Table S5. **Functional annotation of differentially expressed, repressed (S5A) and induced (S5B) genes of Rasless MEFs whose transcriptional pattern is reversed in both BRAF- and MEK1-rescued MEFs.**

The GeneCodis (Gene Annotation Co-occurrence Discovery) functional annotation tool (http://genecodis.dacya.ucm.es) was used to identify statistically significant functional associations linking particular gene subsets contained within the list of Rasless repressed (S5A) or induced (S5B) loci included in Table S4 (Additional file 4, FDR=0.01) to specific Biological Processes from the *Gene Ontology* (GO) database. The column labelled "*Functional category*" identifies the specific functional GO term recognized in each case for the corresponding groups of loci listed under the column labelled "Genes". GO terms descriptions falling under the same, high level, general functional categories (Cell Cycle, DNA and RNA processing, Metabolite processing, DNA damage response, etc) are depicted with distinct, common colors. The column labelled "*Number of Genes*" indicates the specific number of genes linked to the indicated functionality, out of the total number (in parenthesis) of genes recognized by GeneCodis in the list of repressed genes of Rasless cells. The column labeled "*Corrected p-value*" refers to the statistical significance of the functional associations identified, and contains p-values calculated cases using the Hypergeometric Distribution and subsequently corrected by implementing the False Discovery Rate method of Benjamini and Hochberg [113].

S5A. Functional annotation of repressed genes from Rasless MEFs that are induced in both BRAF- and MEK1-rescued MEFs

Functional Category	***Number of Genes***	***Corrected p-value***	***Genes repressed in Table S4***
CELL CYCLE (MITOTIC AND MEIOTIC DIVISION)			
GO:0007049: cell cycle	73(314)	2,20E-65	Ncaph, Timeless, Ercc6l, Mcm5, Cks1b, Plk1, Sass6, Aurkb, Kif11, Bub1, Ndc80, Aspm, Mad2l1, Cdc5l, Dscc1, Cit, Mcm4, Brca1, Mcm3, Rad21, Dlgap5, Sgol1, Ccdc99, Ncapd2, Ccnb2, Cdc25c, Casc5, Lig1, Ncapd3, Kntc1, Rbbp4, Gsg2, Ccng2, Nasp, Chek1, Pttg1, Usp3, Ccna2, Cdc7, Hmga2, Bub1b, Dbf4, Zwilch, Cdca3, Cdc20, Kif2c, Clspn, Cenpe, Tipin, Chtf18, Mcm7, Mastl, Cdkn2c, Prc1, Cdc6, Pkmyt1, Mcm2, Cep55, E2f7, Mcm6, C79407, Fancd2, Nek2, Cdca8, Incenp, Khdrbs1, Nup43, Rbl1, Terf1, Uhrf1, Cdt1, Cks2, Pogz
GO:0051301: cell division	48(314)	3,06E-45	Ncaph, Timeless, Ercc6l, Mcm5, Cks1b, Plk1, Aurkb, Kif11, Bub1, Ndc80, Aspm, Mad2l1, Cit, Rad21, Sgol1, Ccdc99, Ncapd2, Ccnb2, Cdc25c, Casc5, Lig1, Ncapd3, Kntc1, Ccng2, Pttg1, Ccna2, Cdc7, Hmga2, Bub1b, Zwilch, Cdca3, Cdc20, Kif2c, Cenpe, Tipin, Mastl, Prc1, Cdc6, Cep55, C79407, Nek2, Cdca8, Incenp, Nup43, Cdca7, Terf1, Cks2, Pogz
GO:0007067: mitosis	40(314)	4,62E-40	Ncaph, Timeless, Ercc6l, Plk1, Aurkb, Kif11, Bub1, Ndc80, Aspm, Mad2l1, Cit, Rad21, Sgol1, Ccdc99, Ncapd2, Ccnb2, Cdc25c, Casc5, Ncapd3, Kntc1, Ccng2, Pttg1, Ccna2, Hmga2, Bub1b, Zwilch, Cdca3, Cdc20, Kif2c, Cenpe, Tipin, Mastl, Cdc6, Cep55, C79407, Nek2, Cdca8, Incenp, Nup43, Terf1
GO:0007059: chromosome segregation	16(314)	7,11E-18	Srpk1, Bub1, Ndc80, Ctcf, Brca1, Rad21, Sgol1, Casc5, Espl1, Pttg1, Top2a, Kif2c, Cenpf, Nek2, Incenp, Nup43
GO:0033261: regulation of S phase	5(314)	4,65E-08	Timeless, Slbp, Chek1, Cdc7, Tipin
GO:0051726: regulation of cell cycle	10(314)	9,42E-08	Skp2, Ccnb2, Dtl, Zfp703, Ccng2, Ccna2, Mastl, Tacc3, Fignl1, Rbl1
