Supplementary Information

Low-dose anti-HIV drug efavirenz mitigates retinal vascular lesions in a mouse model of Alzheimer's disease

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Table S1. Differentially expressed genes ($P \leq 0.05$) in efavirenz-treated (Tx) retina *vs* control (Cntr) retina in 5XFAD mice as identified by RNAseq.

Gene	Ratio, Tx/Cntr	Gene	Ratio, Tx/Cntr	Gene	Ratio, Tx/Cntr
5730507C01Rik	1.24	*D130040H23Rik*	1.20	*Gm5415*	1.42
Abca13	1.17	*Ddost*	0.90	*Gng13*	0.90
Ache	1.09	*Dock5*	0.72	*Gng7*	1.10
Adgrf4	1.49	*Dpm3*	0.81	*Gpi1*	0.94
Agr2	0.70	*Drd4*	0.92	*Gpnmb*	1.45
Akap6	0.87	*Dscam*	0.90	*Gpr37l1*	1.56
Akr1e1	0.79	*Dusp1*	0.84	*Grem2*	1.29
Alad	0.86	*Dusp11*	1.07	*Gtf2a1*	1.11
Aldoa	0.92	*Dusp26*	1.09	*Guca1b*	1.10
Alpl	0.92	*Ech1*	1.28	*Gvin1*	1.59
Ampd3	0.84	*Edn2*	1.53	*H2-Ob*	1.76
Armh4	0.65	*Efnb2*	1.15	*Hmgb1*	0.91
Bcas1	1.77	*Egln1*	0.92	*Hsp90b1*	0.91
Bfsp2	0.64	*Egr2*	0.63	*Hspb2*	0.62
Bmf	0.80	*Emilin1*	1.42	*Igip*	1.19
Bspry	0.71	*Eno1*	0.90	*Igsf9*	1.16
Bst1	1.18	*Enox1*	0.71	*Il4i1*	0.60
Bub1b	0.89	*Enpp2*	1.14	*Insig1*	0.90
Calm2	0.93	*Entpd4b*	0.84	*Irf9*	1.59
Car12	1.48	*Esrrb*	0.84	*Itih3*	1.52
Cd47	1.12	*Etnppl*	1.41	*Jmjd6*	0.91
Cdc26	1.16	*Fads2*	0.89	*Kcnh5*	0.83
Cdin1	0.80	*Fam89b*	1.70	*Kcnj13*	1.45
Cldn23	1.24	*Fgd1*	1.13	*Kcnv2*	1.07
Clu	0.91	*Fkbp2*	0.84	*Kdm1b*	1.16
Cnrip1	0.91	*Frmpd1*	0.92	*Klhl28*	1.19
Col1a2	1.37	*Gdf15*	0.61	*Lbh*	0.90
Col5a1	1.21	*Gfap*	1.29	*Lgals6*	1.69
Col8a2	1.40	*Glmn*	1.14	*Lmbrd2*	1.14
Cox6b1	0.90	*Gm1140*	1.61	*Lmtk3*	1.10
Crybb1	0.68	*Gm11837*	0.55	*Lpin2*	0.89
Crybb3	0.66	*Gm12657*	1.49	*Lrat*	1.49
Cubn	0.66	*Gm14692*	0.55	*Lrrc8e*	0.72
Cyp4f16	0.77	*Gm45929*	0.72	*Mbp*	1.15

