HIST1H3B|HIST1H2BP|HIST2H3C1|HIST2H3B|HIST1H3C|HIST1H3A
19538	1.92E-06	2.73E-04	174	3502	protein metabolism	UBE2T|HIST2H2AA1|ADAM23|C1RL|STC1|CDK6|APOE|3230401I01RIK|HIST1H2BM|HIST1H1B|CNDP2|DPH5|FBXL14|EIF3S4|ETF1|OPN3|TSSK3|HIST1H2BP|HYOU1|EIF1|CLASP1|TARS|MCPT1|CDC16|D7WSU128E|UBTD1|BRCC3|TUBB3|CSNK1G1|B3GALT6|2610031L17RIK|SIL1|PJA1|MAST2|HEMK1|MAST1|MRPL17|ILF3|PTPRK|PCSK1N|FBXO44|RLF|GM711|RUVBL2|PIGQ|RPL36|4933424A20RIK|HIST1H3D|FBXO6B|EIF5|CAPZA1|PSMB5|RPS12|RWDD4A|USP3|TM4SF4|MCPT4|PRKAR1A|EIF3S3|HIST2H3C2|GAG|X83328|WBSCR18|PRSS15|CRKRS|FBXL21|MCPT2|UBE2E3|PDK3|HIST1H3C|UBE2D3|SPCS1|SUZ12|GSPT2|MAGI1|UBE2M|PARS2|HIST2H2AA2|OASL1|HIST1H3E|TEP1|POMT2|HIST1H3F|USP43|HIST2H3C1|DCAMKL2|UBB|RPS27A|D11BWG0434E|PIAS2|NPR2|ESPL1|PIAS3|MRPL37|NLN|STAMBP|POFUT1|HIST1H3B|FANCC|MEN1|C2|EPHB2|HLCS|PIGT|SMAD1|MRPL14|CDK7|1700030G11RIK|WASF1|PRMT5|FKBP7|TARSL2|UHMK1|KLHL12|STK38L|AMFR|ELF1|C1R|TIMM8A1|SECISBP2|METAP2|PLD2|PGPEP1|RPS5|HECW1|CTNNA1|HIST1H3A|ZDHHC7|VARS2|HIST1H3G|LRPAP1|RPS28|DUSP3|HIST1H3I|PLAT|UBE3B|CUL4A|CDC25C|ADAMTS2|CAPZA2|FBXO38|ADPRH|BAG5|MGAT3|GGN|USP27X|PTPRG|HIST1H3H|CEBPB|BACE2|MID1IP1|1700016G05RIK|D11ERTD730E|BTK|B3GNT6|UBQLN4|CDC7|TRAK1|HS2ST1|9130017K11RIK|PCSK4|PPP1CA|CLN8|CD9|4732466D17RIK|ATG9A|APOA1|HIST2H3B|RPS21|NDUFAF1|PSMA7|LDLR|ROR2|PHKA2
6333	5.57E-06	7.21E-04	20	175	chromatin assembly or disassembly	HIST1H3H|HIST2H2AA1|CBX2|HIST1H3D|HIST1H3G|HIST1H2BM|HIST1H1B|HIST2H2AA2|CHD4|HIST1H3I|SMARCA5|HIST1H3E|HIST2H3C2|HIST1H3F|HIST1H3B|HIST1H2BP|HIST2H3C1|HIST2H3B|HIST1H3C|HIST1H3A
31497	8.46E-06	1.00E-03	17	136	chromatin assembly	HIST1H3H|HIST2H2AA1|HIST1H3D|HIST1H3G|HIST1H2BM|HIST1H1B|HIST2H2AA2|HIST1H3I|HIST1H3E|HIST2H3C2|HIST1H3F|HIST1H3B|HIST1H2BP|HIST2H3C1|HIST2H3B|HIST1H3C|HIST1H3A
6461	1.25E-05	1.37E-03	28	316	protein complex assembly	HIST2H2AA1|HIST1H3D|HIST1H3G|APOE|HIST1H2BM|HIST1H1B|HIST1H3I|HIST2H3C2|CAPZA2|HIST1H3B|HIST1H2BP|FANCC|GGN|HIST1H3C|HIST1H3H|MAGI1|WASF1|HIST2H2AA2|D11ERTD730E|2610031L17RIK|HIST1H3E|HIST1H3F|CD9|HIST2H3C1|HIST2H3B|NDUFAF1|C

