

SUPPLEMENTARY MATERIALS AND METHODS

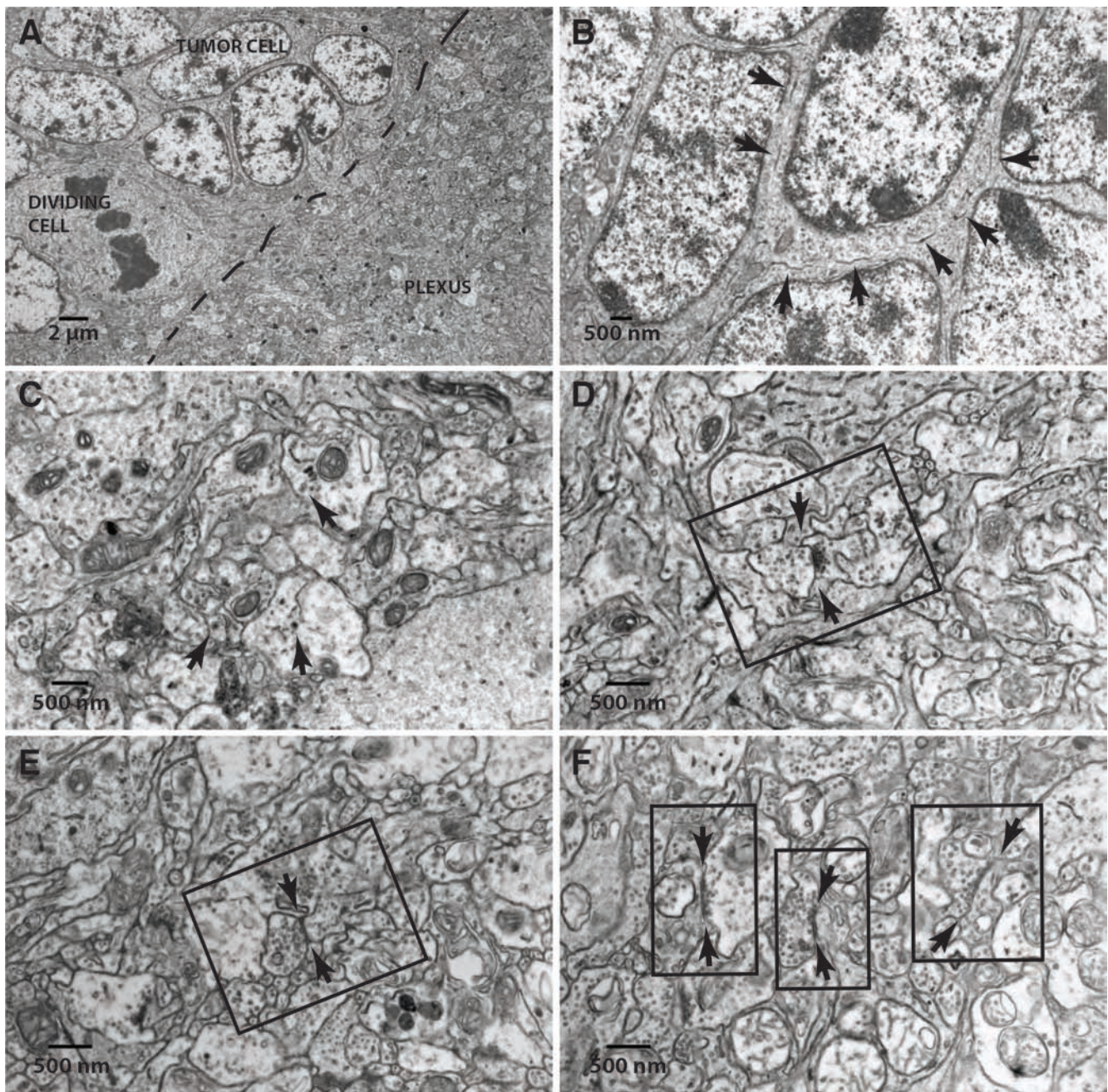
Transmission electron microscopy

All procedures for TEM have been described previously (Johnson et al. 2006). Animals were anesthetized with Avertin until a loss of deep tendon reflexes. Transcardial perfusion was performed with carboxygenated Ames Medium supplemented with

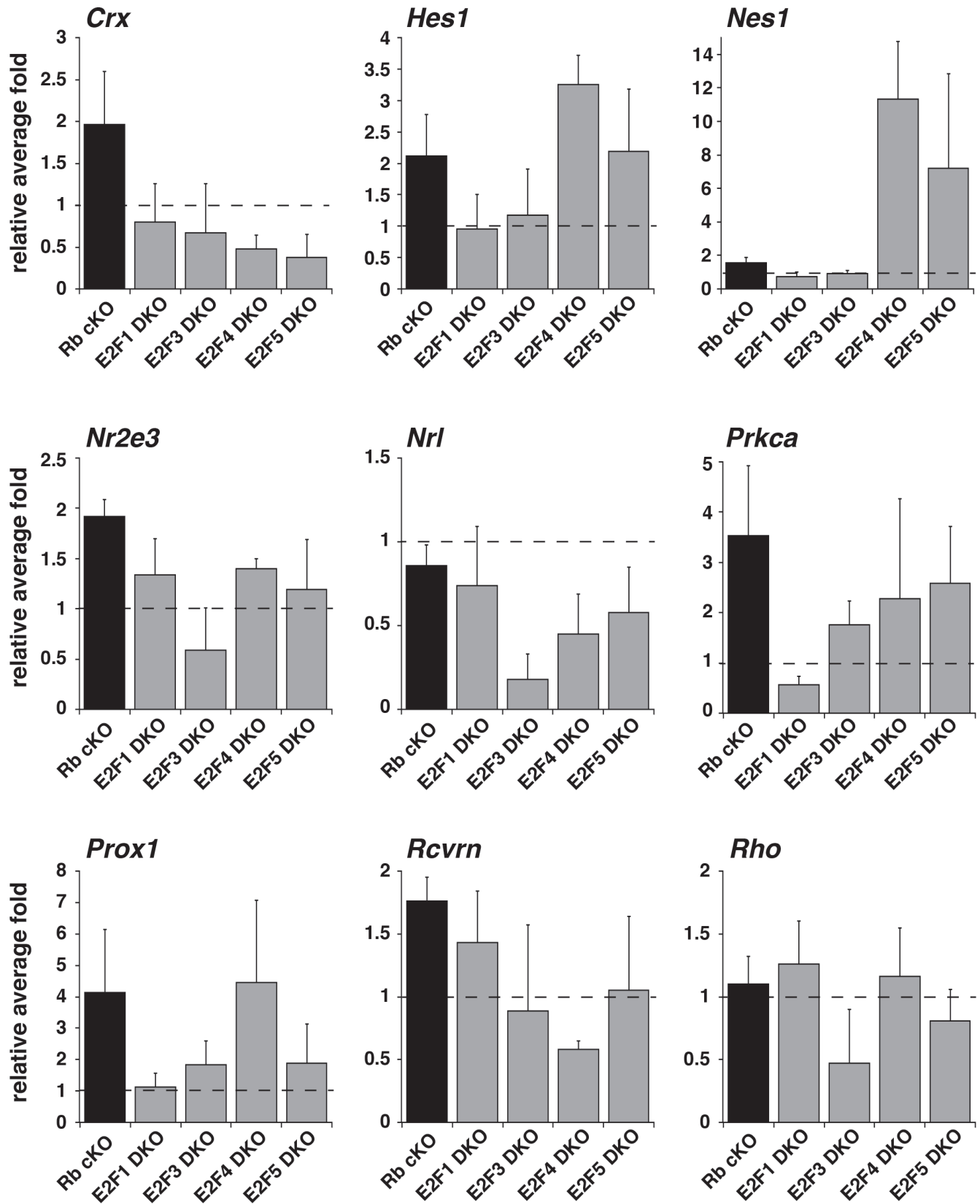
40 mM glucose to clear the vasculature, followed by perfusion with Sorenson's phosphate buffer pH 7.2 with 2% EM grade paraformaldehyde and 1% EM grade glutaraldehyde. Eyes were then harvested, a slit was made in the cornea to aid in diffusion, and the tissue was placed in 3% glutaraldehyde in Sorenson's phosphate buffer overnight. Tissue was washed with 0.2 M cacodylate buffer in 5% sucrose, post-fixed in 1% OsO₄, embedded, sectioned, and viewed by transmission electron microscopy (TEM).