Mex3b	0.79	*Pon1*	1.47	*Slco5a1*	1.20
Mip	0.68	*Ppp1r3e*	1.36	*Smco3*	0.63
Mmp28	1.47	*Prelid1*	0.92	*Smim24*	0.92
Mobp	1.65	*Prkaca*	1.08	*Snhg11*	1.10
Mrps10	1.17	*Prkdc*	1.13	*Srp54a*	1.42
Mtrfr	0.84	*Psd*	1.08	*Srp54b*	1.26
Myl6	0.91	*Ptov1*	1.11	*Srp54c*	1.21
Myo15	1.52	*Rab6a*	0.93	*Sssca1*	0.85
Myo7a	0.80	*Rag1*	0.61	*Ssu72*	0.89
Nat1	0.74	*Rbm4*	0.80	*Stard7*	1.07
Ndufa13	0.91	*Rdh16f2*	0.70	*Stra6*	1.26
Nkd2	1.52	*Ric8b*	1.08	*Styx*	1.09
Nono	0.93	*Rmdn3*	0.89	*Supt16*	1.09
Nr4a3	0.69	*Rnf144a*	0.83	*Svep1*	1.69
Nudc	0.91	*Rpe65*	1.44	*Tead3*	1.15
Nudt3	0.92	*Rpl21*	0.82	*Tfap4*	0.77
Nup62	0.84	*Rpl23a*	0.93	*Thbs1*	1.33
Nutf2	0.86	*Rpl26*	0.78	*Tmem170*	1.27
Oasl2	1.24	*Rpl28*	0.89	*Tmem237*	0.91
Obscn	1.39	*Rpl35*	0.91	*Tmem40*	0.55
Odc1	1.13	*Rpl41*	0.87	*Tnxb*	1.28
Oog4	0.67	*Rpl7a*	0.92	*Tom1*	0.88
Opn3	0.76	*Rplp0*	0.91	*Trappc1*	0.87
Pabpc4	0.90	*Rps10*	0.89	*Trerf1*	1.17
Pcdha9	0.78	*Rps15*	0.93	*Trib2*	1.13
Pcdhga1	0.85	*Rps28*	0.87	*Trove2*	1.10
Pcsk1n	0.93	*Sap18b*	0.89	*Tspyl4*	0.93
Pde6g	0.91	*Sec61g*	0.84	*Tusc2*	0.91
Pfkfb2	1.07	*Sema3e*	0.87	*Tusc3*	1.12
Pfkfb3	0.88	*Sik1*	0.81	*Ubb*	0.91
Pfkl	0.90	*Sirt5*	0.81	*Ube2h*	1.09
Pgm2	0.92	*Six6os1*	1.16	*Ubl5*	0.92
Pi15	0.52	*Skp1a*	1.08	*Unc13c*	1.13
Pkd1	1.07	*Slc12a9*	1.14	*Wdr31*	0.88
Pkm	0.93	*Slc16a8*	1.40	*Wfs1*	0.92
Pla2g12a	1.36	*Slc29a1*	0.75	*Ythdf1*	1.13
Pnma3	0.79	*Slc30a3*	1.35	*Zan*	0.86
Pnp2	0.59	*Slc7a1*	0.81	*Zbtb20*	1.30

Zbtb43	1.13	*Zfp445*	1.07	*Zmat3*	1.18
Zfp383	1.15	*Zfp512b*	1.09		

Table S2. Differentially expressed proteins ($P \leq 0.05$) in efavirenz-treated (Tx) retina *vs* control (Cntr) retina in 5XFAD mice as identified by the label-free approach.

Protein name	# Unique peptides	Sequence Coverage (%)	Tx/Cntr ratio	Protein name	# Unique peptides	Sequence Coverage (%)	Tx/Cntr ratio
ATG7	2	6	0.33	MGN2	1	8	0.13
BZW1	1	7	0.14	MYPT1	2	3	0.67
CD59A	1	14	0.07	NCLN	3	7	0.43
CHKB	1	5	0.20	NDUB1	1	19	0.05
CNBP	3	22	0.14	NDUB7	4	36	0.11
COR2B	2	4	0.50	NFH	1	2	0.50
DCTN1	17	22	0.77	NMT1	5	25	0.20
DDAH2	9	59	0.15	NRCAM	10	13	0.77
DENR	2	12	0.17	NT5C	3	26	0.12
DHX30	1	1	1.00	NU214	1	1	1.00
DUS3	3	24	0.13	PAQR4	1	5	0.20
EIF3I	3	15	0.20	PDE6B	20	47	0.43
EIF3M	2	8	0.25	PDS5B	1	1	1.00
ELMD2	2	9	0.22	PGRC2	4	41	0.10
EMB	2	7	0.29	PLST	5	12	0.42
EMC8	2	13	0.15	PP2AB	1	43	0.02
EPHB2	7	10	0.70	PPIB	5	26	0.19
FCL	3	15	0.20	PTEN	1	4	0.25
GMEB1	1	5	0.20	RAB6A	1	12	0.08
GMPR1	1	4	0.25	RACK1	13	57	0.23
GRK1	21	49	0.43	RAE1L	2	8	0.25
GSHR	6	22	0.27	RD23B	2	7	0.29
GSTT2	1	5	0.20	RN170	1	5	0.20
HCN1	4	8	0.50	SAFB1	4	14	0.29
HMGCL	3	15	0.20	SC6A1	6	15	0.40
IF4G2	5	12	0.42	SCPDL	3	16	0.19
IVD	2	6	0.33	SEC13	5	23	0.22
KBL	3	13	0.23	SFXN5	6	29	0.21
LY6H	1	9	0.11	SNX3	3	25	0.12
LYAR	5	18	0.28	SP16H	4	6	0.67
MACF1	11	3	3.67	SPCS1	1	7	0.14
MARE2	7	39	0.18	SRSF5	1	9	0.11
MCTS1	3	28	0.11	TADBP	8	33	0.24

