

Supporting Documents:

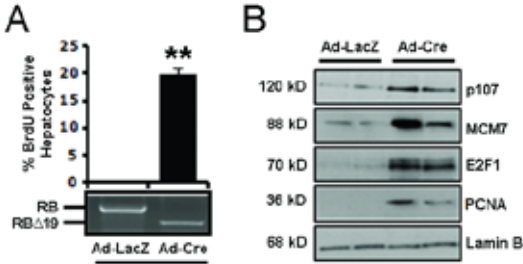
Supplemental Figure Legends.

Supplemental Figure 1. RB deletion modulates proliferation in the liver. (A) Percent BrdU incorporation in livers corresponding to individual genotypes, as indicated by PCR for presence of *RB exon 19*. **(B)** Protein lysates from multiple livers of each treatment, immunoblotted for indicated proteins.

Supplemental Figure 2. Additional enriched molecular networks associated with the liver-specific RB-loss gene signature. (A) Molecular networks of upregulated genes most significantly affected by loss of RB as indicated by IPA. Indicated functional associations included “DNA Replication, Recombination, and Repair, Cell Cycle, Cellular Assembly and Organization” (Left) and “Cell Cycle, Cellular Assembly and Organization, Cellular Function and Maintenance” (Right). **(B)** Molecular networks of downregulated genes most significantly affected by loss of RB as indicated by IPA. Indicated functional associations included “Cellular Development, Hematological System Development and Function, Hematopoiesis” (Left) and “Hematological System Development and Function, Tissue Morphology, Cell-To-Cell Signaling and Interaction” (Right).

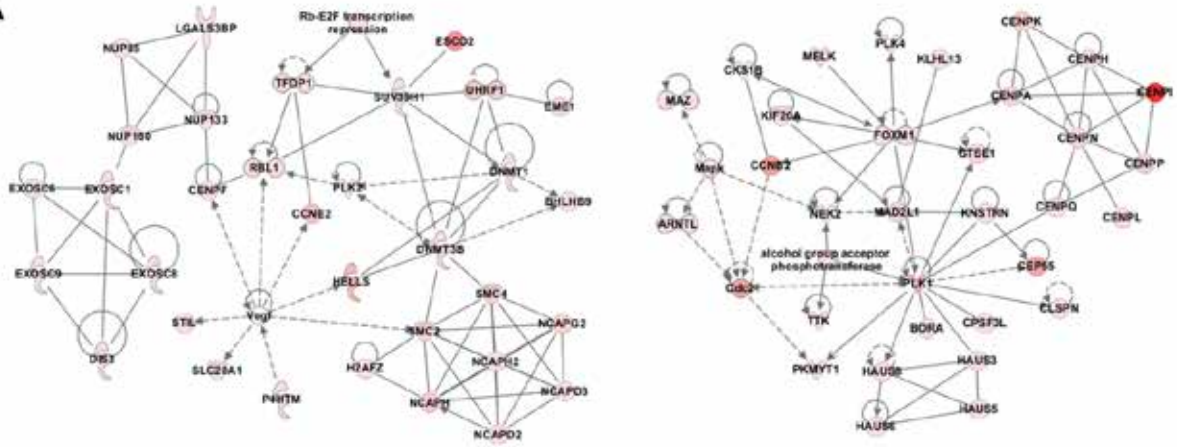
Supplemental Figure 3. RB loss results in differential expression of both NF- κ B and IFN target genes. (A) Graphical representation of differentially expressed NF κ B transcriptional targets in RB-flox mice infected with Ad-Cre as compared to Ad-LacZ. The list of NF κ B targets was compiled from DAVID. **(B)** Graphical representation of type 1 and type 2 IFN mediated genes with altered expression in RB-flox mice infected with Ad-Cre as compared to Ad-LacZ as determined by query of the INTERFEROME database.

Supplemental Figure 1.