<table>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td>TNNA1|HIST1H3A</td></tr>
<tr><td>16070</td><td>5.07E-05</td><td>5.15E-03</td><td>130</td><td>2603</td><td>RNA metabolism</td><td>3230401I01RIK|ZFP715|KLF3|PLAGL2|RPO1-1|ZFHX1A|REX2|RNASEH2A|TARS|A730008L03RIK|4930432O21RIK|CUTL1|SS18L1|RBM4|PRKCBP1|2610031L17RIK|TGIF2|BRD8|MAL|SLA2|CDC40|WWTR1|ILF3|2610305D13RIK|MMS19L|MSC|RG9MTD2|MYT1L|TSHZ3|ERCC2|ZFP397|CBX2|PHF6|TRERF1|CDX4|PRKAR1A|U2AF2|HNRPF|NCOA2|BRWD1|BIRC1C|PHF15|TBX2|BCL6B|DDX54|SRRM2|PRPF18|RG9MTD1|TBX3|SUZ12|ZFP263|C2TA|UGP2|9030624G23RIK|PARS2|D1ERTD161E|TSC22D4|SRRM1|THRAP5|PHF10|NR2F2|SNRPE|RXRB|MECP2|E2F7|IRX3|DRAP1|FOSL1|PIAS2|CHD4|IRX6|PIAS3|NOL5A|PCOLN3|GLIS2|FEM1A|A630042L21RIK|RBMXRT|VAX1|RBAK|SPIN|EDG2|C77668|INVS|C330022B21RIK|FAH|TWIST2|EBF2|SMAD1|CDK7|TXNL4B|ZFP580|SF3B2|ZBTB1|RHOX5|PRMT5|E2F6|TARSL2|ZBTB37|ELF1|NKX2-6|PRPF31|WBP4|ZFP579|E2F8|HOXD8|RELB|BC012278|RHOX4E|VARS2|MYNN|TCERG1|SERTAD2|PAPOLG|SIM1|FOXJ3|2400003N08RIK|NFE2L2|SNRPB2|CEBPB|LHX6|PPP1R12B|NOTCH2|D11ERTD730E|CTCF|RHOX4A|TRAK1|ATF7|OAS2|ROR2</td></tr>
<tr><td>7143</td><td>5.46E-05</td><td>5.18E-03</td><td>4</td><td>7</td><td>female meiosis</td><td>STAG3|PPP1CA|MLH3|SPIN</td></tr>
<tr><td>6325</td><td>6.80E-05</td><td>6.05E-03</td><td>26</td><td>311</td><td>establishment and/or maintenance of chromatin architecture</td><td>HIST2H2AA1|CBX2|HIST1H3D|HIST1H3G|HIST1H2BM|HIST1H1B|CHD4|HIST1H3I|HIST2H3C2|HIST1H2BP|HIST1H3B|MEN1|2400003N08RIK|HIST1H3C|HIST1H3H|SUZ12|SMARCAL1|PRMT5|HIST2H2AA2|HIST1H3E|SMARCA5|BRD8|HIST1H3F|HIST2H3C1|HIST2H3B|HIST1H3A</td></tr>
<tr><td>6464</td><td>8.07E-05</td><td>6.75E-03</td><td>85</td><td>1561</td><td>protein modification</td><td>UBE2T|STC1|RPS27A|CDK6|PIAS2|NPR2|PIAS3|DPH5|FBXL14|STAMBP|POFUT1|OPN3|TSSK3|MEN1|CDC16|D7WSU128E|UBTD1|BRCC3|EPHB2|HLCS|PIGT|SMAD1|CSNK1G1|CDK7|1700030G11RIK|PRMT5|B3GALT6|UHMK1|KLHL12|STK38L|AMFR|ELF1|PJA1|MAST2|HEMK1|MAST1|ILF3|PTPRK|FBXO44|PCSK1N|HECW1|GM711|PIGQ|ZDHHC7|4933424A20RIK|FBXO6B|RWDD4A|USP3|TM4SF4|DUSP3|PLAT|UBE3B|CUL4A|PRKAR1A|CDC25C|CRKRS|FBXL21|FBXO38|ADPRH|MGAT3|UBE2E3|PDK3|PTPRG|UBE2D3|SPCS1|SUZ12|BACE2|UBE2M|BTK|OASL1|B3GNT6|UBQLN4|CDC7|TEP1|POMT2|TRAK1|9130017K11RIK|PPP1CA|USP43|ATG9A|DCAMKL2|UBB|LDLR|ROR2|PHKA2</td></tr>
<tr><td>50791</td><td>1.05E-04</td><td>8.13E-03</td><td>171</td><td>3666</td><td>regulation of physiological process</td><td>CDK6|APOE|KRAS|ZFP715|EIF3S4|KLF3|OPN3|PRDX1|PLAGL2|ZFHX1A|REX2|CLASP1|MINA|CDC16|A730008L03RIK|4930432O21RIK|CUTL1|SS18L1|BGLAP-RS1|PRKCBP1|2610031L17RIK|BGLAP2|TGIF2|BRD8|MAL|TEGT|SLA2|SOCS2|MAST2|WWTR1|ILF3|SERINC3|CCNE2|2610305D13RIK|MMS19L|MSC|MYT1L|TSHZ3|ERCC2|ZFP397|CBX2|PHF6|EIF5|CAPZA1|TRERF1|BNIP2|MFGE8|CDX4|TM4SF4|PRKAR1A|NCOA2|BRWD1|BIRC1C|TBX2|PHF15|BCL6B|DDX54|IHPK2|PIK3CB|UBE2E3|ADRA1D|TBX3|SUZ12|ZFP263|GSPT2|C2TA|UGP2|9030624G23RIK|TSC22D4|D1ERTD161E|THRAP5|PHF10|TEP1|NR2F2|TNNT3|RXRB|MECP2|E2F7|IRX3|FOSL1|DDAH2|DRAP1|CKS2|PIAS2|GDF5|ESPL1|CHD4|IRX6|PIAS3|GRM7|PCOLN3|STAMBP|GLIS2|POFUT1|A630042L21RIK|FEM1A|VAX1|RBAK|MEN1|SPIN|MBD4|EDG2|C330022B21RIK|INVS|C2|FAH|IFNZ|EPHB2|TWIST2|EBF2|ACTN4|SMAD1|NRAS|GRIN2A|ZFP580|CDK7|ZBTB1|RHOX5|PRMT5|E2F6|NPPC|TFPT|BGLAP1|ZBTB37|UHMK1|STK38L|ELF1|NKX2-6|C1R|WBP4|ZFP579|E2F8|HPCA|HOXD8|MTCP1|RELB|CTNNA1|BC012278|AVEN|RHOX4E|CLEC2D|MYNN|GAPDHS|BRMS1|TCERG1|CUL4A|SERTAD2|CAPZA2|SIM1|WRNIP1|FOXJ3|2400003N08RIK|NFE2L2|CEBPB|MID1IP1|LHX6|PPP1R12B|NOTCH2|CTCF|BTK|PRDX2|RHOX4A|DBF4|CDC7|TRAK1|ATF7|PPP1CA|EDG1|APOA1|THPO|ROR2</td></tr>
<tr><td>6323</td><td>1.09E-04</td><td>8.13E-03</td><td>26</td><td>320</td><td>DNA packaging</td><td>HIST2H2AA1|CBX2|HIST1H3D|HIST1H3G|HIST1H2BM|HIST1H1B|CHD4|HIST1H3I|HIST2H3C2|HIST1H2BP|HIST1H3B|MEN1|2400003N08RIK|HIST1H3C|HIST1H3H|SUZ12|SMARCAL1|PRMT5|HIST2H2AA2|HIST1H3E|SMARCA5|BRD8|HIST1H3F|HIST2H3C1|HIST2H3B|HIST1H3A</td></tr>
<tr><td>50789</td><td>1.30E-04</td><td>9.28E-03</td><td>190</td><td>4166</td><td>regulation of biological process</td><td>SPRED3|CDK6|APOE|KRAS|CHRD|ZFP715|EIF3S4|KLF3|OPN3|PRDX1|PLAGL2|ZFHX1A|TMEM9B|REX2|CLASP1|MINA|CDC16|A730008L03RIK|4930432O21RIK|CUTL1|SS18L1|BGLAP-RS1|PRKCBP1|2610031L17RIK|TGIF2|BGLAP2|BRD8|MAL|TEGT|SLA2|SOCS2|MAST2|WWTR1|HEMK1|CHML|ILF3|SERINC3|CCNE2|2610305D13RIK|MMS19L|MSC|RLF|D10ERTD610E|MYT1L|TSHZ3|ERCC2|ZFP397|CBX2|PHF6|EIF5|CAPZA1|TRERF1|BNIP2|MFGE8|CDX4|TM4SF4|P</td></tr>
</table>