MGN	1	8	0.13	TGM2	1	2	0.50
THYN1	4	18	0.22	VAT1	4	15	0.27
TRIM2	3	6	0.50	WBP2	1	4	0.25
UBP14	5	20	0.25				

Supplemental Table S3. List of variants consistent with a dominant inheritance pattern.

<table>
<tr><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th colspan="6">Genotype</th><th></th><th></th><th></th><th></th></tr>
<tr><th>Chr</th><th>Start (bp)</th><th>End (bp)</th><th>Gene</th><th>Ref allele</th><th>Alt allele</th><th>dbSNP</th><th>1153</th><th>68</th><th>942</th><th>1149</th><th>9655</th><th>1150</th><th>Annotation (primary transcript)</th><th>Annotation (alt transcript)</th><th>Transcript: Variant</th><th>Transcript isoforms with annotation</th></tr>
<tr><td>chr1</td><td>20990590</td><td>20990590</td><td>Efhc1</td><td>C</td><td>CTT</td><td>rs260911513</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_027974:c.1876-26_1876-25insTT</td><td>intron_variant(MODIFIER|||c.1876-26_1876-25insTT|648|Efhc1|protein_coding|CODING|NM_027974|10|1)</td></tr>
<tr><td>chr1</td><td>38812397</td><td>38812397</td><td>Lonrf2</td><td>AAC</td><td>A</td><td>rs226794629</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_001029878:c.653+145_653+146delGT</td><td>intron_variant(MODIFIER|||c.653+145_653+146delGT|518|Lonrf2|protein_coding|CODING|NM_001029878|5|1)</td></tr>
<tr><td>chr1</td><td>45391638</td><td>45391638</td><td>Col5a2</td><td>GA</td><td>G</td><td>rs387070045</td><td>het</td><td>hom</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_007737:c.2709+23delT</td><td>intron_variant(MODIFIER|||c.2709+23delT|1497|Col5a2|protein_coding|CODING|NM_007737|40|1)</td></tr>
<tr><td>chr1</td><td>45805341</td><td>45805341</td><td>Wdr75</td><td>G</td><td>GTT</td><td></td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_028599:c.496-35_496-34insTT</td><td>intron_variant(MODIFIER|||c.496-35_496-34insTT|830|Wdr75|protein_coding|CODING|NM_028599|5|1)</td></tr>
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<tr><td>chr1</td><td>80578770</td><td>80578770</td><td>Dock10</td><td>TACACACAC</td><td>T</td><td></td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_175291:c.1686-70_1686-63delGTGTGTGT</td><td>intron_variant(MODIFIER|||c.1686-70_1686-63delGTGTGTGT|2187|Dock10|protein_coding|CODING|NM_175291|14|1)</td></tr>
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<tr><td>chr5</td><td>147526800</td><td>147526800</td><td>Pan3</td><td>CT</td><td>C</td><td>rs261040637</td><td>hom</td><td>het</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_028291:c.1411+121delT</td><td>intron_variant(MODIFIER|||c.1411+121delT|837|Pan3|protein_coding|CODING|NM_028291|9|1)</td></tr>
<tr><td>chr6</td><td>93701094</td><td>93701094</td><td>Magi1</td><td>AAAC</td><td>A</td><td></td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_001029850:c.2568+193_2568+195delGTT</td><td>intron_variant(MODIFIER|||c.2568+193_2568+195delGTT|1471|Magi1|protein_coding|CODING|NM_001029850|16|1),intron_variant(MODIFIER|||c.1884+193_1884+195delGTT|1255|Magi1|protein_coding|CODING|NM_001083320|15|1),intron_variant(MODIFIER|||c.1887+193_1887+195delGTT|1020|Magi1|protein_coding|CODING|NM_001083321|15|1),intron_variant(MODIFIER|||c.2445+193_2445+195delGTT|1171|Magi1|protein_coding|CODING|NM_010367|14|1)</td></tr>
<tr><td>chr6</td><td>125010499</td><td>125010499</td><td>Zfp384</td><td>CT</td><td>C</td><td>rs225093781</td><td>hom</td><td>hom</td><td>hom</td><td>het</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_175557:c.-6+60delT</td><td>intron_variant(MODIFIER|||c.-6+60delT|554|Zfp384|protein_coding|CODING|NM_001252083|2|1),intron_variant(MODIFIER|||c.-6+60delT|584|Zfp384|protein_coding|CODING|NM_175557|2|1)</td></tr>