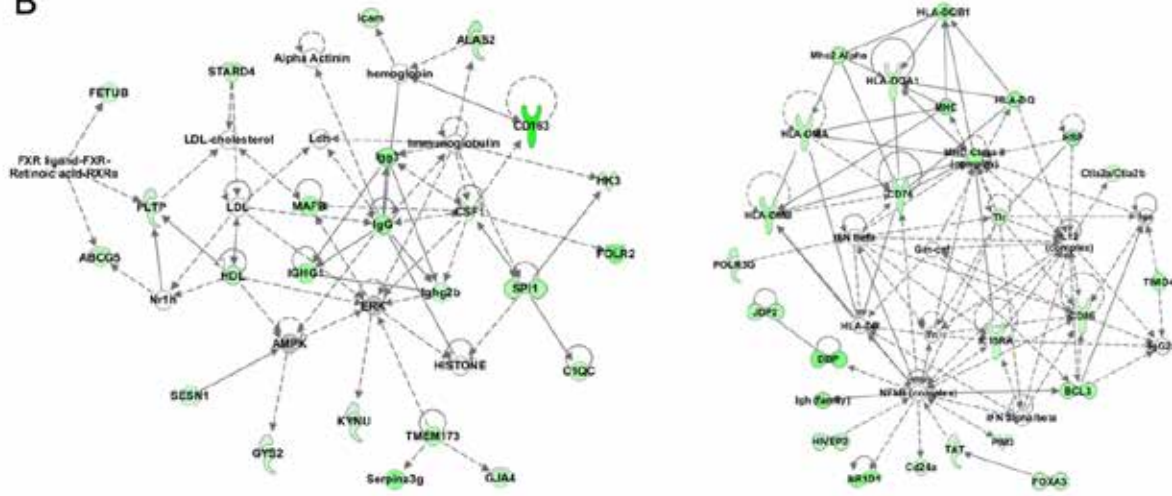


Supplemental Figure 2.

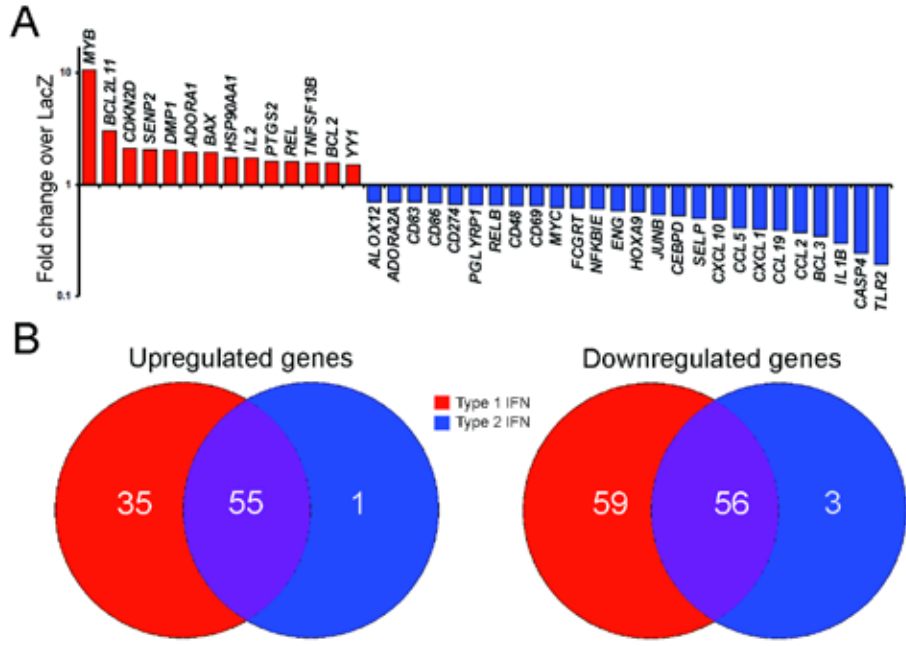
A



B



Supplemental Figure 3.



Supplemental Table 1. The liver-specific RB-loss gene signature.