<table>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td>RKAR1A|NCOA2|BRWD1|BIRC1C|TBX2|PHF15|BCL6B|DDX54|FARP2|IHPK2|PIK3CB|UBE2E3|ADRA1D|TBX3|SUZ12|ZFP263|GSPT2|C2TA|MAGI1|UGP2|9030624G23RIK|TSC22D4|D1ERTD161E|THRAP5|TEP1|PHF10|NR2F2|TNNT3|RXRB|MAPKBP1|MECP2|LRP6|E2F7|IRX3|FOSL1|DDAH2|DRAP1|CKS2|PIAS2|GDF5|ESPL1|CHD4|IRX6|STIP1|ATRN|PIAS3|2600003E23RIK|GRM7|PCOLN3|STAMBP|POFUT1|GLIS2|A630042L21RIK|FEM1A|VAX1|RBAK|MEN1|SPIN|MBD4|EDG2|C330022B21RIK|INVS|C2|FAH|PPP1R1B|IFNZ|EPHB2|TWIST2|EBF2|ACTN4|SMAD1|NRAS|GRIN2A|ZFP580|CDK7|ZBTB1|RHOX5|PRMT5|E2F6|NPPC|TFPT|BGLAP1|ZBTB37|UHMK1|RIC8|STK38L|ELF1|NKX2-6|C1R|WBP4|PLD2|ZFP579|E2F8|HPCA|HOXD8|MTCP1|RELB|CTNNA1|BC012278|AVEN|RHOX4E|CLEC2D|GAPDHS|MYNN|BRMS1|TCERG1|CUL4A|SERTAD2|CAPZA2|WRNIP1|SIM1|FOXJ3|2400003N08RIK|NFE2L2|CEBPB|MID1IP1|LHX6|PPP1R12B|NOTCH2|CTCF|BTK|PRDX2|RHOX4A|DBF4|CDC7|TRAK1|ATF7|PPP1CA|EDG1|CLN8|APOA1|THPO|RGS2|ROR2</td></tr>
<tr><td>43412</td><td>1.73E-04</td><td>1.17E-02</td><td>87</td><td>1643</td><td>biopolymer modification</td><td>UBE2T|STC1|RPS27A|CDK6|PIAS2|NPR2|PIAS3|DPH5|FBXL14|STAMBP|POFUT1|OPN3|TSSK3|MEN1|MBD4|CDC16|D7WSU128E|UBTD1|BRCC3|EPHB2|HLCS|PIGT|SMAD1|CSNK1G1|CDK7|1700030G11RIK|PRMT5|B3GALT6|UHMK1|KLHL12|STK38L|AMFR|ELF1|PJA1|MAST2|HEMK1|MAST1|ILF3|PTPRK|FBXO44|PCSK1N|HECW1|GM711|PIGQ|ZDHHC7|4933424A20RIK|FBXO6B|RWDD4A|USP3|TM4SF4|DUSP3|PLAT|UBE3B|CUL4A|PRKAR1A|CDC25C|CRKRS|FBXL21|FBXO38|ADPRH|MGAT3|UBE2E3|PDK3|PTPRG|UBE2D3|SPCS1|SUZ12|BACE2|UBE2M|CTCF|BTK|OASL1|B3GNT6|UBQLN4|CDC7|TEP1|POMT2|TRAK1|9130017K11RIK|PPP1CA|USP43|ATG9A|DCAMKL2|UBB|LDLR|ROR2|PHKA2</td></tr>
<tr><td>50794</td><td>1.86E-04</td><td>1.20E-02</td><td>173</td><td>3756</td><td>regulation of cellular process</td><td>SPRED3|CDK6|APOE|KRAS|CHRD|ZFP715|EIF3S4|KLF3|PRDX1|PLAGL2|ZFHX1A|TMEM9B|REX2|CLASP1|MINA|CDC16|A730008L03RIK|4930432O21RIK|CUTL1|SS18L1|PRKCBP1|2610031L17RIK|TGIF2|BRD8|MAL|TEGT|SLA2|SOCS2|MAST2|WWTR1|ILF3|SERINC3|CCNE2|2610305D13RIK|MMS19L|MSC|RLF|D10ERTD610E|MYT1L|TSHZ3|ERCC2|ZFP397|CBX2|PHF6|EIF5|CAPZA1|TRERF1|BNIP2|MFGE8|CDX4|TM4SF4|PRKAR1A|NCOA2|BRWD1|BIRC1C|TBX2|PHF15|BCL6B|DDX54|FARP2|IHPK2|PIK3CB|UBE2E3|ADRA1D|TBX3|SUZ12|ZFP263|GSPT2|C2TA|MAGI1|UGP2|9030624G23RIK|TSC22D4|D1ERTD161E|THRAP5|PHF10|TEP1|NR2F2|RXRB|MECP2|LRP6|E2F7|IRX3|FOSL1|DDAH2|DRAP1|CKS2|PIAS2|GDF5|ESPL1|CHD4|IRX6|STIP1|PIAS3|2600003E23RIK|GRM7|PCOLN3|STAMBP|GLIS2|POFUT1|A630042L21RIK|FEM1A|VAX1|RBAK|MEN1|SPIN|MBD4|EDG2|C330022B21RIK|INVS|FAH|IFNZ|TWIST2|EBF2|ACTN4|SMAD1|NRAS|ZFP580|CDK7|ZBTB1|RHOX5|PRMT5|E2F6|TFPT|ZBTB37|UHMK1|RIC8|STK38L|ELF1|NKX2-6|WBP4|PLD2|ZFP579|E2F8|HPCA|HOXD8|MTCP1|RELB|CTNNA1|BC012278|AVEN|RHOX4E|CLEC2D|MYNN|GAPDHS|BRMS1|TCERG1|CUL4A|SERTAD2|CAPZA2|SIM1|WRNIP1|FOXJ3|2400003N08RIK|NFE2L2|CEBPB|MID1IP1|LHX6|PPP1R12B|NOTCH2|CTCF|BTK|PRDX2|RHOX4A|DBF4|CDC7|TRAK1|ATF7|PPP1CA|EDG1|THPO|RGS2|ROR2</td></tr>
<tr><td>48519</td><td>2.04E-04</td><td>1.24E-02</td><td>60</td><td>1036</td><td>negative regulation of biological process</td><td>E2F7|SPRED3|DRAP1|DDAH2|CHRD|PCOLN3|KLF3|STAMBP|VAX1|ZFHX1A|CLASP1|A730008L03RIK|PPP1R1B|TWIST2|CUTL1|ACTN4|SMAD1|MAL|UHMK1|ELF1|SLA2|TEGT|SOCS2|PLD2|WWTR1|HPCA|ILF3|CTNNA1|AVEN|CBX2|CLEC2D|CAPZA1|BNIP2|BRMS1|TM4SF4|CUL4A|SERTAD2|NCOA2|TBX2|BIRC1C|BCL6B|CAPZA2|IHPK2|2400003N08RIK|ADRA1D|TBX3|SUZ12|CEBPB|C2TA|MID1IP1|NOTCH2|CTCF|PRDX2|TEP1|CDC7|ATF7|CLN8|MECP2|RGS2|LRP6</td></tr>
<tr><td>48523</td><td>2.09E-04</td><td>1.24E-02</td><td>56</td><td>949</td><td>negative regulation of cellular process</td><td>E2F7|DRAP1|DDAH2|CHRD|PCOLN3|KLF3|STAMBP|VAX1|ZFHX1A|CLASP1|A730008L03RIK|TWIST2|CUTL1|ACTN4|SMAD1|UHMK1|MAL|ELF1|SLA2|TEGT|PLD2|WWTR1|SOCS2|HPCA|ILF3|CTNNA1|AVEN|CBX2|CLEC2D|CAPZA1|BNIP2|BRMS1|TM4SF4|CUL4A|SERTAD2|NCOA2|TBX2|BIRC1C|BCL6B|CAPZA2|IHPK2|2400003N08RIK|TBX3|SUZ12|CEBPB|C2TA|MID1IP1|NOTCH2|CTCF|PRDX2|TEP1|CDC7|ATF7|MECP2|RGS2|LRP6</td></tr>
<tr><td>51243</td><td>2.70E-04</td><td>1.50E-02</td><td>50</td><td>828</td><td>negative regulation of cellular physiological process</td><td>E2F7|DRAP1|DDAH2|PCOLN3|KLF3|STAMBP|VAX1|ZFHX1A|CLASP1|A730008L03RIK|TWIST2|CUTL1|SMAD1|ACTN4|UHMK1|MAL|ELF1|SLA2|TEGT|WWTR1|HPCA|ILF3|CTNNA1|AVEN|CBX2|CAPZA1|BNIP2|BRMS1|TM4SF4|CUL4A|SERTAD2|NCOA2|TBX2|BIRC1C|BCL6B|CAPZA2|IHPK2|2400003N08RIK|SUZ12|TBX3|CEBPB|C2TA|MID1IP1|NOTCH2|CTCF|PRDX2|TEP1|CDC7|ATF7|MECP2</td></tr>
<tr><td>44260</td><td>2.81E-04</td><td>1.50E-02</td><td>152</td><td>3253</td><td>cellular</td><td>UBE2T|ADAM23|C1RL|STC1|CDK6|APOE|3230401I01RIK|CNDP2|DPH5|FBXL14|EIF3S4|ETF1|OPN3|TSSK3|HYOU1|EIF1|CLASP1|TARS|MCP</td></tr>
</table>