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<tr><td>chr9</td><td>63358105</td><td>63358105</td><td>Map2k5</td><td>C</td><td>CT</td><td>rs263420860</td><td>hom</td><td>het</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_011840:c.185-45_185-46insA</td><td>intron_variant(MODIFIER|||c.185-45_185-46insA|448|Map2k5|protein_coding|CODING|NM_011840|2|1)</td></tr>
<tr><td>chr9</td><td>66463170</td><td>66463170</td><td>Herc1</td><td>GCT</td><td>G</td><td></td><td>hom</td><td>het</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_145617:c.9164+74_9164+75delCT</td><td>intron_variant(MODIFIER|||c.9164+74_9164+75delCT|4859|Herc1|protein_coding|CODING|NM_145617|45|1)</td></tr>
<tr><td>chr9</td><td>66547959</td><td>66547959</td><td>Usp3</td><td>C</td><td>CAAAAAAAA</td><td></td><td>hom</td><td>het</td><td>het</td><td>het</td><td>het</td><td></td><td>splice_region_variant</td><td>protein_coding</td><td>NM_144937:c.285_286insTTTTTTTT</td><td>splice_region_variant(LOW|||c.285_286insTTTTTTTT|520|Usp3|protein_coding|CODING|NM_144937|3|1),intron_variant(MODIFIER|||c.285-4_285-5insTTTTTTTT|520|Usp3|protein_coding|CODING|NM_144937|3|1)</td></tr>
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<tr><td>chr9</td><td>67899903</td><td>67899903</td><td>Vps13c</td><td>TAA</td><td>T</td><td></td><td>hom</td><td>het</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_177184:c.2405+1154_2405+1155delAA</td><td>intron_variant(MODIFIER|||c.2405+1154_2405+1155delAA|3748|Vps13c|protein_coding|CODING|NM_177184|24|1)</td></tr>
<tr><td>chr9</td><td>68769386</td><td>68769386</td><td>Rora</td><td>G</td><td>GT</td><td></td><td>het</td><td>het</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_013646:c.166+115415_166+115416insT</td><td>intron_variant(MODIFIER|||c.166+115415_166+115416insT|523|Rora|protein_coding|CODING|NM_013646|1|1),non_coding_exon_variant(MODIFIER|||n.4042_4043insT||9530091C08Rik||NON_CODING|NR_033299|1|1)</td></tr>
<tr><td>chr9</td><td>75450595</td><td>75450595</td><td>Leo1</td><td>CTT</td><td>C</td><td>rs232490069</td><td>hom</td><td>het</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_001039522:c.1248+24_1248+25delTT</td><td>intron_variant(MODIFIER|||c.1248+24_1248+25delTT|667|Leo1|protein_coding|CODING|NM_001039522|6|1)</td></tr>
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<tr><td>chr10</td><td>14444202</td><td>14444202</td><td>Gpr126</td><td>A</td><td>ATT</td><td></td><td>het</td><td>het</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_001002268:c.1344-54_1344-55insAA</td><td>intron_variant(MODIFIER|||c.1344-54_1344-55insAA|1165|Gpr126|protein_coding|CODING|NM_001002268|8|1)</td></tr>
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<tr><td>chr10</td><td>18470182</td><td>18470182</td><td>Nhsl1</td><td>CGTGT</td><td>C</td><td></td><td>het</td><td>het</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_173390:c.203-2736_203-2733delGTGT</td><td>intron_variant(MODIFIER|||c.203-2736_203-2733delGTGT|1587|Nhsl1|protein_coding|CODING|NM_173390|1|1),intron_variant(MODIFIER|||c.58+18_58+21delGTGT|1583|Nhsl1|protein_coding|CODING|NM_001163592|1|1)</td></tr>
<tr><td>chr11</td><td>106830881</td><td>106830881</td><td>Smurf2</td><td>CTTTTTTT</td><td>C</td><td></td><td>het</td><td>het</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_025481:c.1748+32_1748+38delAAAAAAA</td><td>intron_variant(MODIFIER|||c.1748+32_1748+38delAAAAAAA|748|Smurf2|protein_coding|CODING|NM_025481|15|1)</td></tr>
<tr><td>chr12</td><td>29984749</td><td>29984749</td><td>Pxdn</td><td>T</td><td>TGGG</td><td>rs264717772</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_181395:c.722-117_722-116insGGG</td><td>intron_variant(MODIFIER|||c.722-117_722-116insGGG|1475|Pxdn|protein_coding|CODING|NM_181395|7|1)</td></tr>