Increased Expression RB-flox +Ad-Cre	Decreased Expression RB-flox +Ad-Cre
MTHFD2	SLC25A34
CDC20	TRAPPC9
NUSAP1	COL27A1
KIF22	NGEF
PBK	MAN1C1
SGOL1	MUSTN1
ALDH1L2	B3GNT9
ANKLE1	IER2
CCNE1	MYO1D
FTSJ3	CLCN2
BIRC5	SLC25A33
CCNB1	DOCK9
PRC1	DNAJC12
CKAP2	SCRN2
NCAPD2	S100A4
CDCA8	HS3ST3A1
CCNA2	SLC38A1
FAM81A	TGFB11
TPX2	EBI3
GPX7	SORBS3
INCENP	DENND1C
DUT	CORO2B
LMNB1	ERRF1
PTTG1	GBA2
FANCB	FICD
CDKN1A	DEDD2
PSRC1	ZYX
DDIT4L	TMED8
DNMT1	RFTN1
HAPLN1	MPP4
SHCBP1	FES
PLK1	CHST2
DEFB1	PF4
PTGR1	CD300LG
SYCE2	SOX6
RRM1	SLC12A9
NIPA1	FAM46C
BUB1	ARL4C
RDBP	RASSF6
ESPL1	SELPLG
CENPI	TENC1
CENPN	TNFRSF21
TRIM59	GBP2
CCNF	SERPINE2

COBL	TPPP
LIG1	UPK3B
EZH2	MVP
CHAF1B	PTPLAD2
TMEM9	EVI2A
KNTC1	CYTIP
TTC39A	EPS15L1
CCDC120	RHBDL1
RAD51C	ANGEL1
USP43	LRRC8C
HSD3B1	COL6A1
LSM2	ADCY4
IQGAP3	ELMO3
PPL	ABCA7
MXD3	ACVRL1
COX6B2	CYP26A1
CTPS	ABLIM3
PDXP	WVOX
HN1	HMHA1
CCNB2	IL18BP
CDCA3	MRPL38
GINS2	TMCO4
SLBP	FOXC2
CEP55	NFKBIA
PLEK2	METTL8
NENF	SOX7
TACC3	GBP1
MCM7	VAT1
DLGAP5	LHCGR
PPM1M	DCUN1D4
LRFN3	FRMD6
SMC2	SLC22A3
HAT1	PRELP
NUP133	LY9
CHCHD6	FOS
SPC25	NOTUM
CENPL	SLC1A2
MAST2	ARAP1
CENPK	ACSS2
NFKBIL2	DLGAP4
CPSF3L	TRPM2
NQO1	ADAMTS10
CENPM	PCSK4
TOP2A	PDE1B
RNF144A	CCT6B
UBE2T	PTGS1
RFC1	SHB
GDF15	IRX3

ASF1B	RUFY2
MLKL	FAM102A
REEP5	AVIL
SGOL2	AP4S1
CCHCR1	CALCOCO1
HAUS8	PKNOX2
MAD2L2	ARHGEF10L
SF3A3	HCN3
TTK	TMEM119
PMCH	CD300A
CDCA2	MFSD2
DNA2	CD7
RPA2	HSD3B2
ECT2	KRT10
CKAP2L	ID1
TCF19	TAL1
RACGAP1	SH3YL1
MLF1IP	CDC42EP2
NUF2	ZKSCAN5
MESP2	AKAP8L
OIP5	SLC24A6
ANLN	SLC35D3
MYB	RNF34
RRM2	CD38
MYH7B	SETD4
VNN1	ATRNL1
S100G	LCP2
EME1	KLF9
MELK	STX6
DEPDC1B	ASNS
CDCA5	GPR18
KIF20A	SLC25A29
DBF4	RCL1
SIVA1	AKT2
ESCO2	POLG2
NUP85	TIPARP
PRIM1	SELM
NUP93	ZPBP2
CENPE	PREX1
CCDC34	PTPRC
GTSE1	PLBD2
MORC4	SCARA3
UHMK1	EFCAB4A
CHTF18	TNKS1BP1
MGST2	NFKBIE
TUBB6	CCPG1
AURKA	F13A1
ALS2CR4	ELK3