GO:0007076: mitotic chromosome condensation	5(314)	8,05E-07	Ncaph, Ncapd2, Ncapd3, Ncapg, Akap8
GO:0008608: attachment of spindle microtubules to kinetochore	4(314)	3,05E-06	Ndc80, Sgol1, Casc5, Cenpe
GO:0000070: mitotic sister chromatid segregation	4(314)	1,29E-05	Mad2l1, Cit, Espl1, Nek2
GO:0000076: DNA replication checkpoint	3(314)	7,90E-05	Clspn, Tipin, Cdt1
GO:0000087: M phase of mitotic cell cycle	3(314)	7,90E-05	Dlgap5, Cdc25c, Cenpf
GO:0007131: reciprocal meiotic recombination	4(314)	0,000185328	Msh6, Trip13, Topbp1, Rad51
GO:0000086: G2/M transition of mitotic cell cycle	4(314)	0,000429187	Skp2, Cit, Chek1, Mastl
GO:0051298: centrosome duplication	3(314)	0,000481823	Sass6, Brca1, 6330503K22Rik
GO:0000132: establishment of mitotic	3(314)	0,000727738	Ndc80, Ccdc99, Cenpa

Functional Category	*Number of Genes*	*Corrected p-value*	*Genes repressed in Table S4*
spindle orientation			
GO:0007094: mitotic cell cycle spindle assembly checkpoint	3(314)	0,00105825	Mad2l1, Cenpe, Terf1
GO:0090007: regulation of mitotic anaphase	2(314)	0,00134703	Plk1, Cdc6
GO:0051984: positive regulation of chromosome segregation	2(314)	0,00134703	Cenpe, Cdc6
GO:0007093: mitotic cell cycle checkpoint	3(314)	0,0013998	Mad2l1, Kntc1, Zwilch
GO:0007126: meiosis	5(314)	0,00332418	Mki67, Exo1, Psmc3ip, Nek2, Rad51
GO:0071173: spindle assembly checkpoint	2(314)	0,00337246	Bub1, Casc5
GO:0000910: cytokinesis	4(314)	0,00337984	Aurkb, Cit, Prc1, Incenp
GO:0007127: meiosis I	2(314)	0,00552327	Espl1, Cks2
GO:0051983: regulation of chromosome segregation	2(314)	0,00552327	Bub1, Kif2c
GO:0007091: mitotic metaphase/anaphase transition	2(314)	0,00552327	Cit, Bub1b
GO:0045143: homologous chromosome segregation	2(314)	0,00552327	Espl1, Pttg1
GO:0000089: mitotic metaphase	2(314)	0,00797998	Ndc80, Cdca8
GO:0007099: centriole replication	2(314)	0,0105499	Sass6, 6330503K22Rik
GO:0010389: regulation of G2/M transition of mitotic cell cycle	2(314)	0,0137492	Ccnb2, Cenpf
GO:0007051: spindle organization	2(314)	0,0163194	Kif11, Pcnt
GO:0007090: regulation of S phase of mitotic cell cycle	2(314)	0,0163194	Dbf4, Cdt1
GO:0007052: mitotic spindle organization	2(314)	0,0163194	Ndc80, Stmn1
GO:0045070: positive regulation of viral genome replication	2(314)	0,0163194	Srpk1, Top2a
GO:0000079: regulation of cyclin-dependent protein kinase activity	3(314)	0,0173269	Ccnb2, Ccna2, Cdkn2c
GO:0000084: S phase of mitotic cell cycle	2(314)	0,0234741	Pold1, Ezh2
GO:0000278: mitotic cell cycle	2(314)	0,0278102	Usp3, Cenpf
GO:0071777: positive regulation of cell cycle cytokinesis	1(314)	0,038985	Cdc6
GO:0051310: metaphase plate congression	1(314)	0,038985	Cenpf
GO:0033314: mitotic cell cycle DNA replication checkpoint	1(314)	0,038985	Clspn
GO:0045870: positive regulation of retroviral genome replication	1(314)	0,038985	Top2a
GO:0033260: DNA replication involved in S phase	1(314)	0,038985	Slbp
GO:0045841: negative regulation of mitotic metaphase/anaphase transition	1(314)	0,038985	Mad2l1
GO:0045769: negative regulation of asymmetric cell division	1(314)	0,038985	Aspm
GO:0007063: regulation of sister chromatid cohesion	1(314)	0,038985	Bub1
GO:0007100: mitotic centrosome separation	1(314)	0,038985	Kif11
GO:0090307: spindle assembly involved in mitosis	1(314)	0,038985	Kif11
GO:0046601: positive regulation of centriole replication	1(314)	0,038985	Plk4
GO:0000082: G1/S transition of mitotic cell cycle	3(314)	0,0400578	Skp2, Iqgap3, Cdkn2c
GO:0045736: negative regulation of	2(314)	0,0494391	Plk1, Casp3