					macromolecule metabolism	T1|CDC16|D7WSU128E|UBTD1|BRCC3|TUBB3|CSNK1G1|B3GALT6|SIL1|PJA1|MAST2|HEMK1|GYS1|MAST1|MRPL17|ILF3|PTPRK|FBXO44|PCSK1N|RLF|GM711|RUVBL2|PIGQ|RPL36|4933424A20RIK|FBXO6B|CAPZA1|EIF5|PSMB5|RPS12|RWDD4A|USP3|TM4SF4|PRKAR1A|MCPT4|EIF3S3|GAG|X83328|WBSCR18|CRKRS|PRSS15|FBXL21|MCPT2|UBE2E3|PDK3|UBE2D3|SPCS1|SUZ12|GSPT2|UBE2M|PARS2|OASL1|POMT2|TEP1|USP43|DCAMKL2|UBB|RPS27A|D11BWG0434E|PIAS2|NPR2|ESPL1|PIAS3|MRPL37|NLN|STAMBP|POFUT1|MEN1|C2|EPHB2|HLCS|PIGT|SMAD1|MRPL14|CDK7|1700030G11RIK|WASF1|PRMT5|FKBP7|TARSL2|UHMK1|KLHL12|STK38L|AMFR|ELF1|C1R|TIMM8A1|SECISBP2|METAP2|PLD2|PGPEP1|HECW1|RPS5|ZDHHC7|VARS2|LRPAP1|RPS28|DUSP3|PLAT|UBE3B|CUL4A|CDC25C|ADAMTS2|CAPZA2|FBXO38|ADPRH|BAG5|MGAT3|USP27X|PTPRG|CEBPB|BACE2|MID1IP1|1700016G05RIK|PRKAG3|BTK|B3GNT6|UBQLN4|CDC7|TRAK1|HS2ST1|9130017K11RIK|PCSK4|PPP1CA|CLN8|4732466D17RIK|ATG9A|APOA1|RPS21|NDUFAF1|PSMA7|LDLR|ROR2|PHKA2
51244	2.85E-04	1.50E-02	160	3456	regulation of cellular physiological process	CDK6|APOE|KRAS|ZFP715|EIF3S4|KLF3|PRDX1|PLAGL2|ZFHX1A|REX2|CLASP1|MINA|CDC16|A730008L03RIK|4930432O21RIK|CUTL1|SS18L1|PRKCBP1|2610031L17RIK|TGIF2|BRD8|MAL|SLA2|TEGT|SOCS2|MAST2|WWTR1|ILF3|SERINC3|2610305D13RIK|CCNE2|MMS19L|MSC|MYT1L|TSHZ3|ERCC2|ZFP397|CBX2|CAPZA1|EIF5|PHF6|TRERF1|BNIP2|MFGE8|CDX4|TM4SF4|PRKAR1A|NCOA2|BRWD1|BIRC1C|TBX2|PHF15|BCL6B|DDX54|IHPK2|PIK3CB|UBE2E3|ADRA1D|TBX3|SUZ12|ZFP263|GSPT2|C2TA|UGP2|9030624G23RIK|TSC22D4|D1ERTD161E|THRAP5|PHF10|TEP1|NR2F2|RXRB|MECP2|E2F7|IRX3|FOSL1|DDAH2|DRAP1|CKS2|PIAS2|GDF5|ESPL1|CHD4|IRX6|PIAS3|GRM7|PCOLN3|STAMBP|GLIS2|POFUT1|A630042L21RIK|FEM1A|VAX1|RBAK|MEN1|SPIN|MBD4|EDG2|C330022B21RIK|INVS|FAH|IFNZ|TWIST2|EBF2|ACTN4|SMAD1|NRAS|ZFP580|CDK7|ZBTB1|RHOX5|PRMT5|E2F6|TFPT|ZBTB37|UHMK1|STK38L|ELF1|NKX2-6|WBP4|ZFP579|E2F8|HPCA|HOXD8|MTCP1|RELB|CTNNA1|BC012278|AVEN|RHOX4E|CLEC2D|MYNN|GAPDHS|BRMS1|TCERG1|CUL4A|SERTAD2|CAPZA2|SIM1|WRNIP1|FOXJ3|2400003N08RIK|NFE2L2|CEBPB|MID1IP1|LHX6|PPP1R12B|NOTCH2|CTCF|BTK|PRDX2|RHOX4A|DBF4|CDC7|TRAK1|ATF7|PPP1CA|EDG1|THPO|ROR2
44267	3.12E-04	1.59E-02	150	3210	cellular protein metabolism	UBE2T|ADAM23|C1RL|STC1|CDK6|APOE|3230401I01RIK|CNDP2|DPH5|FBXL14|EIF3S4|ETF1|OPN3|TSSK3|HYOU1|EIF1|CLASP1|TARS|MCPT1|CDC16|D7WSU128E|UBTD1|BRCC3|TUBB3|CSNK1G1|B3GALT6|SIL1|PJA1|MAST2|HEMK1|MAST1|MRPL17|ILF3|PTPRK|FBXO44|PCSK1N|RLF|GM711|RUVBL2|PIGQ|RPL36|4933424A20RIK|FBXO6B|CAPZA1|EIF5|PSMB5|RPS12|RWDD4A|USP3|TM4SF4|PRKAR1A|MCPT4|EIF3S3|GAG|X83328|WBSCR18|CRKRS|PRSS15|FBXL21|MCPT2|UBE2E3|PDK3|UBE2D3|SPCS1|SUZ12|GSPT2|UBE2M|PARS2|OASL1|POMT2|TEP1|USP43|DCAMKL2|UBB|RPS27A|D11BWG0434E|PIAS2|NPR2|ESPL1|PIAS3|MRPL37|NLN|STAMBP|POFUT1|MEN1|C2|EPHB2|HLCS|PIGT|SMAD1|MRPL14|CDK7|1700030G11RIK|WASF1|PRMT5|FKBP7|TARSL2|UHMK1|KLHL12|STK38L|AMFR|ELF1|C1R|TIMM8A1|SECISBP2|METAP2|PLD2|PGPEP1|HECW1|RPS5|ZDHHC7|VARS2|LRPAP1|RPS28|DUSP3|PLAT|UBE3B|CUL4A|CDC25C|ADAMTS2|CAPZA2|FBXO38|ADPRH|BAG5|MGAT3|USP27X|PTPRG|CEBPB|BACE2|MID1IP1|1700016G05RIK|BTK|B3GNT6|UBQLN4|CDC7|TRAK1|HS2ST1|9130017K11RIK|PCSK4|PPP1CA|CLN8|4732466D17RIK|ATG9A|APOA1|RPS21|NDUFAF1|PSMA7|LDLR|ROR2|PHKA2
43118	4.00E-04	1.96E-02	51	864	negative regulation of physiological process	E2F7|DRAP1|DDAH2|PCOLN3|KLF3|STAMBP|VAX1|ZFHX1A|CLASP1|A730008L03RIK|TWIST2|CUTL1|SMAD1|ACTN4|UHMK1|MAL|ELF1|SLA2|TEGT|WWTR1|HPCA|ILF3|CTNNA1|AVEN|CBX2|CAPZA1|BNIP2|BRMS1|TM4SF4|CUL4A|SERTAD2|NCOA2|TBX2|BIRC1C|BCL6B|CAPZA2|IHPK2|2400003N08RIK|ADRA1D|SUZ12|TBX3|CEBPB|C2TA|MID1IP1|NOTCH2|CTCF|PRDX2|TEP1|CDC7|ATF7|MECP2
6357	6.51E-04	3.02E-02	30	438	regulation of transcription from RNA polymerase II promoter	CBX2|DRAP1|FOSL1|PRKAR1A|NCOA2|BRWD1|TBX2|GLIS2|KLF3|BCL6B|PLAGL2|VAX1|ZFHX1A|EDG2|TBX3|SUZ12|TWIST2|CUTL1|SMAD1|E2F6|CTCF|2610031L17RIK|THRAP5|BRD8|TRAK1|ATF7|NR2F2|ELF1|SLA2|WWTR1
7049	6.59E-04	3.02E-02	45	752	cell cycle	E2F7|MYH10|CKS1B|CDK6|CKS2|BRMS1|KRAS|ESPL1|CDCA8|CUL4A|SPO11|CDC25C|STAG3|PCOLN3|DIP3B|MEN1|PIK3CB|SPIN|CDC16|GSPT2|IFNZ|ACTN4|NRAS|CDK7|TXNL4B|NOTCH2|PRMT5|RANBP1|E2F6|CTCF|DBF4|CDC7|TEP1|UHMK1|PPP1CA|MLH3|MEI1|SYCP1|E2F8|M