COL12A1	PEX12
NSMCE1	CD69
FEN1	CALML4
PDK3	CHD6
WDHD1	SPRY4
HEY2	HOXA9
NANS	ENG
CCNE2	OSGIN1
ZCCHC3	TNFAIP8L2
G2E3	SLC2A8
TUBGCP2	SLC41A1
AQP8	FBXO36
ORC6L	CD37
BRCA2	TNFRSF1B
ATPIF1	NEB
CDKN2C	PIM2
APITD1	JUNB
CRIP2	TMC4
POLA1	CEBPD
TAF1D	SLC25A35
IPO9	MCOLN1
CDA	ANK3
REM2	CLDN14
IFI44	TSPYL5
GPC1	VAMP4
ADAT2	POLI
WDR77	ANGPTL6
FBXO5	C1QA
PKMYT1	BCL2L15
DHRS13	AGPAT4
ARSG	ZDHHC14
NCAPH	CXCL1
WFDC12	GABRR2
RAD51L1	NPFF
WBP5	GRIK5
ATAD2	F3
DSN1	AMOTL2
LGALS1	CLEC1B
TRAIP	CLN3
ARHGAP11A	EGR1
UMPS	NTRK2
NUP210	RAPGEF3
EXOSC8	NKG7
NDC80	SLC11A1
RUNDC3B	S100A8
PBX3	ADM
RFC5	TIE1
CDCA7L	MVD

ACPL2	GPR110
AURKB	TLR7
TMPO	PRKCB
PRELID2	MEGF8
CYP17A1	CD44
OTUD1	ID3
FANCD2	CASP1
TRIP13	ELAC1
RANBP1	MARCO
TFDP1	DHRS1
ZDHHC18	DHX8
AS3MT	BANK1
MFGE8	LAMA2
ZWILCH	GNE
CAMK2N2	THBD
WDR76	AGXT2L1
NCAPG2	ZMYM5
POLE2	PFDN2
PKHD1	OSMR
MRE11A	KLHL35
KIF20B	HCK
PCGF2	ARRDC4
TFAM	KIF21B
HSPA14	HLCS
RBBP8	TSHZ3
VPS36	TSPAN13
MTMR11	MBLAC2
CSTF2	SPATA2L
PMF1	TMEM140
DCK	PYROXD2
LBR	DACH2
TMEM48	LILRB3
MCM3	CCL24
PARP2	TSHZ2
FLRT1	OAF
BIK	CD53
PPM1G	RCSD1
SMC4	HSPA2
MSH6	LDB2
CDT1	DNAJB14
PSIP1	TPD52L1
NAP1L1	CNN2
MTNR1A	NAT1
CDKN1C	CPNE8
UBE2CBP	SIK1
RFC4	RAMP2
DONSON	TNRC6B
CDC45L	ENPP1

CBX6	PAMR1
LYAR	LSS
COL1A1	ANTXR1
DDX39	TMEM106A
RAD54L	AKAP12
POLD1	SGCD
CENPH	CD3E
RGS12	TBX2
NEK2	EMR1
PQLC3	TRPC4AP
BAX	TPO
FXN	ARAP3
HMMR	HABP4
POLD3	TPM2
MAGOHB	CYP4B1
TMEM139	BCCIP
AGA	DOCK6
LYSMD2	BIRC3
MCM2	PDE7B
PPP4R1	PMAIP1
CARHSP1	SYDE1
GYPC	NTN1
CCDC11	NLRP3
PFDN4	TNIP1
LARP7	ENTPD2
PCK2	LECT2
MYEF2	MORN1
NOTCH1	SLC6A16
UNC119	TEF
CENPA	MAFF
CDC42BPA	PPP1R9A
RCN2	DNAJB2
BUB1B	TGFB1
PLK4	MEIG1
SLC25A31	SOAT1
BBS12	RAB20
SAMD10	RGL1
TCIRG1	TCP11L2
NUP205	ANKRD12
SERPINB8	ABI3
TOMM22	CYP2S1
FAM83D	ID2
CDCA7	CCL5
BCL7C	VEGFA
MCM4	FADS2
TSGA14	TAF9B
PALB2	FAM26F
MAD2L1	ABCC1