Functional Category	*Number of Genes*	*Corrected p-value*	*Genes repressed in Table S4*
cyclin-dependent protein kinase activity			
DNA AND RNA PROCESSING			
GO:0006260: DNA replication	32(314)	7,49E-35	Mcm5, Pole2, Rbbp7, Dscc1, Mcm4, Prim1, Sin3a, Brca1, Mcm3, Gins1, Dtl, Supt16h, Cdc25c, Lig1, Rbbp4, Nasp, Chek1, Cdc7, Rpa2, Tk1, Dbf4, Rfc5, Clspn, Chtf18, Mcm7, Cdc6, Mcm2, Ssrp1, Pold1, Mcm6, Rfc4, Cdt1
GO:0006355: regulation of transcription, DNA-dependent	54(314)	3,08E-14	Nono, Cdca7l, Timeless, Sirt1, Whsc1, Mybbp1a, Kat2a, Paxip1, Med13l, Zfp57, Dnmt1, Rbbp7, Cdc5l, Ctcf, Sin3a, Hnrnpd, Cand1, Asxl3, Ash2l, Trim28, Supt16h, Six4, Zfp217, Zfp703, Rbbp4, Ewsr1, Sf1, Asf1b, Asxl1, Hmga2, Tead2, Top2a, Patz1, Mlf1ip, Actl6a, Ilf3, Mycn, Ssrp1, E2f7, C79407, Etv4, Whsc2, Apex1, Khdrbs1, Cdca7, Ezh2, Tmpo, Rbl1, Terf1, Uhrf1, Tfam, Smarcc1, Hnrpdl, Pogz
GO:0008380: RNA splicing	22(314)	4,38E-14	Nono, Rbmxrt, Cpsf2, Prpf19, Hnrnpc, Srpk1, Cdc5l, Hnrnpu, Rnps1, Hnrnpd, Cstf2, Polr2b, Sf1, Sf3a1, Snw1, Hnrnpa2b1, Snrpg, Nudt21, Gemin8, Syncrip, Zrsr2, Zcchc8
GO:0006397: mRNA processing	21(314)	8,88E-13	Nono, Rbmxrt, Cpsf2, Prpf19, Cpsf6, Hnrnpc, Srpk1, Cdc5l, Hnrnpu, Rnps1, Cstf2, Sf1, Sf3a1, Slbp, Snw1, Hnrnpa2b1, Nudt21, Gemin8, Syncrip, Zrsr2, Zcchc8
GO:0006351: transcription, DNA-dependent	49(314)	1,73E-12	Nono, Cdca7l, Timeless, Sirt1, Whsc1, Mybbp1a, Kat2a, Paxip1, Med13l, Zfp57, Dnmt1, Rbbp7, Cdc5l, Ctcf, Prim1, Sin3a, Hnrnpd, Cand1, Asxl3, Ash2l, Trim28, Supt16h, Rbbp4, Polr2b, Ewsr1, Sf1, Hmgb1, Asf1b, Asxl1, Hmga2, Hmgb2, Tead2, Mlf1ip, Actl6a, Polr3b, Ilf3, Ssrp1, E2f7, Etv4, Whsc2, Apex1, Khdrbs1, Cdca7, Ezh2, Rbl1, Uhrf1, Tfam, Smarcc1, Hnrpdl
GO:0006310: DNA recombination	11(314)	7,33E-11	Nono, Paxip1, Brca1, Exo1, Psmc3ip, Lig1, Recql4, Rpa2, Rad51ap1, Apex1, Rad51
GO:0006270: DNA-dependent DNA replication initiation	6(314)	1,10E-08	Mcm5, Mcm4, Mcm3, Mcm7, Mcm2, Mcm6
GO:0045892: negative regulation of transcription, DNA-dependent	17(314)	2,47E-08	Timeless, Sirt1, Cbx5, Mybbp1a, Dnmt1, Ctcf, Sin3a, Brca1, Trim28, Zfp703, Cbx3, Snw1, Hmgb2, Cenpf, Patz1, Ilf3, Khdrbs1
GO:0006268: DNA unwinding involved in replication	5(314)	4,65E-08	Mcm4, Mcm7, Mcm2, Mcm6, Rad51
GO:0006164: purine nucleotide biosynthetic process	4(314)	0,000185328	Impdh2, Mthfd1, Adsl, Gmps
GO:0007004: telomere maintenance via telomerase	3(314)	0,0013998	Dkc1, Ptges3, Terf1
GO:0006261: DNA-dependent DNA replication	3(314)	0,00222991	Pole2, Top2a, Pold1
GO:0010216: maintenance of DNA methylation	2(314)	0,00337246	Dnmt1, Ctcf
GO:0006177: GMP biosynthetic process	2(314)	0,00337246	Impdh2, Gmps
GO:0006306: DNA methylation	3(314)	0,00453625	Dnmt1, Ctcf, Mbd4
GO:0009168: purine ribonucleoside monophosphate biosynthetic process	3(314)	0,00453625	Impdh2, Adsl, Gmps
GO:0050684: regulation of mRNA processing	2(314)	0,00552327	Srpk1, Safb
GO:0051571: positive regulation of histone H3-K4 methylation	2(314)	0,00552327	Paxip1, Dnmt1
GO:0000122: negative regulation of transcription from RNA polymerase II promoter	9(314)	0,00778043	Sirt1, Whsc1, Zfp57, Rbbp7, Sin3a, Trim28, Hmgb1, Hmga2, Rbl1
GO:0006398: histone mRNA 3'-end processing	2(314)	0,00797998	Cpsf2, Slbp
GO:0070934: CRD-mediated mRNA stabilization	2(314)	0,00797998	Hnrnpu, Syncrip
GO:0009048: dosage compensation, by inactivation of X chromosome	2(314)	0,00797998	Ctcf, Brca1
GO:0006396: RNA processing	4(314)	0,00946223	Dkc1, Exosc8, Larp7, Sf3a1