Real-time Primers and Probes

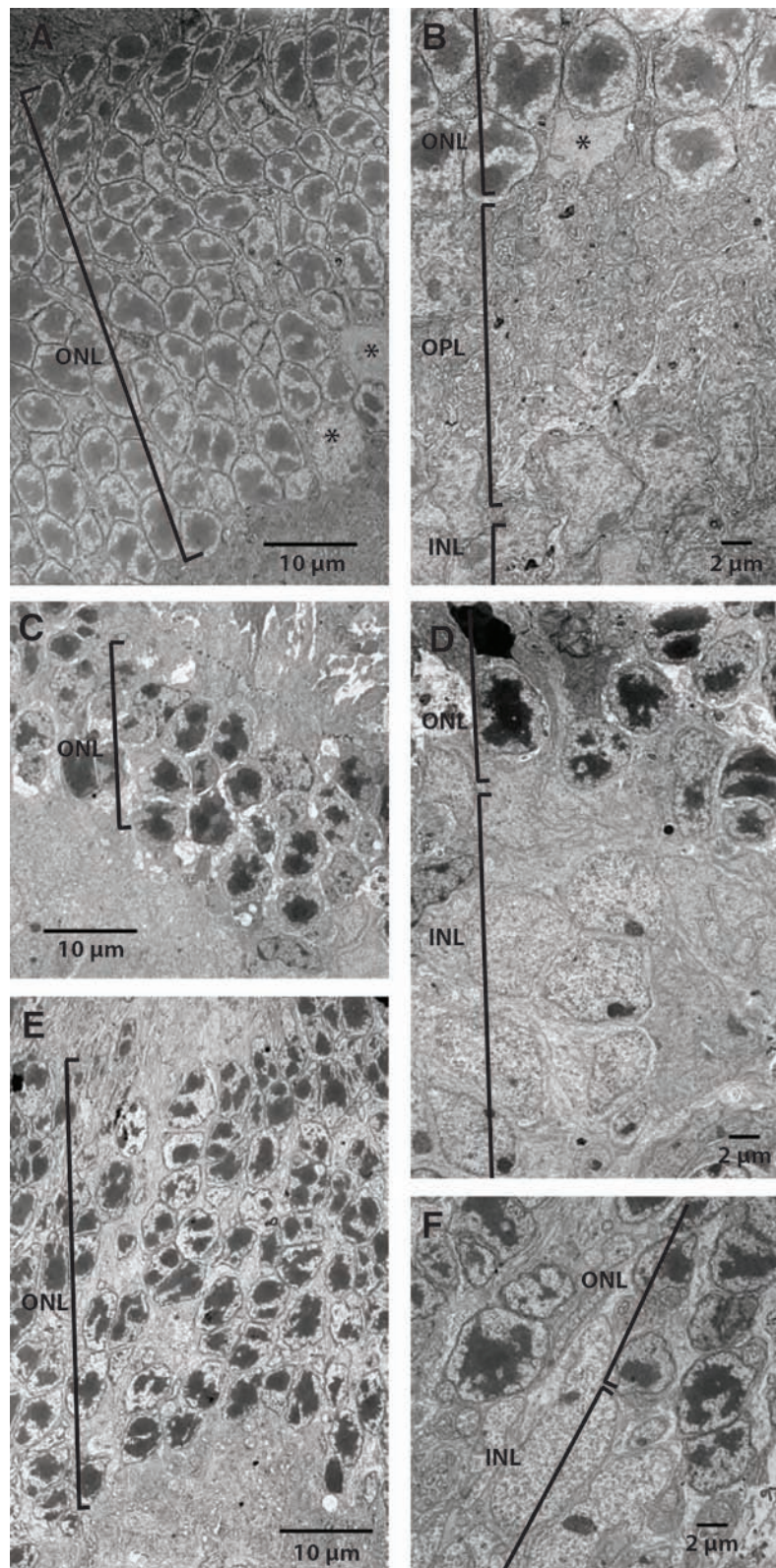
Gene	Forward	Reverse	Probe
mArr3	TGACTTGGATGTGATTGGTCTGA	GGAGCCACTTGCTTGGTTTG	ATTCGCAAAGATCTCTATG
mBrn3b	CCGGTTTCGCAGTGAAGAA	GCTCTGTACAACCTTGACAAATTCC	AACCAAAACCACAAACAACACAACACGAAA
mCalb1	CACATGTAACCTCTGTTTCGTGTATCCTT	TCACAATAAAGAATCCAGGCAATTAA	AGTGTGTCCTCTGCTGGTTATTGGTGACAA
mChx10	TGAGGCAAGGCCCATGTC	CGGGAGTATGTCCAGGATGTCT	AGGCCCGCAATTACCCCCACG
mCRALBP	CTGTCCAGGGTGGAGGTCAT	CCCCAGCACCAAGGATCAC	TCCCTTCTCTCCACCCATCTTGGA
mCrx	TCTGTGTGTACAGACATGACCACTAA	CATCAAGCTTCTTTTGCAITTTGT	CTGAGCTGGGATGCTGTGGCTTGATAAA
mGAPDH	CTCCACTCACGGCAAATTCA	CGCTCTGGAAGATGGTGAT	AAGGCCGAGAATGGGAAGCTTGTCATC
mGFAP	ATCGAGAAGGTCCGCTTCT	GGCTCGAAGCTGGTTCAAGTT	AGCAAAAACAAGGCGCTGGCAGC
mGS	GGTGCCAAGTTTGTAGTGATGAG	ACTTTCCCGTACTGCATCCT	CTTGGCTTAGAAGTGAGGCTCCCTTGAGG
mGnat1	TGACCAATAATGAAGCCATGCT	TCTTTGCCCATGGTTGATCA	TGGCTCAGAGCAGAGTCCAACCCCTA
mGPI-1	TCCGTGTCCCTTCTCACCAT	GGCAGTTCAGACCAGCTTCT	CTCCCTGCCCAGAGCGCACC
mGrm6	TTCCTGAAGACAGAGACTAAATTGACA	GGCAAGCCCTGACTTTACCA	TCTGGGCGGGCATTCAAACCC
mHes1	AGAGCCTCAGGCCACTGCTA	TTCGTTTTTAGTGTCCGTCAGAAG	CCGTAAAGTCCCTAGCCACCTCT
mNes1	CAACGCCCCCTTCTTCTG	GAGCAGTCTCGTGGGAAAGC	CACCTGCTGGAAGAGGCTTGGGC
mNr2e3	AGGCTGGAAGTTGAACAAAAGC	TCCAGTCTCCCTCCTTTCCC	AGGCACGTTTATCCTGTGTTCAAGACCAGA
mNrl	AACTTCTGAGCATCGTGGCA	TGAAGAGTCGTGACCTGCAAA	CTGGTCTTTGCTGGAGATGAGTTCCT
mPax6	CACCGCCCTCACCAACAC	AGGTTGTTTGCCATGGTGAAG	AGTGCTTTGCCACCCATGCCA
mPrkca	CGCGAGGACAGCCTGTCT	AGAACCCTTCAAAATCAGATTGGT	CCACCAGATCAGCTGGTCATTGCTAACATA
mProx1	TTAGAACAGGCTCGTGGTGAGA	TGAAGCAAAGTAAATAGCAACTAGTGACA	TGAGCTTGGCCGTGTGGACTTAGAGG
mRevrn	GCAGCTTCGATGCCAACAG	TCATGTGCAGAGCAATCACGTA	TACGCTGGACTTCAAGGA
mSyt1	CCACTGCCCTCCAAATCTACTC	ACAACGGTGTGATAACAATACATTCA	TCTTTTAAGCAATATGATGTGTAGATAGAGC