FAM89A	LRRC16A
PDE7A	NCALD
ARNTL	GIMAP6
SASS6	AFAP1L1
P4HTM	NFKB2
NUDT5	FERMT3
CLOCK	SMAD7
ACTL6A	LPIN2
GPR172B	TCHH
SNRPD3	ERI3
GSG2	ALAS1
CYTSB	RGS10
FAM101B	SBSN
SKP2	IL10RA
PPIL1	CDKN2B
CYP39A1	DSE
CAND2	LRRC33
TSSC4	COL5A1
SAE1	OSGEP
IDH2	DPYS
PARP1	PDILT
DDIT4	MYO7A
RHBDF1	TIFA
HELLS	KCNH8
TRIM68	SUSD4
YPEL1	ZFP36
CCDC99	GRASP
E2F2	CRIP1
ERMP1	CSF1R
PAFAH1B3	THYN1
TMEM43	ROPN1L
CCDC67	GRAP
E2F8	SRD5A1
RFC2	PIK3R6
IFT80	POR
MAEL	TNFAIP8
WDR67	IFITM1
BRIP1	ABCC9
PRUNE	SPRN
SNRPD1	SDS
CENPJ	KCTD11
CENPF	LAPTM5
MCM5	PFKFB3
TFRC	AXL
CDC25A	GNAT1
TMPRSS4	GALNT14
APRT	CADM4
ADCY6	ABCG8

MDC1	NFKBID
NUP155	DNAJB5
CAV2	TGFB3
ARC	FHL2
HIST2H2BE	GEM
STEAP2	TINAGL1
NAP1L3	BMX
RPS6KA1	PPAPDC3
FAM118B	RABIF
PTPN21	SOD3
FRY	FYN
CAPRIN1	CYP1A2
CAPRIN2	CCL2
CD276	PCDHB17
RBBP7	GNA14
SSRP1	NOX4
ZFP41	DNAJA4
HAUS5	LYL1
LIMD2	CBS
TIMM50	TLR2
DDX11	TDRKH
PPWD1	IRF5
GRIA3	KCNK6
EXOSC9	RASGEF1B
RSPH9	TROVE2
ITGB1BP1	PLCG2
MYO5C	FXD7
RAD51AP1	PDK2
ITGAE	ATP5S
AK1	HOXB5
FANCF	IGJ
H2AFX	CD14
NRM	UPP1
NMB	GIMAP4
HAUS6	PIGP
KPNA3	CEACAM1
CENPQ	IDO2
MCM6	RND1
HEY1	LACTB
SETD8	LIFR
PANX1	GFOD2
FBXO43	SDR42E1
ATP2B2	OAT
PRCP	IGSF6
MAZ	LSP1
RAD51	NECAB2
HOMER3	KLF2
PLK2	CYB5D2

GMNN	KLHL6
MAP4K4	PIGR
ANAPC5	PTGER2
PNKD	CXCL10
CD36	TGFBR3
MCM8	TPRKB
SNN	ARHGAP6
FIGNL1	IKBKE
NT5DC2	HOOK2
PTRH1	PODXL
TYW3	DAB2
GOLM1	TM7SF2
TINF2	GIMAP7
MYH10	TCF21
RAB15	SUCNR1
SNX7	ELL
KLHL13	AMOTL1
TIPIN	CXCL13
KCTD3	GLIPR1
ZMYND19	ARG2
TUG1	SLC25A25
NCAPD3	SC4MOL
CRYM	EVI2B
CRAT	TACC2
EXOSC6	FCGRT
E2F1	LST1
UBA2	HAPLN4
ENDOD1	EFEMP1
CCNG1	FPR2
LONRF3	TM4SF1
SLC20A1	C1QB
CLDN1	GAMT
PRR5	CSRNP1
KIF18A	FDX1
EEP1	WDR86
TTLL4	SOX15
IPO5	GCH1
REEP4	FCER1G
GADD45B	FAM134B
STIL	HMOX1
ODF2L	CCDC114
TRAF4	IL15RA
SMARCC1	RBM11
HIRIP3	FXYD2
MTBP	HTRA1
SVIL	ARHGAP30
LMO4	STXBP1
RNF168	SCN1B