GO:0006266: DNA ligation	2(314)	0,0105499	Lig1, Top2a
GO:0006259: DNA metabolic process	3(314)	0,0106837	Pttg1, Top2a, Rad51
GO:0000398: nuclear mRNA splicing, via spliceosome	3(314)	0,0154716	Sf3a1, Snw1, Zrsr2
GO:0043488: regulation of mRNA	2(314)	0,0202844	Hnrnpd, Apex1

Functional Category	***Number of Genes***	***Corrected p-value***	***Genes repressed in Table S4***
stability			
GO:0045893: positive regulation of transcription, DNA-dependent	9(314)	0,0234362	Ctcf, Trim28, Six4, Ccna2, Hmgb2, Ilf3, Etv4, Tfam, Smarcc1
GO:0006349: regulation of gene expression by genetic imprinting	2(314)	0,0278102	Zfp57, Ctcf
GO:0016578: histone deubiquitination	2(314)	0,0308515	Kat2a, Usp3
GO:0016180: snRNA processing	2(314)	0,0308515	Ints5, Ints7
GO:0051106: positive regulation of DNA ligation	1(314)	0,038985	Rad51
GO:0006348: chromatin silencing at telomere	1(314)	0,038985	Hat1
GO:0009152: purine ribonucleotide biosynthetic process	1(314)	0,038985	Adsl
GO:0046104: thymidine metabolic process	1(314)	0,038985	Tk1
GO:0032075: positive regulation of nuclease activity	1(314)	0,038985	Hmgb2
GO:0000105: histidine biosynthetic process	1(314)	0,038985	Mthfd1
GO:0031060: regulation of histone methylation	1(314)	0,038985	Ctcf
GO:0000416: positive regulation of histone H3-K36 methylation	1(314)	0,038985	Paxip1
GO:0031937: positive regulation of chromatin silencing	1(314)	0,038985	Sirt1
GO:0006343: establishment of chromatin silencing	1(314)	0,038985	Sirt1
GO:0006378: mRNA polyadenylation	2(314)	0,0395876	Cpsf6, Nudt21
GO:0051568: histone H3-K4 methylation	2(314)	0,0395876	Paxip1, Ash2l
GO:0032259: methylation	5(314)	0,0397787	Whsc1, Dnmt1, Tyw3, Emg1, Ezh2
GO:0045944: positive regulation of transcription from RNA polymerase II promoter	10(314)	0,0401959	Psmc3ip, Six4, Hmgb1, Snw1, Hmgb2, Tead2, Top2a, Rbm14, Cenpk, Smarcc1
GO:0006364: rRNA processing	4(314)	0,0419854	Sirt1, Dkc1, Exosc8, Emg1
GO:0043388: positive regulation of DNA binding	2(314)	0,0447025	Hmgb1, Hmgb2
GO:0008156: negative regulation of DNA replication	2(314)	0,0491857	Hmgb1, Terf1
GO:0016575: histone deacetylation	2(314)	0,0494391	Sirt1, Rbm14
METABOLITE PROCESSING (PROTEIN, CARBOHYDRATE AND LIPID PROCESSING)			
GO:0006468: protein phosphorylation	22(314)	1,36E-07	Prkar2b, Plk4, Plk1, Aurkb, Srpk1, Bub1, Ptpre, Vrk3, Cit, Trim28, Gsg2, Chek1, Cdc7, Prkd1, Bub1b, Melk, Prkg2, Mastl, Ttk, Pkmyt1, Abl2, Nek2
GO:0016310: phosphorylation	21(314)	1,46E-05	Skp2, Plk4, Plk1, Srpk1, Bub1, Cit, Gsg2, Chek1, Cdc7, Bub1b, Tk1, Dbf4, Melk, Mastl, Cdkn2c, Ttk, Pkmyt1, Akap8, Abl2, Nek2, Cks2
GO:0009060: aerobic respiration	2(314)	0,0105499	Fxn, Adsl
GO:0046855: inositol phosphate dephosphorylation	2(314)	0,0105499	Synj2, Impa1
GO:0042325: regulation of phosphorylation	3(314)	0,0131104	Prkar2b, Cd24a, Mcm7
GO:0006020: inositol metabolic process	2(314)	0,0137492	Slc5a3, Impa1
GO:0051353: positive regulation of oxidoreductase activity	2(314)	0,0163194	Fxn, Abl2
GO:0010722: regulation of ferrochelatase activity	1(314)	0,038985	Fxn
GO:0016567: protein ubiquitination	5(314)	0,0406218	Rfwd3, Plk1, Prpf19, Brca1, Cand1
GO:0000209: protein polyubiquitination	3(314)	0,0446759	Skp2, Prpf19, Dtl
DNA DAMAGE RESPONSE			
GO:0006974: response to DNA damage stimulus	36(314)	4,90E-29	Nono, Timeless, Sirt1, Rfwd3, Prpf19, Paxip1, Msh6, Casp3, Brca1, Rad21, Usp1, Ash2l, Exo1, Dtl, Supt16h, Lig1, Rad54l, Chek1, Pttg1, Usp3, Top2a,

Functional Category	*Number of Genes*	*Corrected p-value*	*Genes repressed in Table S4*