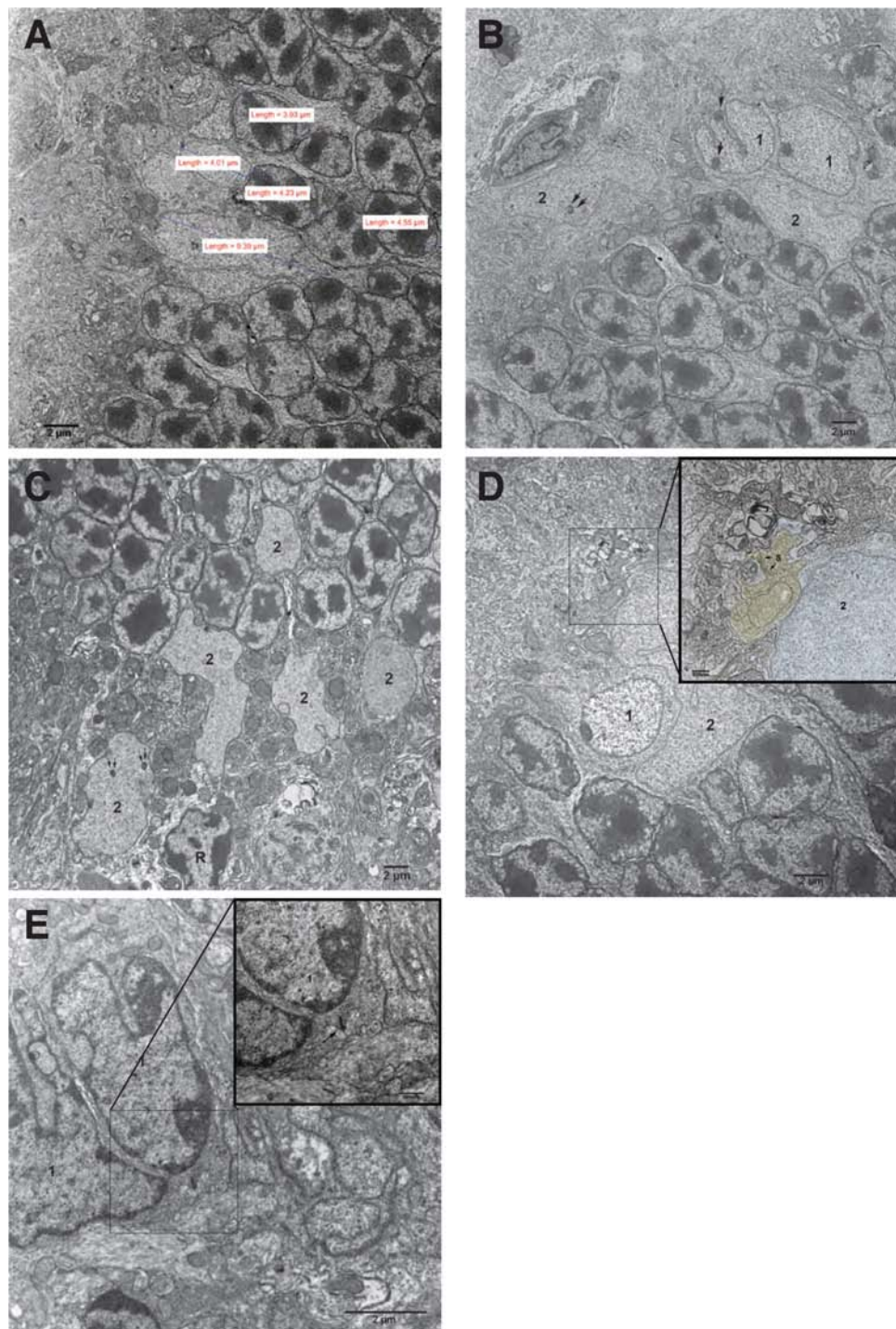
Supplementary Figure S1: Transmission Electron Microscopy from E2f5 TKO Tumors. (A-E) Transmission electron microscopy (TEM) from a *Chx10-Cre;Rb^{lox/lox};p107^{-/-};E2f5^{lox/lox}* (*E2f5 TKO*) tumor show that these tumors have all of the differentiation features of 7D and human retinoblastomas with (A) dividing cells, tightly packed tumor cells with areas of plexus, (B) cell to cell junctions among the tumor cell soma (arrows), (C) dense core vesicles (arrows), (D-E) and processes and synapses (box). The synapses seen in *E2f5 TKO* tumors are amacrine-like synapses. (F) TEM of amacrine synapses (boxes) at the inner plexiform layer from a *Chx10-Cre;Rb^{lox/lox};E2f5^{lox/lox}* (*E2f5 DKO*) retina shown as comparison of the amacrine-like synapses seen in retinoblastoma tumors.



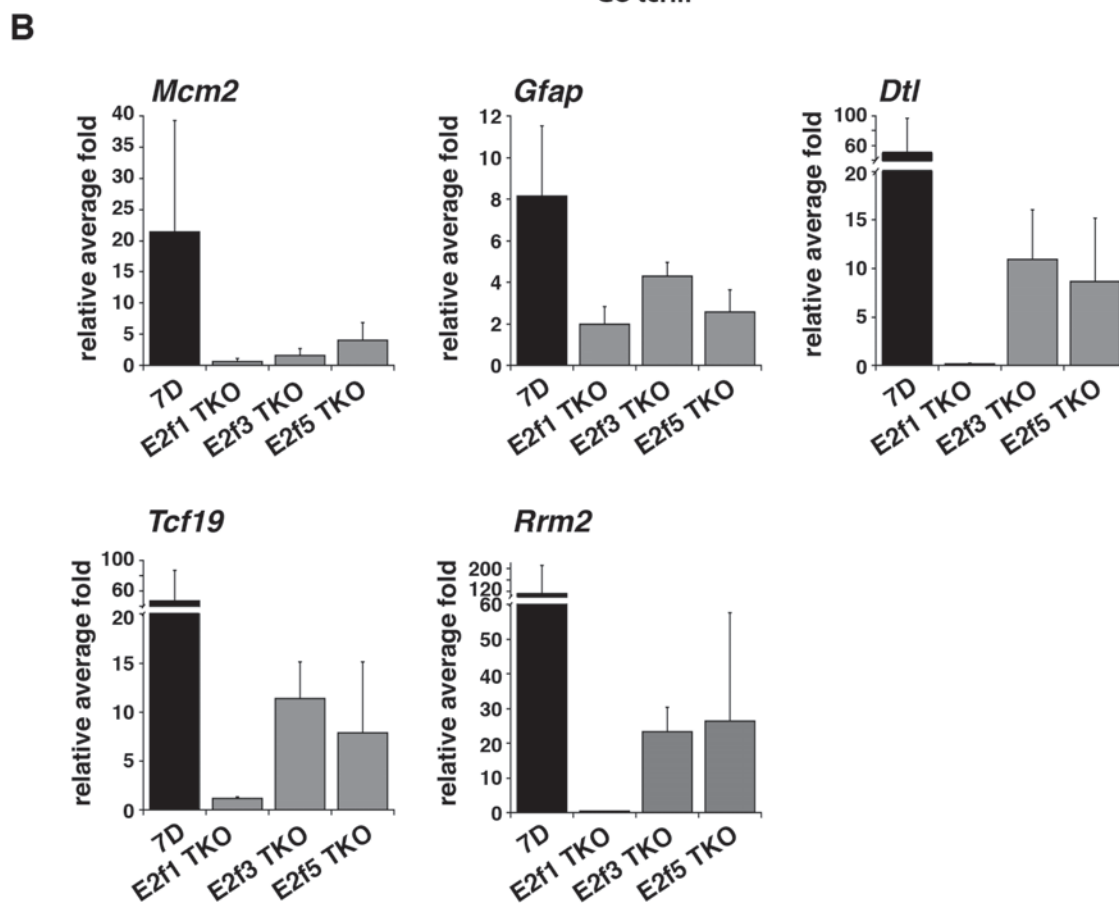
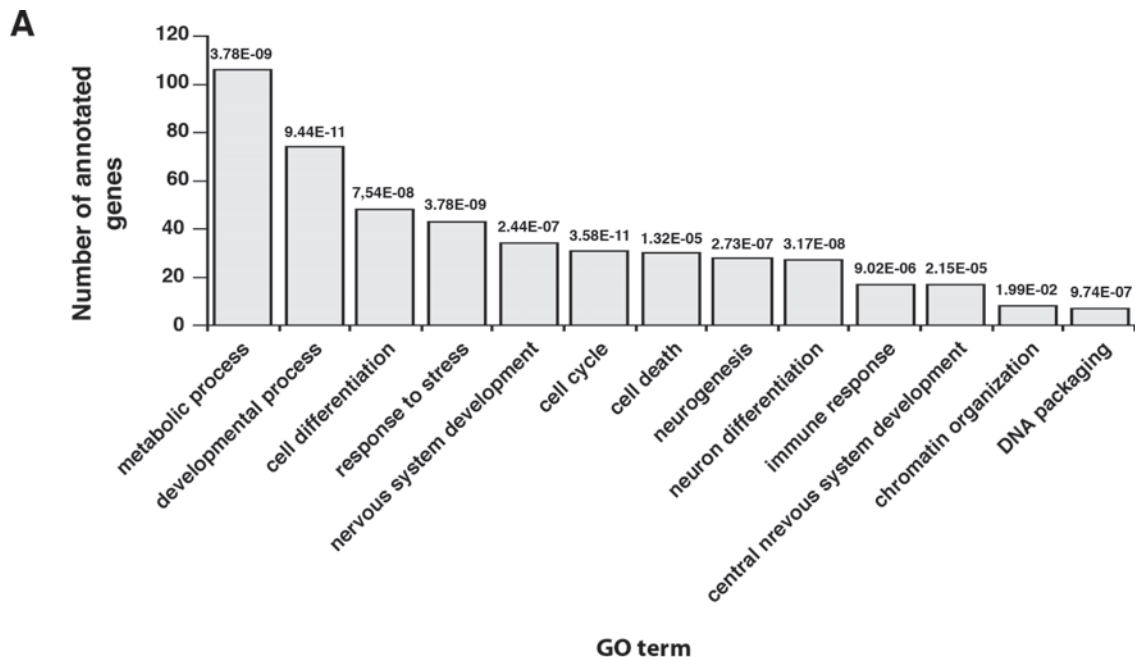
Supplementary Figure S2: Real Time RT-PCR Analysis of Retinal Development Genes. Real time RT-PCR analyses for P21 retinae from E2f DKO mice for various retinal development genes. Relative average fold was calculated compared to wt. Each bar is the mean and standard deviation of 5 biological replicates ran in duplicate.