						TCP1|ILF3|THPO|CCNE2|RGS2|RELB
6512	8.64E-04	3.73E-02	26	366	ubiquitin cycle	UBE2T|FBXO6B|PIAS2|RWDD4A|USP3|CUL4A|UBE3B|PIAS3|FBXL14|FBXL21|STAMBP|FBXO38|UBE2E3|CDC16|UBE2D3|BRCC3|SUZ12|UBE2M|9130017K11RIK|KLHL12|AMFR|USP43|PJA1|ATG9A|FBXO44|HECW1
6366	8.79E-04	3.73E-02	36	570	transcription from RNA polymerase II promoter	CBX2|FOSL1|DRAP1|TCERG1|PRKAR1A|NCOA2|BRWD1|TBX2|BCL6B|GLIS2|KLF3|PLAGL2|VAX1|ZFHX1A|NFE2L2|EDG2|TBX3|SUZ12|CEBPB|TWIST2|CUTL1|SMAD1|CDK7|E2F6|CTCF|2610031L17RIK|THRAP5|BRD8|TRAK1|ATF7|NR2F2|ELF1|SLA2|WWTR1|MSC|ERCC2
7127	8.91E-04	3.73E-02	6	32	meiosis I	STAG3|MLH3|CKS2|SYCP1|ESPL1|SPO11
6996	1.05E-03	4.27E-02	64	1197	organelle organization and biogenesis	HIST2H2AA1|APOE|CKS2|HIST1H2BM|HIST1H1B|ESPL1|CHD4|NOL5A|KRT2-1|PCOLN3|HIST1H3B|HIST1H2BP|MEN1|CLASP1|PEX16|KIF20A|DNAIC1|TUBB3|SMARCAL1|PLA2G1B|ACTN4|ABCD1|MRPL14|WASF1|TCTE3|RANBP1|PRMT5|NEB|SMARCA5|BRD8|ELF1|TIMM8A1|MAST1|MRPL17|MYH8|RPS5|LSP1|HIST1H3A|CBX2|MYH10|HIST1H3D|CAPZA1|HIST1H3G|RPS12|HIST1H3I|HIST2H3C2|CAPZA2|2400003N08RIK|HIST1H3C|HIST1H3H|SUZ12|MID1IP1|ACTG1|APXL|STX6|HIST2H2AA2|HIST1H3E|TEP1|MYH13|HIST1H3F|CLN8|ATG9A|HIST2H3C1|HIST2H3B
16481	1.08E-03	4.28E-02	21	275	negative regulation of transcription	TBX3|A730008L03RIK|SUZ12|CUTL1|CBX2|TWIST2|C2TA|DRAP1|CTCF|NCOA2|PCOLN3|TBX2|BCL6B|KLF3|SLA2|VAX1|MECP2|WWTR1|ZFHX1A|ILF3|2400003N08RIK
6355	1.19E-03	4.59E-02	103	2133	regulation of transcription, DNA-dependent	ZFP715|KLF3|PLAGL2|ZFHX1A|REX2|A730008L03RIK|4930432O21RIK|CUTL1|SS18L1|PRKCBP1|2610031L17RIK|TGIF2|BRD8|MAL|SLA2|WWTR1|ILF3|2610305D13RIK|MSC|MMS19L|MYT1L|ERCC2|TSHZ3|ZFP397|CBX2|PHF6|TRERF1|CDX4|PRKAR1A|NCOA2|PHF15|TBX2|BIRC1C|BRWD1|BCL6B|DDX54|SUZ12|ZFP263|TBX3|C2TA|UGP2|9030624G23RIK|D1ERTD161E|TSC22D4|THRAP5|PHF10|NR2F2|RXRB|MECP2|E2F7|IRX3|DRAP1|FOSL1|PIAS2|IRX6|CHD4|PIAS3|PCOLN3|GLIS2|FEM1A|A630042L21RIK|VAX1|RBAK|SPIN|EDG2|INVS|C330022B21RIK|FAH|TWIST2|EBF2|SMAD1|CDK7|ZFP580|ZBTB1|PRMT5|RHOX5|E2F6|ZBTB37|ELF1|NKX2-6|WBP4|ZFP579|E2F8|HOXD8|RELB|BC012278|RHOX4E|MYNN|TCERG1|SERTAD2|SIM1|FOXJ3|2400003N08RIK|NFE2L2|CEBPB|LHX6|PPP1R12B|NOTCH2|CTCF|RHOX4A|TRAK1|ATF7|ROR2
9892	1.32E-03	4.96E-02	26	377	negative regulation of metabolism	CBX2|CAPZA1|DRAP1|PCOLN3|NCOA2|TBX2|KLF3|BCL6B|CAPZA2|VAX1|ZFHX1A|2400003N08RIK|CLASP1|SUZ12|A730008L03RIK|TBX3|TWIST2|CUTL1|C2TA|MID1IP1|CTCF|ELF1|SLA2|WWTR1|MECP2|ILF3