RBL1	RGS1
PLD6	SGSM1
PHLDB1	ROBO1
WFDC2	RNF10
NFATC2IP	SHPK
NUCKS1	CASP12
HNMT	TLR4
MMP17	USO1
PFAS	PPP1R3F
NVL	GMPPA
CDC25C	ENTPD4
ITGA5	S100A9
LSM3	DARC
RTN4RL1	PDGFRA
FBXO45	HIVEP2
FKBP3	PLXDC1
SOX12	ZAP70
TXNDC16	CSF1
RHOQ	LPCAT2
DTL	DGKA
PAQR4	MASP1
PSAT1	IRX1
IFI27L1	THRSP
PHF13	CFP
DNMT3B	HES6
TJP2	ENTPD1
PDZRN3	FMNL2
BHLHB9	HSPA1A
ZBTB45	ECM1
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CHIC1	FYB
PGP	ALOX5AP
GUCY2C	EIF2C3
GBE1	GPR146
LRIG3	MAFK
DIO3OS	ARHGAP26
CTNNAL1	ESRRG
ZDHHC2	CALHM2
SNX24	CDC37
TOPBP1	AGXT
CLSPN	CD97
DPY30	HCST
SUSD3	ZDHHC9
POLE	CYTL1
GEMIN8	LTBP4
RG9MTD2	RENBP
CPSF6	GYS2
RAB23	FETUB

SCRIB	PIM3
TRIM24	SERTAD1
SPINK5	ZSWIM6
RRAS2	HIST1H3A
PTRH2	GAPDHS
PHF10	NCF4
SUV39H1	HABP2
HFE2	SLC46A1
GLOD5	VPREB3
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EXO1	ICAM2
SMC6	HSPA1L
BLM	PDE2A
RFC3	TYROBP
GLDC	CABYR
PLCL2	PCK1
KIF11	MPV17L
EPHB4	PPM1K
RNPEP	PCBD2
NSL1	PLEKHA2
EFNA2	EMILIN2
ALG8	APOB48R
LSM8	CEBPB
CDK2	ITGB2
MLEC	KCNJ8
CEP76	COL6A2
ZIK1	KLF15
RECQL	ONECUT2
FANCM	PLTP
WDR8	EXTL1
CENPT	SERINC2
LMF2	SLC4A3
RASL11B	SELP
CLN6	HYI
SMC3	KYNU
PRKAA1	CTGF
PAXIP1	TMEM173
TRIOBP	DNASE1L3
AP4M1	RAC2
CDKN3	MARCKS
NUP160	LRMP
DIS3	UNC13B
TYMS	FABP7
FKBP5	AIF1
CASP7	SLC39A11
LEFTY1	BCL3
MAPK7	ALAS2
HCFC2	SLC6A12

HAMP	IGFBP2
IL17RB	C1QC
DAPK2	COQ10B
RQCD1	CTRL
FAM54A	MACROD1
GPSM2	GJA4
TRMT12	CATSPER2
LRRC3	SLC22A7
CHEK1	NPR2
ANAPC4	FOXA3
HUNK	CD86
H1FX	SEMA3C
RANBP3	P2RY6
ETAA1	PLEKHB1
PDGFC	ABCG5
NME4	TIMD4
PTPRU	CD5L
TEAD2	P2RY13
AAAS	TMCC2
SENP1	CD74
NUP43	NPL2
PLEKHG5	GPX3
RNASEH2B	HK3
DCTPP1	FPR1
SMYD4	TAT
AIM1	GDPD3
ATP10D	ACAD10
SUV39H2	C5AR1
SULF2	SLC38A3
RAB34	IL1B
NFE2L2	CYBA
NUP107	DBP
RIC8B	IMPDH1
BRCA1	MOXD1
NUP62	PDLIM4
PMS1	CD207
CNTLN	TRHDE
CNTROB	SLC15A3
TLR1	JDP2
LANCL2	COLEC10
NOP58	CASP4
WHSC1	CD3D
ARPP19	CD163
SSNA1	CCL8
CC2D2A	FOLR2
ZNHIT3	CLEC4F
TUBB2A	MAFB
PIN1	CRIP3