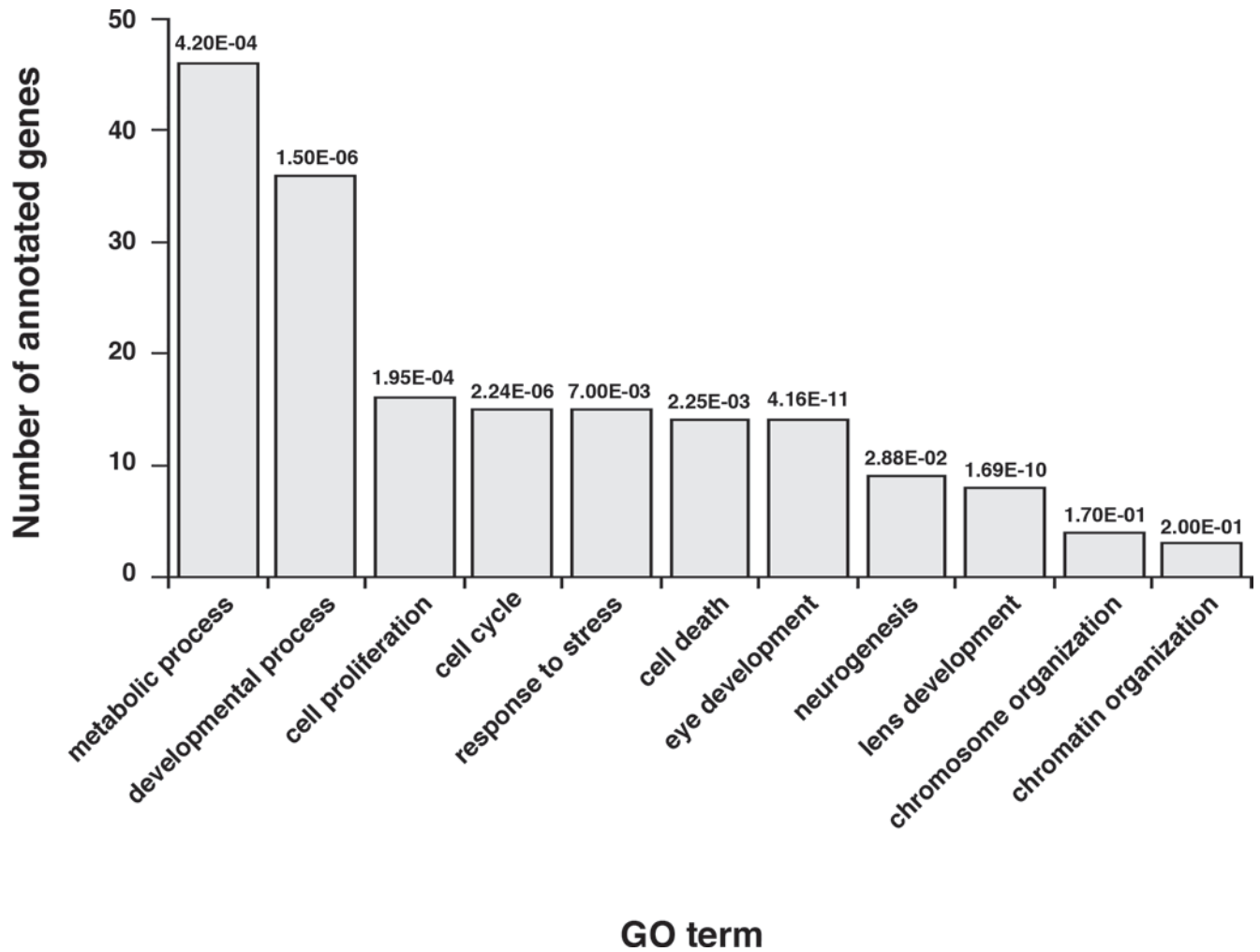
Supplementary Figure S3: Transmission Electron Microscopy from E2f DKO Retinae. (A-F) Transmission electron microscopy (TEM) from P21 E2f DKO retinae. (A-B) *Chx10-Cre;Rb^{lox/lox};E2f1^{-/-}* (*E2f1* DKO) retinae show normal thickness of (A) the outer nuclear layer (ONL) and (B) outer plexiform layer (OPL) with some evidence of persistent progenitors (asterisk). (C-D) *Chx10-Cre;Rb^{lox/lox};E2f3^{lox/lox}* (*E2f3* DKO) retinae show thinning of (C) the ONL and (D) OPL. (E-F) *Chx10-Cre;Rb^{lox/lox};E2f5^{lox/lox}* (*E2f5* DKO) retinae also show thinning of the (E) ONL and (F) OPL. INL: inner nuclear layer.



Supplementary Figure S4: Transmission Electron Microscopy Showing Persistent Progenitor Cells in E2f TKO Retinae. TEM analysis of E2f TKO retinae show (A) The “length” of unusual cells with pale nuclei termed “persistent progenitors” varies from the average diameter of normal rods to more than twice as large. Also, their chromatin is less condensed than normal rods. (B) The differences in the size and shape of these cells may reflect two stages. Stage 1 cells are approximately the size of normal rods but with some nuclear invagination. Their chromatin is more dispersed and some present nucleoli. Stage 2 cells are large in size, often elongated. Their nucleus is highly pleomorphic, with no evidence of chromatin condensation. No nucleoli are present but small dark circular inclusion bodies are often seen within the pale nucleus. Clumps of persistent progenitors in both stages are usually found on the proximal edge of the OPL within the ONL. (C) Both cell stages (stage2) and normal rods (R) can be displaced into the outer plexiform layer (OPL). Displaced rod somata are often elongated. (D) Example of stage 1 and stage 2 cell. Inset: Stage 2 cell could be traced, showing process projecting into OPL in close apposition to neighboring rod spherule. (E) Two stage 1 cells are shown, one appears to contain spherule elements: synaptic ribbon and junction with two horizontal cells.