<tr><td>chr12</td><td>50366266</td><td>50366266</td><td>Prkd1</td><td>G</td><td>GT</td><td></td><td>het</td><td>het</td><td>hom</td><td>hom</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_008858:c.2085+36_2085+35insA</td><td>intron_variant(MODIFIER|||c.2085+36_2085+35insA|918|Prkd1|protein_coding|CODING|NM_008858|15|1)</td></tr>
<tr><td>chr12</td><td>50490135</td><td>50490135</td><td>Prkd1</td><td>CT</td><td>C</td><td></td><td>hom</td><td>hom</td><td>hom</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_008858:c.259-95delA</td><td>intron_variant(MODIFIER|||c.259-95delA|918|Prkd1|protein_coding|CODING|NM_008858|1|1)</td></tr>
<tr><td>chr12</td><td>55410409</td><td>55410409</td><td>Psma6</td><td>GTT</td><td>G</td><td></td><td>hom</td><td>het</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_011968:c.409+128_409+129delTT</td><td>intron_variant(MODIFIER|||n.22+39694_22+39695delTT||Mir1198||NON_CODING|NR_035430|1|1),intron_variant(MODIFIER|||c.409+128_409+129delTT|246|Psma6|protein_coding|CODING|NM_011968|4|1)</td></tr>
<tr><td>chr12</td><td>56340178</td><td>56340178</td><td>Mbip</td><td>T</td><td>TA</td><td></td><td>hom</td><td>het</td><td>het</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_145442:c.565+23_565+22insT</td><td>intron_variant(MODIFIER|||c.565+23_565+22insT|341|Mbip|protein_coding|CODING|NM_145442|4|1)</td></tr>
<tr><td>chr13</td><td>4078094</td><td>4078094</td><td>Akr1c14</td><td>GAGAGAGAG</td><td>G</td><td></td><td>het</td><td>hom</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_134072:c.447+48_447+57delGAGAGAGAGA</td><td>intron_variant(MODIFIER|||c.447+48_447+57delGAGAGAGAGA|323|Akr1c14|protein_coding|CODING|NM_134072|4|1)</td></tr>
<tr><td>chr15</td><td>6837600</td><td>6837600</td><td>Osmr</td><td>GAAA</td><td>G</td><td></td><td>het</td><td>het</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_011019:c.1122+89_1122+91delTTT</td><td>intron_variant(MODIFIER|||c.1122+89_1122+91delTTT|971|Osmr|protein_coding|CODING|NM_011019|8|1)</td></tr>
<tr><td>chr15</td><td>8121958</td><td>8121958</td><td>Nup155</td><td>TGTGTGTGT</td><td>C</td><td></td><td>het</td><td>het</td><td>het</td><td>het</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_133227:c.1094-97_1094-88delTGTGTGTGTG</td><td>intron_variant(MODIFIER|||c.1094-97_1094-88delTGTGTGTGTG|1391|Nup155|protein_coding|CODING|NM_133227|10|1)</td></tr>
<tr><td>chr15</td><td>10591698</td><td>10591698</td><td>Rai14</td><td>T</td><td>TACAC</td><td></td><td>het</td><td>het</td><td>het</td><td>het</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_001166408:c.737-83_737-84insGTGT</td><td>intron_variant(MODIFIER|||c.737-83_737-84insGTGT|979|Rai14|protein_coding|CODING|NM_001166408|9|1),intron_variant(MODIFIER|||c.737-83_737-84insGTGT|979|Rai14|protein_coding|CODING|NM_030690|9|1)</td></tr>
<tr><td>chr16</td><td>7223821</td><td>7223821</td><td>Rbfox1</td><td>T</td><td>TACAC</td><td></td><td>hom</td><td>het</td><td>hom</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_183188:c.88-489_88-488insACAC</td><td>intron_variant(MODIFIER|||c.28-489_28-488insACAC|396|Rbfox1|protein_coding|CODING|NM_021477|5|1),intron_variant(MODIFIER|||c.88-489_88-488insACAC|417|Rbfox1|protein_coding|CODING|NM_183188|1|1)</td></tr>
<tr><td>chrX</td><td>49494731</td><td>49494731</td><td>Arhgap36</td><td>GCT</td><td>G</td><td></td><td>het</td><td>hom</td><td>het</td><td>het</td><td>het</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_001081123:c.283+21_283+22delCT</td><td>intron_variant(MODIFIER|||c.283+21_283+22delCT|590|Arhgap36|protein_coding|CODING|NM_001081123|3|1)</td></tr>
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Supplemental Table S4. List of variants consistent with a recessive inheritance pattern.