Table S2. Affymetrix analysis of gene upregulation in response to H_2O_2 in ES cells. M430 2.0 array data obtained from three untreated and three H_2O_2-treated RNA samples were compared using DChip software. SIRT1-associated genes with a ≥ 15% transcriptional increase ($P < 0.1$) are shown. All genes with ≥ $2\log_2$ SIRT1 binding were subjected to validation by q-RT-PCR. Genes that were validated by q-RT-PCR using independently derived samples are highlighted in blue. Genes that could not be validated are shown in red.

affy_probe	Accession	gene	fold change	P value	S1 ChIP ($\log_2$)
1421683_at	NM_011560	t-complex-associated testis expressed 3	2.57	0.001	2.63
1417488_at	NM_010235	fos-like antigen 1	1.98	0.004	1.515
1422980_a_at	NM_018742	blocked early in transport 1 homolog (S. cerevisiae)-like	1.72	0.003	1.676
1437063_at	NM_010192	feminization 1 homolog a (C. elegans)	1.45	0.062	2.342
1436595_at	NM_172762	RNA binding motif protein 34	1.43	0.040	2.81
1434299_x_at	NM_025931	RAB, member of RAS oncogene family-like 4	1.4	0.003	1.06
1427552_a_at	NM_010363	glutathione transferase zeta 1 (maleylacetoacetate isomerase)	1.36	0.014	2.91
1452289_a_at	NM_028019	ring finger protein 135	1.3	0.033	1.063
1417165_at	NM_010773	methyl-CpG binding domain protein 2	1.3	0.050	1.101
1447480_at	NM_207667	Fibroblast growth factor 14	1.26	0.086	1.639
1417815_a_at	NM_012032	serine incorporator 3	1.25	0.059	2.461
1438982_s_at	NM_029798	RIKEN cDNA 2810417J12 gene	1.25	0.036	1.495
1423711_at	NM_027175	NADH dehydrogenase 1 alpha subcomplex, assembly factor 1	1.25	0.036	2.741
1424583_at	NM_145519	FERM, RhoGEF and pleckstrin domain protein 2	1.24	0.072	2.013
1434975_x_at	NM_001004146	RIKEN cDNA 4933439C20 gene	1.22	0.031	1.141
1420642_a_at	NM_025946	RIKEN cDNA 2010100O12 gene	1.21	0.035	1.179
1416841_at	NM_025423	RIKEN cDNA 1110059E24 gene	1.21	0.013	1.75
1424494_s_at	NM_029798	RIKEN cDNA 2810417J12 gene	1.2	0.025	1.495
1422797_at	NM_031248	mitogen activated protein binding protein interacting protein	1.2	0.010	1.795
1424045_at	NM_027457	RIKEN cDNA 5730437N04 gene	1.19	0.027	1.882
1426387_x_at	NM_177298	phosphatidylserine decarboxylase	1.19	0.051	3.043
1454092_a_at	NM_181410	general transcription factor IIH, polypeptide 3	1.19	0.013	1.26
1423610_at	NM_019648	methionine aminopeptidase 2	1.18	0.012	3.489
1433719_at	NM_177909	solute carrier family 9 (sodium/hydrogen exchanger), isoform 9	1.17	0.091	2.851
1426894_s_at	NM_153560	RIKEN cDNA C230093N12 gene	1.17	0.091	1.406
1420486_at	NM_023554	nucleolar protein 7	1.17	0.029	2.449
1448455_at	NM_012000	ceroid-lipofuscinosis, neuronal 8	1.17	0.038	1.93
1424883_s_at	NM_146083	splicing factor, arginine/serine-rich 7	1.16	0.023	1.042
1460182_at	NM_080557	sorting nexin 4	1.16	0.016	1.997
1415962_at	NM_080635	eukaryotic translation initiation factor 3, subunit 3 (gamma)	1.15	0.024	3.967

Table S3. Chromosomal aberrations of SIRT1 knock-down cells (KD) in response to H_2O_2 treatment. Cells were treated with H_2O_2 for 1 h, followed by 48 h recovery. Metaphases were analyzed by T-FISH. Numbers represent totals from two independent experiments, P values are based on Fisher's Exact Test, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ comparing H_2O_2 treated vs. untreated cells; ††† $P < 0.001$ comparing SIRT1 KD to control.

	untreated		H_2O_2	
	control	SIRT1-KD	control	SIRT1 KD
Total Metaphases	90	98	86	74
Fragments/ Chromatid breaks	5	1	7	9**
Chromosome breaks	5	2	3	4
Chromosome fusions/ circles	3	11	6	23**,†††
Total aberrations	**14.4%**	**13.3%**	**18.6%**	**48.6%**
Aberrant metaphases	**13.2%**	**12.3%**	**17.5%**	**30.4%**

Table S4. List of SIRT1-target genes (FDR<0.005) that are deregulated with age in the neocotrex of B6C3F$_1$ mice ($P<0.005$).