			Rpa2, Mbd4, Clspn, Tipin, Apitd1, Mcm7, Topbp1, Rad51ap1, Ssrp1, Fancd2, Alkbh1, Gen1, Apex1, Rad51, Uhrf1
GO:0006281: DNA repair	29(314)	9,92E-23	Nono, Rfwd3, Prpf19, Paxip1, Msh6, Brca1, Rad21, Usp1, Exo1, Supt16h, Lig1, Rad54l, Chek1, Pttg1, Usp3, Rpa2, Mbd4, Clspn, Kif22, Apitd1, Topbp1, Rad51ap1, Ssrp1, Fancd2, Alkbh1, Gen1, Apex1, Rad51, Uhrf1
GO:0006297: nucleotide-excision repair, DNA gap filling	6(314)	3,96E-07	Pole2, Lig1, Rpa2, Rfc5, Pold1, Rfc4
GO:0031572: G2/M transition DNA damage checkpoint	5(314)	4,65E-06	Plk1, Brca1, Dtl, Chek1, Clspn
GO:0010212: response to ionizing radiation	5(314)	0,000163094	Rfwd3, Paxip1, Brca1, Rad54l, Topbp1
GO:0009411: response to UV	5(314)	0,000232741	Msh6, Casp3, Usp1, Dtl, Tipin
GO:0050918: positive chemotaxis	4(314)	0,000429187	Scrib, Hmgb2, Fgf7, Alkbh1
GO:0006288: base-excision repair, DNA ligation	2(314)	0,00134703	Hmgb1, Hmgb2
GO:0045739: positive regulation of DNA repair	3(314)	0,00915821	Sirt1, Brca1, Apex1
GO:0000724: double-strand break repair via homologous recombination	3(314)	0,0141938	Brca1, Rad54l, Rad51
GO:0043627: response to estrogen stimulus	3(314)	0,0222209	Brca1, Ash2l, Cd24a
GO:0070301: cellular response to hydrogen peroxide	2(314)	0,0234741	Fxn, Apex1
GO:0006298: mismatch repair	2(314)	0,0308515	Msh6, Exo1
GO:0048545: response to steroid hormone stimulus	2(314)	0,0308515	Hmgb2, Spp1
GO:0006302: double-strand break repair	3(314)	0,0322914	Brca1, Trip13, Rad54l
GO:0042060: wound healing	3(314)	0,0370525	Scrib, Vangl2, Fgf7
GO:0050831: male-specific defense response to bacterium	1(314)	0,038985	Hmgb1
GO:0006282: regulation of DNA repair	1(314)	0,038985	Usp1
GO:0070370: cellular heat acclimation	1(314)	0,038985	Rbbp7
GO:0000077: DNA damage checkpoint	2(314)	0,0441243	Chek1, Tipin
CYTOSKELETON-REGULATED PROCESSES			
GO:0016568: chromatin modification	15(314)	4,81E-08	Whsc1, Dnmt1, Rbbp7, Ctcf, Ash2l, Rbbp4, Gsg2, Asf1b, Asxl1, Usp3, Hat1, Actl6a, Ezh2, Rbl1, Smarcc1
GO:0030261: chromosome condensation	4(314)	0,000230568	Ncaph, Ncapd2, Ncapd3, Top2a
GO:0007018: microtubule-based movement	6(314)	0,000627124	Kif4, Kif11, Kif20a, Kif2c, Cenpe, Kif22
GO:0006334: nucleosome assembly	5(314)	0,00140607	H2afv, Asf1b, Cenpa, Mcm2, H2afz
GO:0051382: kinetochore assembly	2(314)	0,00337246	Cenpa, Pogz
GO:0006999: nuclear pore organization	2(314)	0,00337246	Pom121, Nup133
GO:0006338: chromatin remodeling	4(314)	0,00475204	Rbbp7, Rbbp4, Actl6a, Smarcc1
GO:0051262: protein tetramerization	3(314)	0,00784636	Cpsf6, Adsl, Nudt21
GO:0051276: chromosome organization	3(314)	0,00806018	Rad54l, Pttg1, Cdca8
GO:0007019: microtubule depolymerization	2(314)	0,0105499	Kif2c, Stmn1
GO:0031532: actin cytoskeleton reorganization	3(314)	0,0131104	Hmgb1, Fgf7, Eps8
GO:0000245: spliceosome assembly	2(314)	0,0202844	Prpf19, Zrsr2
GO:0033108: mitochondrial respiratory chain complex assembly	1(314)	0,038985	Tfam
GO:0043486: histone exchange	1(314)	0,038985	Nasp
GO:0030866: cortical actin cytoskeleton organization	2(314)	0,0395876	Llgl1, Arf6
CELL PROLIFERATION AND GROWTH			

Functional Category	*Number of Genes*	*Corrected p-value*	*Genes repressed in Table S4*
GO:0008283: cell proliferation	9(314)	0,000185875	Prkar2b, Kat2a, Mki67, Scrib, Nasp, Ptges3, Mcm7, Tacc3, Uhrf1
GO:0008284: positive regulation of cell proliferation	11(314)	0,00202872	Cdca7l, Fxn, Ash2l, Zfp703, Recql4, Hmgb1, Cdc7, Fgf7, Cdc20, Tipin, Mycn