Supplementary Figure S5: Real Time RT-PCR Validation of Putative Rb-Target Genes Involved in Retinal Development. (A) Histogram from the Gene Ontology (GO) analysis of the 322 genes that are putative Rb-targets involved in retinal development. Each bar is the number of annotated genes from a subset of the GO terms found. Numbers above the bars depict the respective P-values. (B) Real time RT-PCR validation of a subset of genes involved in retinal development show a significant increase in gene expression in the *Chx10-Cre;Rb^{lox/lox};p107^{-/-}* (7D), *Chx10-Cre;Rb^{lox/lox};p107^{-/-};E2f3^{lox/lox}* (E2f3 TKO) and *Chx10-Cre;Rb^{lox/lox};p107^{-/-};E2f5^{lox/lox}* (E2f5 TKO) mouse strains that display retinal development defects but not in *Chx10-Cre;Rb^{lox/lox};p107^{-/-};E2f1^{-/-}* (E2f1 TKO) which rescue the developmental defects. Each bar is the mean and standard deviation of 5 biological replicates ran in duplicate.



Supplementary Figure S6: Gene Ontology Analysis of Putative Rb-Target Genes Involved in Retinoblastoma. Histogram from the Gene Ontology (GO) analysis of the 148 genes that are putative Rb-targets involved in retinal tumorigenesis. Each bar is the number of annotated genes from a subset of the GO terms found. Numbers above the bars depict the respective P-values.

Supplementary Table S1. Retinal Differentiation Gene List

genesymbol	genetitle
130004C03	hypothetical LOC403343
1500011B03Rik	RIKEN cDNA 1500011B03 gene
1500015O10Rik	RIKEN cDNA 1500015O10 gene
1700007K13Rik	RIKEN cDNA 1700007K13 gene
1700023H06Rik	RIKEN cDNA 1700023H06 gene
2010011I20Rik	RIKEN cDNA 2010011I20 gene
2010315B03Rik	RIKEN cDNA 2010315B03 gene
2310067E19Rik	RIKEN cDNA 2310067E19 gene
2610507I01Rik	RIKEN cDNA 2610507I01 gene
2700089E24Rik	RIKEN cDNA 2700089E24 gene
2810039B14Rik	RIKEN cDNA 2810039B14 gene
2810055F11Rik	RIKEN cDNA 2810055F11 gene
2900046D03Rik	RIKEN cDNA 2900046D03 gene
2900052N01Rik	RIKEN cDNA 2900052N01 gene
3110035E14Rik	RIKEN cDNA 3110035E14 gene
4632432E15Rik	RIKEN cDNA 4632432E15 gene
4833420G17Rik	RIKEN cDNA 4833420G17 gene
4933406J10Rik	RIKEN cDNA 4933406J10 gene
4933409K07Rik/// Gm10590///Gm3893/// Gm5859///Gm7819	RIKEN cDNA 4933409K07 gene///predicted gene 10590///predicted gene 3893///predict
5730408A14Rik	RIKEN cDNA 5730408A14 gene
5730552O08Rik	RIKEN cDNA 5730552O08 gene
5830443J22Rik	RIKEN cDNA 5830443J22 gene
6030438J01	hypothetical protein 6030438J01
6330418B08Rik	RIKEN cDNA 6330418B08 gene
6530402F18Rik	RIKEN cDNA 6530402F18 gene
6720422M22Rik	RIKEN cDNA 6720422M22 gene
7120451J01Rik/// LOC100503726	RIKEN cDNA 7120451J01 gene///hypothetical protein LOC100503726
9230105E10Rik	RIKEN cDNA 9230105E10 gene
9330161A08Rik	RIKEN cDNA 9330161A08 gene
9430025M13Rik	RIKEN cDNA 9430025M13 gene
9430065F17Rik	RIKEN cDNA 9430065F17 gene
9630009C16	hypothetical protein 9630009C16
A030001D20Rik	RIKEN cDNA A030001D20 gene
A2m	alpha-2-macroglobulin

(Continued)

genesymbol	genetitle
A430105J06Rik	RIKEN cDNA A430105J06 gene
A930004D18Rik	RIKEN cDNA A930004D18 gene
A930028C08Rik	RIKEN cDNA A930028C08 gene
A930030B08Rik	RIKEN cDNA A930030B08 gene
A930036A04Rik	RIKEN cDNA A930036A04 gene
Aard	alanine and arginine rich domain containing protein
Abca9	ATP-binding cassette, sub-family A (ABC1), member 9
Adarb2	adenosine deaminase, RNA-specific, B2
Ahrr	aryl-hydrocarbon receptor repressor
AI835735	expressed sequence AI835735
Akap5	A kinase (PRKA) anchor protein 5
Ankrd33b	ankyrin repeat domain 33B
Antxr2	anthrax toxin receptor 2
Apobec1	apolipoprotein B mRNA editing enzyme, catalytic polypeptide 1
Apobec2	apolipoprotein B mRNA editing enzyme, catalytic polypeptide 2
Apoc1	apolipoprotein C-I
Arhgap26	Rho GTPase activating protein 26
Arhgap31	Rho GTPase activating protein 31
Arsk	arylsulfatase K
Atad2	ATPase family, AAA domain containing 2
Atp1a2	ATPase, Na ⁺ /K ⁺ transporting, alpha 2 polypeptide
B2m	beta-2 microglobulin
BC023969	cDNA sequence BC023969
BC064078	cDNA sequence BC064078
Bcan	brevican
BE949265	cDNA sequence BE949265
Bmp2	bone morphogenetic protein 2
C030034I22Rik	RIKEN cDNA C030034I22 gene
C130071C03Rik	RIKEN cDNA C130071C03 gene
C1qa	complement component 1, q subcomponent, alpha polypeptide
C1qb	complement component 1, q subcomponent, beta polypeptide
C1qc	complement component 1, q subcomponent, C chain
C4b	complement component 4B (Childo blood group)
C4bp-ps1	complement component 4 binding protein, pseudogene 1
Carhsp1	calcium regulated heat stable protein 1
Ccde24	coiled-coil domain containing 24

(Continued)

genesymbol	genetitle
Ccl21a///Ccl21b///Ccl21c/// Gm10591///Gm13304/// Gm1987///LOC100041593	chemokine (C-C motif) ligand 21A (serine)///chemokine (C-C motif) ligand 21B (leucine)
Ccne2	cyclin E2
Cd44	CD44 antigen
Cd53	CD53 antigen
Cd59a	CD59a antigen
Cdc20	cell division cycle 20 homolog (S. cerevisiae)
Cdca8	cell division cycle associated 8
Cdk1	cyclin-dependent kinase 1
Cdkn1a	cyclin-dependent kinase inhibitor 1A (P21)
Cdt1	chromatin licensing and DNA replication factor 1
Cenpf	centromere protein F
Cenpk	centromere protein K
Cep164	centrosomal protein 164
Chek1	checkpoint kinase 1 homolog (S. pombe)
Chl1	cell adhesion molecule with homology to L1CAM
Chrdl1	chordin-like 1
Ckap2	cytoskeleton associated protein 2
Cks1b	CDC28 protein kinase 1b
Cldn7	claudin 7
Clspn	claspin homolog (Xenopus laevis)
Col18a1	collagen, type XVIII, alpha 1
Col19a1	collagen, type XIX, alpha 1
Col1a2	collagen, type I, alpha 2
Col2a1	collagen, type II, alpha 1
Col9a3	collagen, type IX, alpha 3
Comt1	catechol-O-methyltransferase 1
Crhbp	corticotropin releasing hormone binding protein
Crym	crystallin, mu
Csrp2	cysteine and glycine-rich protein 2
Ctss	cathepsin S
Cxcl12	chemokine (C-X-C motif) ligand 12
Cxcl13	chemokine (C-X-C motif) ligand 13
Cxcl14	chemokine (C-X-C motif) ligand 14
D17H6S56E-5	DNA segment, Chr 17, human D6S56E 5
D4Wsu53e	DNA segment, Chr 4, Wayne State University 53, expressed