Entrez Gene ID	probe set	gene	fold change	P value
320951, 66776	1435426_s_at	RIKEN cDNA 4933439C20, phosphatidylserine decarboxylase	4.79	0.00436
16792	1436905_x_at	lysosomal-associated protein transmembrane 5	2.1	0.000042
211499	1424454_at	transmembrane protein 87A	1.77	0.000499
50909	1417009_at	complement component 1, r subcomponent	1.72	0.002932
19718	1457669_x_at	replication factor C (activator 1) 2	1.7	0.000121
23792	1423378_at	a disintegrin and metallopeptidase domain 23	1.66	0.000028
67448	1418912_at	plexin domain containing 2	1.63	0.000041
67095	1459666_at	trafficking protein, kinesin binding 1	1.62	0.000864
12175	1422490_at	BCL2/adenovirus E1B interacting protein 1, NIP2	1.56	0.000042
331004	1433719_at	solute carrier family 9 (sodium/hydrogen exchanger), isoform 9	1.56	0.00014
66838	1453141_at	RIKEN cDNA 0610009L18 gene	1.53	0.001976
329251	1434786_at	protein phosphatase 1, regulatory (inhibitor) subunit 12B	1.52	0.000323
69714	1438963_s_at	TCF3 (E2A) fusion partner	1.51	0.002245
11973	1420038_at	VATPase, H+ transporting, lysosomal V1 subunit E1	1.49	0.000268
13047	1451435_at	cut-like 1 (Drosophila)	1.47	0.000947
27053	1433966_x_at	asparagine synthetase	1.43	0.000941
97064	1417818_at	WW domain containing transcription regulator 1	1.42	0.00014
12846	1418701_at	catechol-O-methyltransferase	1.41	0.000144
72479	1426856_at	hydroxysteroid dehydrogenase like 2	1.41	0.000299
109263	1427171_at	rearranged L-myc fusion sequence	1.39	0.001796
75007	1438321_x_at	RIKEN cDNA 4930504E06 gene	1.39	0.002745
20643	1451294_s_at	small nuclear ribonucleoprotein E	1.38	0.000335
240614	1435167_at	RAN binding protein 6	1.38	0.000409
106583	1455310_at	RNA binding motif protein 16	1.38	0.002638
64164	1458364_s_at	interferon alpha responsive gene	1.36	0.000242
66114	1418081_at	Williams-Beuren syndrome chromosome region 18 homolog (human)	1.36	0.002663
56280	1423764_s_at	mitochondrial ribosomal protein L37	1.35	0.000071
13018	1418330_at	CCCTC-binding factor	1.35	0.000719
71990	1438853_x_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 54	1.33	0.000211
114873	1441706_at	Down syndrome cell adhesion molecule-like 1	1.33	0.002378
67489	1416631_at	adaptor-related protein complex AP-4, beta 1	1.32	0.004436
75695	1447852_x_at	RIKEN cDNA 2900002H16 gene	1.3	0.002295
229722	1442113_at	RIKEN cDNA 5330417C22 gene	1.3	0.004258
52202	1436595_at	RNA binding motif protein 34	1.29	0.002776
66162	1434545_x_at	bolA-like 2 (E. coli)	1.28	0.002077
20932	1416213_x_at	surfeit gene 4	1.28	0.003058
13026	1438011_at	phosphate cytidylyltransferase 1, choline, alpha isoform	1.27	0.000117
78829	1448412_a_at	TSC22 domain family 4	1.27	0.001027
241296	1434694_at	leucine rich repeat containing 8A	1.27	0.001334
320910	1436223_at	integrin beta 8	1.27	0.004578
26943	1434548_at	serine incorporator 3	1.25	0.00041
17933	1429738_at	myelin transcription factor 1-like	1.25	0.00088
218544	1451529_at	small glutamine-rich tetratricopeptide repeat (TPR)-containing, beta	1.25	0.001029
14784	1449111_a_at	growth factor receptor bound protein 2	1.24	0.001892

71069	1447624_s_at	storkhead box 2	1.23	0.000502
56307	1434120_a_at	methionine aminopeptidase 2	1.22	0.001864
19735	1447830_s_at	regulator of G-protein signaling 2	1.22	0.004918
60315	1424088_at	melanocyte proliferating gene 1	1.21	0.002547
17125	1448208_at	MAD homolog 1 (Drosophila)	1.21	0.003539
54399	1422980_a_at	blocked early in transport 1 homolog (S. cerevisiae)-like	1.21	0.004001
78825	1425185_at	RIKEN cDNA 5830417C01 gene	1.21	0.004368
216578	1427241_at	poly(A) polymerase gamma	1.2	0.000996
80985	1421870_at	tripartite motif-containing 44	1.2	0.001747
69536	1430287_s_at	HemK methyltransferase family member 1	1.2	0.003087
70544	1424045_at	RIKEN cDNA 5730437N04 gene	1.2	0.004037
77579	1452740_at	myosin, heavy polypeptide 10, non-muscle	1.19	0.00073
16976	1426697_a_at	low density lipoprotein receptor-related protein associated protein 1	1.19	0.001593
207425	1452820_at	bromodomain and WD repeat domain containing 2	1.19	0.002536
51796	1447447_s_at	serine/arginine repetitive matrix 1	1.17	0.003672
20918	1423799_at	eukaryotic translation initiation factor 1	1.13	0.002394
68365	1419246_s_at	RAB14, member RAS oncogene family	1.12	0.001018
69207	1452371_at	splicing factor, arginine/serine-rich 11	-1.14	0.001748
67331	1438604_at	ATPase, Class I, type 8B, member 3	-1.19	0.002219
72057	1449085_at	PHD finger protein 10	-1.24	0.00039
78656	1452350_at	bromodomain containing 8	-1.26	0.004776
216028	1434761_at	leucine rich repeat transmembrane neuronal 3	-1.32	0.003804
27397	1450867_at	mitochondrial ribosomal protein L17	-1.34	0.000634
18092	1452018_at	NK2 transcription factor related, locus 6 (Drosophila)	-1.36	0.000448
320951	1460585_x_at	phosphatidylserine decarboxylase	-1.53	0.000599
387314	1439855_at	cDNA sequence BC023818	-1.53	0.003681
114893	1425986_a_at	DCUN1D1 DCN1, defective in cullin neddylation 1, domain containing 1 (S. cerevisiae)	-1.7	0.001794
218763	1451245_at	leucine rich repeat containing 3B	-1.78	0.002955
68283	1429916_at	RIKEN cDNA 9530077C05 gene	-1.86	0.004644

Table S5. Primers used in this study. * 74 bp sequence is repeated spaced by 160-190 bp. Predominant PCR product is ~230bp. LC: light cycler (Roche), LC480: Roche 96 wp q-PCR instrument.