GO:0033601: positive regulation of mammary gland epithelial cell proliferation	2(314)	0,00797998	Iqgap3, Zfp703
GO:0001833: inner cell mass cell proliferation	2(314)	0,0308515	Prpf19, Gins1
GO:0030889: negative regulation of B cell proliferation	2(314)	0,0308515	Casp3, Cd24a
GO:0046014: negative regulation of T cell homeostatic proliferation	1(314)	0,038985	Cd24a
GO:0042103: positive regulation of T cell homeostatic proliferation	1(314)	0,038985	Cd24a
TRANSPORT (METABOLITES, IONS AND VESICLES)			
GO:0051028: mRNA transport	6(314)	0,000376719	Nup54, Pom121, Nup107, Slbp, Nup133, Nup43
GO:0048488: synaptic vesicle endocytosis	2(314)	0,0234741	Scrib, Cd24a
GO:0032597: B cell receptor transport into membrane raft	1(314)	0,038985	Cd24a
GO:0032600: chemokine receptor transport out of membrane raft	1(314)	0,038985	Cd24a
GO:0046831: regulation of RNA export from nucleus	1(314)	0,038985	Khdrbs1
GO:0015031: protein transport	10(314)	0,0447186	Nup54, Pom121, Kif20a, Nasp, Nup107, Kpnb1, Cenpf, Nup133, Nup43, Arf6
DEVELOPMENTAL PROCESS			
GO:0001843: neural tube closure	5(314)	0,00195095	Kat2a, Scrib, Vangl2, Tead2, Stil
GO:0003149: membranous septum morphogenesis	2(314)	0,00797998	Whsc1, Vangl2
GO:0045665: negative regulation of neuron differentiation	4(314)	0,00995345	Prpf19, Aspm, Cit, Cd24a
GO:0048538: thymus development	3(314)	0,0131104	Ccnb2, Six4, Bcl2l11
GO:0007399: nervous system development	8(314)	0,015502	Kat2a, Nrp1, Cit, Hmgb1, Hmgb2, Actl6a, Stmn1, Smarcc1
GO:0016446: somatic hypermutation of immunoglobulin genes	2(314)	0,0163194	Msh6, Exo1
GO:0048699: generation of neurons	2(314)	0,0163194	Cit, Six4
GO:0001701: in utero embryonic development	7(314)	0,0228412	Kat2a, Sin3a, Ccnb2, Pcnt, Alkbh1, Stil, Bcl2l11
GO:0048339: paraxial mesoderm development	2(314)	0,0234741	Tead2, Nup133
GO:0030903: notochord development	2(314)	0,0234741	Tead2, Stil
GO:0007275: multicellular organismal development	16(314)	0,027824	Timeless, Sirt1, Spred2, Zfp57, Nrp1, Cit, Six4, Scrib, Vangl2, Plxnb1, Cenpe, H2afz, Stmn1, Fancd2, Stil, Uhrf1
GO:0008584: male gonad development	3(314)	0,0325403	Hmgb2, Patz1, Bcl2l11
GO:0060998: regulation of dendritic spine development	1(314)	0,038985	Arf6
GO:0051154: negative regulation of striated muscle cell differentiation	1(314)	0,038985	Ezh2
GO:0045605: negative regulation of epidermal cell differentiation	1(314)	0,038985	Ezh2
GO:0035148: tube formation	1(314)	0,038985	Bcl2l11
GO:0003402: planar cell polarity pathway involved in axis elongation	1(314)	0,038985	Vangl2
GO:0060420: regulation of heart growth	1(314)	0,038985	Dusp6
GO:0060717: chorion development	1(314)	0,038985	Paxip1
GO:0003290: atrial septum secundum morphogenesis	1(314)	0,038985	Whsc1
GO:0003289: atrial septum primum	1(314)	0,038985	Whsc1

Functional Category	*Number of Genes*	*Corrected p-value*	*Genes repressed in Table S4*
morphogenesis			
GO:0030324: lung development	4(314)	0,039477	Timeless, Hmgb1, Fgf7, Mycn
CELL DEATH			
GO:0008630: DNA damage response, signal transduction resulting in induction of apoptosis	3(314)	0,00383482	Msh6, Brca1, Mbd4
GO:0006915: apoptosis	13(314)	0,00780888	Sirt1, Bub1, Casp3, Tmem173, Ect2, Rad21, Gramd4, Casp2, Pcnt, Bub1b, Bcl2l11, Arf6, 1810011O10Rik
GO:0008624: induction of apoptosis by extracellular signals	5(314)	0,00971646	Casp3, Ect2, Casp2, Cd24a, Bcl2l11
GO:0043065: positive regulation of apoptosis	7(314)	0,0152979	Casp3, Casp2, Scrib, Dusp6, Hmgb1, Top2a, Bcl2l11