(Continued)

genesymbol	genetitle
Daam1	dishevelled associated activator of morphogenesis 1
Dctd	dCMP deaminase
Dcx	doublecortin
Dixdc1	DIX domain containing 1
Dleu7	deleted in lymphocytic leukemia, 7
Dnahc9	dynein, axonemal, heavy chain 9
Dtl	denticleless homolog (Drosophila)
Dusp12	dual specificity phosphatase 12
Edn2	endothelin 2
Elavl1	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 1 (Hu antigen R)
Emp1	epithelial membrane protein 1
Eno4	enolase 4
Eps8	epidermal growth factor receptor pathway substrate 8
Eps8l1	EPS8-like 1
Erc1	ELKS/RAB6-interacting/CAST family member 1
Fam107b	family with sequence similarity 107, member B
Fam111a	family with sequence similarity 111, member A
Fam129a	family with sequence similarity 129, member A
Fam129a	family with sequence similarity 129, member A
Fam5c	family with sequence similarity 5, member C
Fbln1	fibulin 1
Fbn2	fibrillin 2
Fcgr3	Fc receptor, IgG, low affinity III
Figl1	fidgetin-like 1
Fscn2	fascin homolog 2, actin-bundling protein, retinal (Strongylocentrotus purpuratus)
Fyco1	FYVE and coiled-coil domain containing 1
Gabrb3	gamma-aminobutyric acid (GABA) A receptor, subunit beta 3
Gas5	growth arrest specific 5
Gas7	growth arrest specific 7
Gbp10///Mpa2l	guanylate-binding protein 10///macrophage activation 2 like
Gbp6	guanylate binding protein 6
Gckr	glucokinase regulatory protein
Gdpd3	glycerophosphodiester phosphodiesterase domain containing 3
Gfap	glial fibrillary acidic protein
Gins1	GINS complex subunit 1 (Psf1 homolog)
Gja1	gap junction protein, alpha 1
Glb1l3	galactosidase, beta 1 like 3

(Continued)

genesymbol	genetitle
Gm10037	predicted gene 10037
Gm10393///Plac9	predicted gene 10393///placenta specific 9
Gm11276///Hist1h2ao	predicted gene 11276///histone cluster 1, H2ao
Gm12758	predicted gene 12758
Gm2115	predicted gene 2115
Gm3893///Gm5859/// Gm7819	predicted gene 3893///predicted pseudogene 5859///predicted gene 7819
Gm7120	predicted gene 7120
Gmcl1	germ cell-less homolog 1 (Drosophila)
Gpc3	glypican 3
Gpr137b	G protein-coupled receptor 137B
Gpr34	G protein-coupled receptor 34
Grik1	glutamate receptor, ionotropic, kainate 1
Grm3	glutamate receptor, metabotropic 3
Guca1b	guanylate cyclase activator 1B
H2-T10///H2-T22/// H2-T9	histocompatibility 2, T region locus 10///histocompatibility 2, T region locus 22
H2afj	H2A histone family, member J
Hcls1	hematopoietic cell specific Lyn substrate 1
Hddc3	HD domain containing 3
Heatr1	HEAT repeat containing 1
Hebp1	heme binding protein 1
Hells	helicase, lymphoid specific
Heph	hephaestin
Herc6	hect domain and RLD 6
Hist1h2be	Histone cluster 1, H2be
Ifit2	interferon-induced protein with tetratricopeptide repeats 2
Ifitm3	interferon induced transmembrane protein 3
Igfbpl1	insulin-like growth factor binding protein-like 1
Ildr2	immunoglobulin-like domain containing receptor 2
Insl5	insulin-like 5
Irf3	interferon regulatory factor 3
Kbtbd11	kelch repeat and BTB (POZ) domain containing 11
Kcne11	potassium voltage-gated channel, Isk-related family, member 1-like, pseudogene
Klf2	Kruppel-like factor 2 (lung)
Krt24	keratin 24
Laptm5	lysosomal-associated protein transmembrane 5
Lars2	leucyl-tRNA synthetase, mitochondrial

(Continued)

genesymbol	genetitle
Lgi3	leucine-rich repeat LGI family, member 3
LOC630164///Xlr3a///Xlr3b///Xlr3c	x-linked lymphocyte-regulated protein 3B-like///X-linked lymphocyte-regulated 3A ///
LOC676974	glucose-6-phosphate isomerase-like
Ltbp1	latent transforming growth factor beta binding protein 1
Lyplal1	lysophospholipase-like 1
Lyz1	lysozyme 1
Lztf1	leucine zipper transcription factor-like 1
Madd	MAP-kinase activating death domain
Man2a2	mannosidase 2, alpha 2
Mapk6	mitogen-activated protein kinase 6
March6	membrane-associated ring finger (C3HC4) 6
Matn2	matrilin 2
Mcm2	minichromosome maintenance deficient 2 mitotin (S. cerevisiae)
Mcm3	minichromosome maintenance deficient 3 (S. cerevisiae)
Mcm5	minichromosome maintenance deficient 5, cell division cycle 46 (S. cerevisiae)
Mcm6	minichromosome maintenance deficient 6 (MIS5 homolog, S. pombe) (S. cerevisiae)
Mcm7	minichromosome maintenance deficient 7 (S. cerevisiae)
Mcoln1	mucolipin 1
Mdk	midkine
Mef2c	myocyte enhancer factor 2C
Mki67	antigen identified by monoclonal antibody Ki 67
Mpeg1	macrophage expressed gene 1
Mt2	metallothionein 2
Myb	myeloblastosis oncogene
Mybl1	myeloblastosis oncogene-like 1
Mycl1	v-myc myelocytomatosis viral oncogene homolog 1, lung carcinoma derived (avian)
Myo7a	myosin VIIA
Ncaph	non-SMC condensin I complex, subunit H
Ndel1	nuclear distribution gene E-like homolog 1 (A. nidulans)
Ndufa12	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 12
Neurog2	neurogenin 2
Nfib	nuclear factor I/B
Nfix	nuclear factor I/X
Nmral1	NmrA-like family domain containing 1
Nnat	neuronatin
Nrip2	nuclear receptor interacting protein 2
Nusap1	nucleolar and spindle associated protein 1

(Continued)

genesymbol	genetitle
Ogn	osteoglycin
Opn1sw	opsin 1 (cone pigments), short-wave-sensitive (color blindness, tritan)
P2ry12	purinergic receptor P2Y, G-protein coupled 12
Paip1	polyadenylate binding protein-interacting protein 1
Parp3	poly (ADP-ribose) polymerase family, member 3
Pbk	PDZ binding kinase
Pcolce	procollagen C-endopeptidase enhancer protein
Pcp2	Purkinje cell protein 2 (L7)
Pde3b	phosphodiesterase 3B, cGMP-inhibited
Pde6h	phosphodiesterase 6H, cGMP-specific, cone, gamma
Pdzrn3	PDZ domain containing RING finger 3
Pex19	peroxisomal biogenesis factor 19
Pisd-ps3	phosphatidylserine decarboxylase, pseudogene 3
Pitpnm3	PITPNM family member 3
Pla2g16	phospholipase A2, group XVI
Plcd3	phospholipase C, delta 3
Plekhf1	pleckstrin homology domain containing, family F (with FYVE domain) member 1
Pnpla3	patatin-like phospholipase domain containing 3
Pole2	polymerase (DNA directed), epsilon 2 (p59 subunit)
Ppara	peroxisome proliferator activated receptor alpha
Ppcdc	phosphopantothenoylecysteine decarboxylase
Ppic	peptidylprolyl isomerase C
Ppox	protoporphyrinogen oxidase
Ppp1r12b	protein phosphatase 1, regulatory (inhibitor) subunit 12B
Pre1	protein regulator of cytokinesis 1
Prep	prolylcarboxypeptidase (angiotensinase C)
Prelp	proline arginine-rich end leucine-rich repeat
Prim1	DNA primase, p49 subunit
Prkca	protein kinase C, alpha
Prph2	peripherin 2
Psma3	Proteasome (prosome, macropain) subunit, alpha type 3
Ptprz1	protein tyrosine phosphatase, receptor type Z, polypeptide 1
Ptx3	pentraxin related gene
Pycard	PYD and CARD domain containing
Qars	glutaminyl-tRNA synthetase
Rab31	RAB31, member RAS oncogene family
Rabgef1	RAB guanine nucleotide exchange factor (GEF) 1