Gene	SEQUENCE (5'-3')	AT	SYBRKit/ Instrument	Size (bp)
ChIP				
Farp2 (F)	F: TGCAAGTCTGAAGTGGAAGGACCA	56	QIAgen/LC	432
	R: AAGGCGACGGGAGGATTCTATCTT			
DRGFP	F: TCTTCTTCAAGGACGACGGCAACT	60	Roche/LC480	145
	R: TTGTAGTTGTACTCCAGCTTGTGC			
Gapdh	F: CCAATGTGTCCGTCGTGGATCT	56	Roche/LC	155
	R: GTTGAAGTCGCAGGAGACAACC			
LINE1	F: ATGGCGAAAGGCAAACGTAAG	56	Roche/LC	114
	R: ATTTTCGGTTGTGTTGGGGTG			
Major sat. rep.	F: GACGACTTGAAAAATGACGAAATC	56	Roche/LC	74*
	R: CATATTCCAGGTCCTTCAGTGTGC			
Prkag3	F: TCCAGCAGGAAACCCAATAGTCCA	56	QIAgen/LC	586
	R: TGGCTTCCTTCACTTTCTCCTCCA			
Slc9a9	F: TGTGCCGGGTTGAACTGTCTTACT	56	QIAgen/LC	338
	R: TAGACTGGCGCCCACAGAATTTCA			
NHEJ				
NHEJ	F: AGGGCGGGGTTCGGCTTCTGG	60	N/A	725
	R: CCTTCGGGCATGGCGGACTTGA			
RT-PCR				
β-actin	F: GGCCAGGTCATCACTATTGGCAAC	60	Roche/LC480	228
	R: CAGAGCAGTAATCTCCTTCTGCAT			
B2m	F: TGGTCTTTCTGGTGCTTGTCTCAC	60	Roche/LC480	151
	R: ATTTCAATGTGAGGCGGGTGGAAC			
Gapdh	F: GGAGCCAAAAGGGTCATCATCTC	60	Roche/LC480	234
	R: AGAGGGGCCATCCACAGTCTTCT			
Hprt	F: GCCTAAGATGAGCGCAAGTTG	60	Roche/LC480	101
	R: TACTAGGCAGATGGCCACAGG			
Rps16	F: AATGGGCTCATCAAGGTGAACGGA	60	Roche/LC480	185
	R: TTTGAGATGGACTGTCGGATGGCA			

Bet1l	F: ACCAGGCTTAAATCGCTGGCTTTG	60	Roche/LC480	186
	R: GACCACAGCCATACCACACAGAA			
Btg2	F: TGAGCGAGCAGAGACTCAAGGTTT	60	Roche/LC480	113
	R: ACAGCGATAGCCAGAACCTTTGGA			
Farp2	F: ATCCAAGCAGCCAAGACTATCGGT	60	Roche/LC480	241
	R: AAAGCTGGTTCTCAACAGCTGCAC			
Gstz1	F: TGGGACAGGAGAACCAGATGCAAT	60	Roche/LC480	132
	R: AGCACACATCAGCCATGGATACCT			
Pisd	F: AGGGAATGAGCTGTACCACTGTGT	60	Roche/LC480	310
	R: ATTGTAGGAGCCCTTGCTGTACCT			
Ptp4a3	F: GTTCAAAGACCCACACACGCACAA	60	Roche/LC480	147
	R: AGAAAGACAGCCGTGGGTACAGAT			
Prkag3	F: ATGCACTTCATGCAGGAACACACC	60	Roche/LC480	297
	R: AGGCTTGAAGCAGCCTTGTAGGTA			
Serinc3	F: TTTACCTCACGTGGTCAGCCATGA	60	Roche/LC480	104
	R: TGCAGGAGACACAGTTGGTGAAGT			
Slc9a9	F: AGGCAACGCCATACTGGAGAAGAT	60	Roche/LC480	166
	R: ACAGGAGATGGCTGTTCCCAAGAA			
Slc19a2	F: TCTCCTGATTGCTGCTGCAGTGTA	60	Roche/LC480	192
	R: AATGCCAGGGCAATGAAGGTGTTC			
Tbcel	F: TGTGCTCACGTGTCAGAACTCGAT	60	Roche/LC480	187
	R: TGTTGAGGACAAGTTTGCGAACCC			
Tetc3	F: GGCAGATCGAATATTGGCAGCAGT	60	Roche/LC480	196
	R: AGCAAACACCAAGGCCAATACCAC			
Jarid1c	F: AGATTCCCAATGTAGAACGGCGGA	60	Roche/LC480	168
	R: AGTGAGAGCGTAGCAAGGAACCAA			
Zfp622	F: AAGCTCTTCACAGATGGTGACGCT	60	Roche/LC480	124
	R: TCTTGTCTGTGGACAAGGCCTCAA			
Cnn3	F: TGCGCAACTGGATAGAAGAGGTGA	60	Roche/LC480	115
	R: ACAGAGCCTGGCTGTAGCTTGTTT			
Nucks1	F: AGAAGATGATGAGGCGCCATTCCA	60	Roche/LC480	187
	R: TGGCGTCACTGTTGCCTTTAGTCT			
Vim	F: AATCCTTCCCGCGATCCCTTCTTT	60	Roche/LC480	101
	R: ACGAGGACACAGACCTGGTAGACAT			
Gnao1	F: TGTGGTCTACAGCAACACCATCCA	60	Roche/LC480	124
	R: ACTCACCACGTCACACACCATCTT			
Ubc	F: AAAGATCCAGGACAAGGAGGGCAT	60	Roche/LC480	179

	R: TCTTGCCTGTCAGGGTCTTCACAA			
Aim1l	F: CGCCAAACCTGGAGCATCAATGAA	60	Roche/LC480	140
	R: TGGGAAAGTCTGTCCTTGGTTGGT			
Cxcl16	F: ACCCTTGTCTCTTGCGTTCTTCCT	60	Roche/LC480	147
	R: ATGTGATCCAAAGTACCCTGCGGT			
Gfap	F: TGGCCACCAGTAACATGCAAGAGA	60	Roche/LC480	121
	R: TAGTCGTTAGCTTCGTGCTTGGCT			

Supplemental References

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