WDR89
MESDC1
PTPLB
WDR90
ENOPH1
VPS37D
E2F7
RXRG
DOCK7
SLC16A7
CGN
GAR1
SPAG5
CCR1
NKAP
MTHFD1L
CTDSPL
TUSC1
ATAD5
HAUS1
ALS2CL
TAF6
HAUS4
ZBTB25
TWSG1
MBNL3
WDSUB1
RFWD3
KLF11
BCL2L11
ELOVL7
SSTR2
GINS3
CKAP5
CDC6
TRMT2A
ELMO2
PARD6G
DFNA5
PTBP2
MED9
SIPA1L2
MEX3B
MDM2
MED27
SMTN
CYB5R1
GAS1

RCC2
EED
CCDC52
TMEM184C
ITGA10
MBD1
TIMM22
POLA2
PHLDA3
ATP10A
IL33
OMD
IGSF1
NEO1
OXCT1
MRAS
SSX2IP
CKLF
RAD21
MUM1
IFT74
DSCC1
TMEM107
LAG3
RFK
MAP4K2
EVC
NUPL1
PLCH1
S1PR2
MSL3
ARL6IP6
MET
ACTR6
ZMYND8
SNX26
SNX16
SFT2D3
ARRDC3
UBAP2
LCMT1
RAG1AP1
BCDIN3D
XAF1
KLHDC6
ERCC6L
RHOD
MAD1L1

A2M
CBLN3
TEX9
NGFRAP1
PKN3
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STX2
PANK4
POLK
MPHOSPH6
GINS1
ABHD10
CITED1
GNB1L
CEP72
AMIGO2
GTPBP10
AK7
MSRB2
TRIM37
PLXNB1
PRDM14
CHML
VRK1
TTF2
SLC6A8
KDEL1C
NAPEPLD
UBA6
LRRC39
L3MBTL2
ASB15
EFCAB7
SLC43A3
MCM9
POLD2
WDR35
USP49
TNNC1
EXOC4
PPIL3
HCCS
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DOT1L

ASF1A
PARP12
ITPKA
PRPF3
SUPT16H
FRK
ADORA1
RPA3
OSBPL5
FIBIN
NUDT11
CHRD2
HS2ST1
PIWIL2
GTPBP3
TNFRSF14
RHPN2
GAS2L3
ASTE1
SHF
PLEKHH1
DMRTA1
ABHD2
AEN
REC8
MARS2
GPX8
FAP
RIF1
SYT12
RAB31
ZDHHC24
DDX55
MTHFD2L
SNHG1
UBTD2
CASP2
NMRAL1
ZMAT3
ZDHHC13
ARHGEF19
SNX14
SPIN4
TMX1
TECTB
SS18
ORC1L
PYGB

TPM4
SAMD9L
RTTN
APAF1
PPOX
RPRD1A
ARHGAP17
SUZ12
FABP4
ARHGEF7
KLF16
LIN54
SESTD1
MDM1
RAD18
INHBA
IGF2BP2
VNN3
MED14
FIGN
PPP1R8
TUBD1
FAM110A
RPP30
SLC10A3
FAM40B
CDC25B
LZIC
QPCT
KLHL8
NPAT
CCDC96
MED6
ARHGEF16
H19

List of genes with significantly different expression between Ad-Cre and Ad-LacZ treatment of RB^{f/f} mice. Raw intensity data were processed to produce the Robust Multi-array average (RMA) and the resultant values were analyzed by SAM software. Following SAM analysis, genes were filtered to ensure inclusion of only genes that were +/- $\geq 20\%$ expression in the Ad-Cre mice versus the control (Ad-LacZ).