(Continued)

genesymbol	genetitle
Rcn2	reticulocalbin 2
Retn	resistin
Rgs13	regulator of G-protein signaling 13
Rnase4	ribonuclease, RNase A family 4
Rnf207	ring finger protein 207
Rpgrip1	retinitis pigmentosa GTPase regulator interacting protein 1
Rprd1b	regulation of nuclear pre-mRNA domain containing 1B
Rps25	ribosomal protein S25
Rps9	ribosomal protein S9
Rrm2	ribonucleotide reductase M2
S100a4	S100 calcium binding protein A4
S100a6	S100 calcium binding protein A6 (calcyclin)
Scn2b	sodium channel, voltage-gated, type II, beta
Scn7a	sodium channel, voltage-gated, type VII, alpha
Sdha	succinate dehydrogenase complex, subunit A, flavoprotein (Fp)
Sec22a	SEC22 vesicle trafficking protein homologue A (<i>S. cerevisiae</i>)
Serinc3	serine incorporator 3
Serping1	serine (or cysteine) peptidase inhibitor, clade G, member 1
Sh2d1a	SH2 domain protein 1A
Slc13a4	solute carrier family 13 (sodium/sulfate symporters), member 4
Slc38a6	solute carrier family 38, member 6
Slco4a1	solute carrier organic anion transporter family, member 4a1
Smc2	structural maintenance of chromosomes 2
Socs2	suppressor of cytokine signaling 2
Sox11	SRY-box containing gene 11
Sox4	SRY-box containing gene 4
Spc25	SPC25, NDC80 kinetochore complex component, homolog (<i>S. cerevisiae</i>)
Srp54b	signal recognition particle 54B
Srpk2	serine/arginine-rich protein specific kinase 2
Stard7	START domain containing 7
Stk17b	serine/threonine kinase 17b (apoptosis-inducing)
Suclg2	succinate-Coenzyme A ligase, GDP-forming, beta subunit
Syne2	synaptic nuclear envelope 2
Sys1	SYS1 Golgi-localized integral membrane protein homolog (<i>S. cerevisiae</i>)
Tcf19	transcription factor 19
Tcfap2c	transcription factor AP-2, gamma
Tctn3	tectonic family member 3

(Continued)

genesymbol	genetitle
Tgm2	transglutaminase 2, C polypeptide
Tia1	cytotoxic granule-associated RNA binding protein 1
Timm44	translocase of inner mitochondrial membrane 44
Tmem150c	transmembrane protein 150C
Tmlhe	trimethyllysine hydroxylase, epsilon
Tmx4	thioredoxin-related transmembrane protein 4
Tnfrsf21	tumor necrosis factor receptor superfamily, member 21
Tnnt1	troponin T1, skeletal, slow
Top2a	topoisomerase (DNA) II alpha
Trim59	tripartite motif-containing 59
Tspan6	tetraspanin 6
Ttc21a	Tetratricopeptide repeat domain 21A
Tubel	epsilon-tubulin 1
Tyrobp	TYRO protein tyrosine kinase binding protein
Ube2c	ubiquitin-conjugating enzyme E2C
Ube2m	ubiquitin-conjugating enzyme E2M (UBC12 homolog, yeast)
Uhrf1	ubiquitin-like, containing PHD and RING finger domains, 1
Ung	uracil DNA glycosylase
Vamp3	vesicle-associated membrane protein 3
Vax2os1	Vax2 opposite strand transcript 1
Vcan	versican
Vmn2r29	vomer nasal 2, receptor 29
Vps13b	vacuolar protein sorting 13B (yeast)
Wdfy1	WD repeat and FYVE domain containing 1
Wdr89	WD repeat domain 89
Wisp1	WNT1 inducible signaling pathway protein 1
Wnt5a	wingless-related MMTV integration site 5A
Xaf1	XIAP associated factor 1
Zcchc24	zinc finger, CCHC domain containing 24
Zfp420	zinc finger protein 420
Zfp874a	zinc finger protein 874a
Zic1	zinc finger protein of the cerebellum 1
Zic5	zinc finger protein of the cerebellum 5

Supplementary Table S2. Tumorigenesis Gene List

genesymbol	genetitle	Epigenetic	Deregulated in human RB
1190002F15Rik	RIKEN cDNA 1190002F15 gene	No	No
1200003I10Rik/// 1200015M12Rik/// A130040M12Rik/// E430024C06Rik	RIKEN cDNA 1200003I10 gene///RIKEN cDNA 1200015M12 gene///RIKEN cDNA A130040M12 gen	No	No
1200015M12Rik/// A130040M12Rik/// E430024C06Rik	RIKEN cDNA 1200015M12 gene///RIKEN cDNA A130040M12 gene///RIKEN cDNA E430024C06 gen	No	No
2810417H13Rik	RIKEN cDNA 2810417H13 gene	Yes	No
3110003A17Rik	RIKEN cDNA 3110003A17 gene	No	No
4833408G04Rik	RIKEN cDNA 4833408G04 gene	No	No
5330426P16Rik	RIKEN cDNA 5330426P16 gene	No	No
9030411K21Rik	RIKEN cDNA 9030411K21 gene	No	No
9430047L24Rik	RIKEN cDNA 9430047L24 gene	No	No
9530085L11Rik	RIKEN cDNA 9530085L11 gene	No	No
A330094K24Rik	RIKEN cDNA A330094K24 gene	No	No
A530083I20Rik	RIKEN cDNA A530083I20 gene	No	No
Abcb1a	ATP-binding cassette, sub-family B (MDR/TAP), member 1A	No	No
Abcc9	ATP-binding cassette, sub-family C (CFTR/MRP), member 9	No	No
Abce1	ATP-binding cassette, sub-family E (OABP), member 1	No	No
Acaa1a///Acaa1b	acetyl-Coenzyme A acyltransferase 1A///acetyl-Coenzyme A acyltransferase 1B	No	No
Agpat3	1-acylglycerol-3-phosphate O-acyltransferase 3	Yes	Yes
Aipl1	aryl hydrocarbon receptor-interacting protein-like 1	Yes	No
Akna	AT-hook transcription factor	No	Yes
Ankrd33	ankyrin repeat domain 33	No	Yes
Anln	anillin, actin binding protein	Yes	No
Arhgap11a	Rho GTPase activating protein 11A	Yes	No
Armc9	armadillo repeat containing 9	Yes	Yes
Aspm	asp (abnormal spindle)-like, microcephaly associated (Drosophila)	Yes	No
BC019943	cDNA sequence BC019943	No	No
BC059841	cDNA sequence BC059841	No	No
Bfsp1	beaded filament structural protein 1, in lens-CP94	No	No
Bub1	budding uninhibited by benzimidazoles 1 homolog (S. cerevisiae)	Yes	No
Car8	carbonic anhydrase 8	No	No
Ccnb1	cyclin B1	Yes	No
Cd24a	CD24a antigen	No	No
Cdc20	cell division cycle 20 homolog (S. cerevisiae)	Yes	No