GO:0043525: positive regulation of neuron apoptosis	3(314)	0,0280321	Casp3, Casp2, Bcl2l11
GO:0010942: positive regulation of cell death	2(314)	0,0447025	Hmgb1, Mycn
GO:0043066: negative regulation of apoptosis	7(314)	0,0449741	Mad2l1, Fxn, Casp3, Sin3a, Casp2, Stil, Fignl1
SIGNALING			
GO:0070373: negative regulation of ERK1 and ERK2 cascade	2(314)	0,0395876	Vrk3, Dusp6
GO:0000188: inactivation of MAPK activity	2(314)	0,0447025	Spred2, Dusp6
OTHER			
GO:0034501: protein localization to kinetochore	3(314)	0,000309679	Aurkb, Ccdc99, Bub1b
GO:0043029: T cell homeostasis	3(314)	0,00577017	Casp3, Ccnb2, Bcl2l11
GO:0071168: protein localization to chromatin	2(314)	0,00337246	Plk1, Rad21
GO:0045190: isotype switching	2(314)	0,0308515	Msh6, Exo1
GO:0045830: positive regulation of isotype switching	1(314)	0,038985	Paxip1
GO:0001309: age-dependent telomere shortening	1(314)	0,038985	Terf1
GO:0032913: negative regulation of transforming growth factor-beta3 production	1(314)	0,038985	Cd24a
GO:0034107: negative regulation of erythrocyte clearance	1(314)	0,038985	Cd24a
GO:0034119: negative regulation of erythrocyte aggregation	1(314)	0,038985	Cd24a
GO:2000145: regulation of cell motility	1(314)	0,038985	Brca1
GO:0033003: regulation of mast cell activation	1(314)	0,038985	Ptpre
GO:0035090: maintenance of apical/basal cell polarity	1(314)	0,038985	Llgl1
GO:0001782: B cell homeostasis	2(314)	0,0441243	Casp3, Bcl2l11

S5B. Functional annotation of induced genes from Rasless MEFs that are repressed in both BRAF- and MEK1-rescued MEFs

Functional Category	*Number of Genes*	*Corrected p-value*	*Genes upregulated in Table S4*
TRANSPORT (METABOLITES, IONS AND VESICLES)			
GO:0006810: transport	17(86)	4,83E-05	Slc6a6, Tmco3, Slc31a2, Stx8, Ap3m2, Kpna1, Slc9a6, Exoc3, Dynlt3, Rab2b, Slc26a11, Slco3a1, Rab7l1, Slc1a4, Vamp3, Atp6v0a1, Vps29
GO:0016192: vesicle-mediated transport	5(86)	0,00443869	Stx8, Ap3m2, Rab2b, Vamp3, Stx7
GO:0015031: protein transport	7(86)	0,00900847	Ap3m2, Kpna1, Exoc3, Rab2b, Rab7l1, Vamp3, Vps29
GO:0006906: vesicle fusion	2(86)	0,0136743	Stx8, Stx7
GO:0006896: Golgi to vacuole transport	1(86)	0,0202459	Vps29
GO:0034589: hydroxyproline transport	1(86)	0,0202459	Slc1a4
GO:0015826: threonine transport	1(86)	0,0202459	Slc1a4
GO:0001762: beta-alanine transport	1(86)	0,0202459	Slc6a6
GO:0015734: taurine transport	1(86)	0,0202459	Slc6a6
GO:0008333: endosome to lysosome transport	2(86)	0,0309299	Stx8, Stx7
GO:0015811: L-cystine transport	1(86)	0,0312005	Slc1a4
GO:0006811: ion transport	6(86)	0,0346205	Tmco3, Slc31a2, Slc9a6, Slc26a11, Slco3a1, Atp6v0a1
GO:0015732: prostaglandin transport	1(86)	0,0355682	Slco3a1
GO:0015825: L-serine transport	1(86)	0,0355682	Slc1a4
GO:0006886: intracellular protein transport	3(86)	0,0360536	Ap3m2, Kpna1, Stx7
GO:0003333: amino acid transmembrane transport	2(86)	0,0365263	Slc6a6, Slc1a4
GO:0006865: amino acid transport	2(86)	0,0368832	Slc6a6, Slc1a4
GO:0015808: L-alanine transport	1(86)	0,0403518	Slc1a4
GO:0035524: proline transmembrane transport	1(86)	0,0453434	Slc1a4
GO:0035434: copper ion transmembrane transport	1(86)	0,0453434	Slc31a2
GO:0015824: proline transport	1(86)	0,0486711	Slc1a4
METABOLITE PROCESSING (PROTEIN, CARBOHYDRATE AND LIPID PROCESSING)			
GO:0006657: CDP-choline pathway	2(86)	0,00377501	Pcyt1a, Chpt1
GO:0008654: phospholipid biosynthetic process	3(86)	0,0110616	Pcyt1a, Abhd5, Chpt1
GO:0006656: phosphatidylcholine biosynthetic process	2(86)	0,012102	Pcyt1a, Chpt1
GO:0043438: acetoacetic acid metabolic process	1(86)	0,0202459	Tyrp1
GO:0070178: D-serine metabolic process	1(86)	0,0202459	Srr
GO:0070179: D-serine biosynthetic process	1(86)	0,0202459	Srr
GO:0009069: serine family amino acid metabolic process	1(86)	0,0202459	Srr
GO:0006583: melanin biosynthetic process from tyrosine	1(86)	0,0312005	Tyrp1
GO:0015939: pantothenate metabolic process	1(86)	0,0312005	Vnn1
GO:0045964: positive regulation of dopamine metabolic process	1(86)	0,0312005	Maob
GO:0001933: negative regulation of protein phosphorylation	2(86)	0,0327589	Prnp, Impact

Functional Category	*Number of Genes*	*Corrected p-value*	*Genes upregulated in Table S4*
GO:0006695: cholesterol biosynthetic process	2(86)	0,0329598	Insig2, Cyb5r3
GO:0016126: sterol biosynthetic process	2(86)	0,0329598	Insig2, Cyb5r3
GO:0006663: platelet activating factor biosynthetic process	1(86)	0,0355682	Chpt1
GO:0046068: cGMP metabolic process	1(86)	0,0355682	Rora
GO:0006582: melanin metabolic process	1(86)	0,0355682	Tyrp1
GO:0051084: 'de novo' posttranslational protein folding	1(86)	0,0355682	Entpd5
GO:0010894: negative regulation of steroid biosynthetic process	1(86)	0,0403518	Insig2
GO:0071569: protein ufmylation	1(86)	0,0403518	Ufm1
GO:0006563: L-serine metabolic process	1(86)	0,0453434	Srr
GO:0042866: pyruvate biosynthetic process	1(86)	0,0453434	Srr
GO:0006654: phosphatidic acid biosynthetic process	1(86)	0,0486711	Abhd5
GO:0050435: beta-amyloid metabolic process	1(86)	0,0486711	Bace1
GO:0010898: positive regulation of triglyceride catabolic process	1(86)	0,0486711	Abhd5
CELL DEATH			
GO:0006916: anti-apoptosis	4(86)	0,0130928	Birc7, Prnp, Vnn1, Tsc22d3
GO:0048102: autophagic cell death	1(86)	0,0403518	Acp2
CYTOSKELETON-REGULATED PROCESSES			
GO:0016584: nucleosome positioning	1(86)	0,0486711	Hist1h1e
GO:0045103: intermediate filament-based process	1(86)	0,0355682	Sync
DEVELOPMENTAL PROCESS			
GO:0060668: regulation of branching involved in salivary gland morphogenesis by extracellular matrix-epithelial cell signaling	1(86)	0,0202459	Ntn4
GO:0010842: retina layer formation	1(86)	0,0355682	Ptprm
GO:0048642: negative regulation of skeletal muscle tissue development	1(86)	0,0355682	Tsc22d3
GO:0060363: cranial suture morphogenesis	1(86)	0,0453434	Insig2
GO:0035117: embryonic arm morphogenesis	1(86)	0,0453434	Wnt9a
SIGNALING			
GO:0070885: negative regulation of calcineurin-NFAT signaling pathway	1(86)	0,0202459	Prnp
GO:0014066: regulation of phosphatidylinositol 3-kinase cascade	1(86)	0,0312005	Entpd5
GO:0007264: small GTPase mediated signal transduction	4(86)	0,033574	Rasl12, Rab2b, Rab7l1, Rit1
GO:0014063: negative regulation of serotonin secretion	1(86)	0,0355682	Maob
GO:0001921: positive regulation of	1(86)	0,0486711	Vamp3

Functional Category	*Number of Genes*	*Corrected p-value*	*Genes upregulated in Table S4*
receptor recycling			
CELL PROLIFERATION AND GROWTH			
GO:0046007: negative regulation of activated T cell proliferation	1(86)	0,0403518	Prnp
OTHER			
GO:0002544: chronic inflammatory response	1(86)	0,0202459	Vnn1
GO:0009628: response to abiotic stimulus	1(86)	0,0202459	Pcyt1a
GO:0030967: ER-nuclear sterol response pathway	1(86)	0,0312005	Insig2
GO:0006991: response to sterol depletion	1(86)	0,0312005	Insig2
GO:0043030: regulation of macrophage activation	1(86)	0,0403518	Rora
GO:0010891: negative regulation of sequestering of triglyceride	1(86)	0,0403518	Abhd5
GO:0002526: acute inflammatory response	1(86)	0,0486711	Vnn1