(Continued)

genesymbol	genetitle	Epigenetic	Deregulated in human RB
Cdc6	cell division cycle 6 homolog (S. cerevisiae)	Yes	No
Cdca3	cell division cycle associated 3	Yes	No
Cdca7	cell division cycle associated 7	No	No
Cdca7l	cell division cycle associated 7 like	Yes	No
Cdk2	cyclin-dependent kinase 2	Yes	No
Cds1	CDP-diacylglycerol synthase 1	No	No
Cks2	CDC28 protein kinase regulatory subunit 2	Yes	No
Cnnm4	cyclin M4	No	Yes
Col24a1	collagen, type XXIV, alpha 1	No	No
Col6a3	collagen, type VI, alpha 3	No	No
Crocc	ciliary rootlet coiled-coil, rootletin	Yes	No
Cryaa	crystallin, alpha A	No	No
Cryab	crystallin, alpha B	Yes	No
Cryba1	crystallin, beta A1	Yes	No
Cryba2	crystallin, beta A2	No	No
Cryba4	crystallin, beta A4	Yes	No
Crybb1	crystallin, beta B1	No	No
Crybb2	crystallin, beta B2	No	No
Crybb3	crystallin, beta B3	No	No
Cryga	crystallin, gamma A	No	No
Crygb	crystallin, gamma B	No	No
Crygc	crystallin, gamma C	No	No
Crygd	crystallin, gamma D	No	Yes
Crygf	crystallin, gamma F	No	No
Crygn	crystallin, gamma N	No	No
Crygs	crystallin, gamma S	No	No
D17H6S56E-5	DNA segment, Chr 17, human D6S56E 5	Yes	No
Dcx	doublecortin	Yes	Yes
Ddx6	DEAD (Asp-Glu-Ala-Asp) box polypeptide 6	No	Yes
Dnajc28	DnaJ (Hsp40) homolog, subfamily C, member 28	No	No
Dohh// LOC100503793	deoxyhypusine hydroxylase/monooxygenase//hypothetical protein LOC100503793	No	No
Dpf3	D4, zinc and double PHD fingers, family 3	No	No
Dyx1c1	dyslexia susceptibility 1 candidate 1 homolog (human)	No	No
E2f7	E2F transcription factor 7	No	No
E2f8	E2F transcription factor 8	Yes	No
Eno4	enolase 4	No	No

(Continued)

genesymbol	genetitle	Epigenetic	Deregulated in human RB
Fabp5	fatty acid binding protein 5, epidermal	No	No
Fabp5///Gm3601	fatty acid binding protein 5, epidermal///predicted gene 3601	No	No
Fabp7	fatty acid binding protein 7, brain	No	Yes
Fam161a	family with sequence similarity 161, member A	No	No
Fbxo5	F-box protein 5	Yes	No
Flad1///Lenep	RFad1, flavin adenine dinucleotide synthetase, homolog (yeast)/// lens epithelial prot	No	No
Gas2l3	growth arrest-specific 2 like 3	Yes	Yes
Giyd2	GIY-YIG domain containing 2	Yes	No
Gm7659	Predicted gene 7659	No	No
Gm9918	predicted gene 9918	No	No
Gpr116	G protein-coupled receptor 116	No	Yes
H2-Q6///LOC68395	histocompatibility 2, Q region locus 6///histocompatibility 2, Q region locus 6-like	No	No
H2-Q7	histocompatibility 2, Q region locus 7	No	No
H2-T24	histocompatibility 2, T region locus 24	No	No
Hells	helicase, lymphoid specific	Yes	No
Hk2	hexokinase 2	No	No
Impg1	interphotoreceptor matrix proteoglycan 1	No	No
Jam2	junction adhesion molecule 2	No	Yes
Katnal2	katanin p60 subunit A-like 2	No	No
Kcnj14	potassium inwardly-rectifying channel, subfamily J, member 14	No	No
Lim2	lens intrinsic membrane protein 2	No	No
LOC100503456	hypothetical LOC100503456	No	No
LOC100505359///Xlr4a///Xlr4b///Xlr4c	x-linked lymphocyte-regulated protein 3A-like///X-linked lymphocyte-regulated 4A ///	No	No
Lrit2	leucine-rich repeat, immunoglobulin-like and transmembrane domains 2	No	No
Lrp2bp	Lrp2 binding protein	No	No
Lrrc67	leucine rich repeat containing 67	No	No
Mcm4	minichromosome maintenance deficient 4 homolog (S. cerevisiae)	No	No
Mcm7	minichromosome maintenance deficient 7 (S. cerevisiae)	Yes	No
Meig1	meiosis expressed gene 1	No	No
Ncapg2	non-SMC condensin II complex, subunit G2	No	Yes
Nfya	nuclear transcription factor-Y alpha	No	No
Nsg2	neuron specific gene family member 2	No	No
Nupr1	nuclear protein 1	No	No

(Continued)

genesymbol	genetitle	Epigenetic	Deregulated in human RB
Nxn1	nucleoredoxin-like 1	No	No
Pde6a	phosphodiesterase 6A, cGMP-specific, rod, alpha	No	No
Pdia5	protein disulfide isomerase associated 5	No	Yes
Pfk1	phosphofructokinase, liver, B-type	No	Yes
Pigo	phosphatidylinositol glycan anchor biosynthesis, class O	No	No
Pim1	proviral integration site 1	Yes	No
Pla2r1	phospholipase A2 receptor 1	No	No
Pole	polymerase (DNA directed), epsilon	Yes	No
Pon1	paraoxonase 1	No	No
Prdx4	peroxiredoxin 4	Yes	No
Racgap1	Rac GTPase-activating protein 1	Yes	No
Rad51ap1	RAD51 associated protein 1	Yes	No
Rbm39	RNA binding motif protein 39	No	No
Rgr	retinal G protein coupled receptor	No	No
Rgs20	regulator of G-protein signaling 20	No	No
Rora	RAR-related orphan receptor alpha	No	No
Rs1	retinoschisis (X-linked, juvenile) 1 (human)	No	Yes
Rspo2	R-spondin 2 homolog (<i>Xenopus laevis</i>)	Yes	Yes
Samd7	sterile alpha motif domain containing 7	No	No
Sec22c	SEC22 vesicle trafficking protein homolog C (<i>S. cerevisiae</i>)	No	No
Serpina3n	serine (or cysteine) peptidase inhibitor, clade A, member 3N	No	No
Sgcg	sarcoglycan, gamma (dystrophin-associated glycoprotein)	No	No
Shcbp1	Shc SH2-domain binding protein 1	Yes	No
Slc17a1	solute carrier family 17 (sodium phosphate), member 1	No	No
Slc24a1	solute carrier family 24 (sodium/potassium/calcium exchanger), member 1	No	No
Slco4a1	solute carrier organic anion transporter family, member 4a1	No	Yes
Socs3	suppressor of cytokine signaling 3	No	No
Sox4	SRY-box containing gene 4	No	Yes
Spata1	spermatogenesis associated 1	Yes	No
Stk36	serine/threonine kinase 36 (fused homolog, <i>Drosophila</i>)	No	No
Stxbp1	syntaxin binding protein 1	No	No
Synpo2	synaptopodin 2	No	No
Tek	endothelial-specific receptor tyrosine kinase	No	No
Tm4sf1	transmembrane 4 superfamily member 1	Yes	Yes
Tmlhe	trimethyllysine hydroxylase, epsilon	No	Yes
Topbp1	topoisomerase (DNA) II binding protein 1	Yes	No

(Continued)

genesymbol	genetitle	Epigenetic	Deregulated in human RB
Traf3ip3	TRAF3 interacting protein 3	No	No
Ube2t	ubiquitin-conjugating enzyme E2T (putative)	Yes	No
Ubt2	ubiquitin domain containing 2	No	Yes
Ubxn7	UBX domain protein 7	No	No
Vtn	vitronectin	Yes	Yes
Wdr31	WD repeat domain 31	Yes	No
Wdr47	WD repeat domain 47	No	No
Xiap	X-linked inhibitor of apoptosis	No	No
Ypel2	yippee-like 2 (Drosophila)	No	Yes
Zfp882	zinc finger protein 882	No	No
Zik1	zinc finger protein interacting with K protein 1	No	No