<table>
<tr><th rowspan="2">Chr</th><th rowspan="2">Start (bp)</th><th rowspan="2">End (bp)</th><th rowspan="2">Gene</th><th rowspan="2">Ref Allele</th><th rowspan="2">Alt allele</th><th rowspan="2">dbSNP</th><th colspan="6">Genotype</th><th rowspan="2">Annotation (primary transcript)</th><th rowspan="2">Annotation (alt transcript)</th><th rowspan="2">Transcript: Variant</th><th rowspan="2">Transcript isoforms with annotation</th></tr>
<tr><th>1153</th><th>68</th><th>942</th><th>1149</th><th>9655</th><th>1150</th></tr>
<tr><td>chr1</td><td>20814934</td><td>20814934</td><td>Mcm3</td><td>G</td><td>GGGA</td><td>rs242440541</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>het</td><td>splice_region_variant</td><td>protein_coding</td><td>NM_008563:c.532_533insTCC</td><td>splice_region_variant(LOW|||c.532_533insTCC|812|Mcm3|protein_coding|CODING|NM_008563|4|1),intron_variant(MODIFIER|||c.532-7_532-8insTCC|812|Mcm3|protein_coding|CODING|NM_008563|4|1)</td></tr>
<tr><td>chr1</td><td>20990590</td><td>20990590</td><td>Efhc1</td><td>C</td><td>CTT</td><td>rs260911513</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_027974:c.1876-26_1876-25insTT</td><td>intron_variant(MODIFIER|||c.1876-26_1876-25insTT|648|Efhc1|protein_coding|CODING|NM_027974|10|1)</td></tr>
<tr><td>chr1</td><td>38812397</td><td>38812397</td><td>Lonrf2</td><td>AAC</td><td>A</td><td>rs226794629</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_001029878:c.653+145_653+146delGT</td><td>intron_variant(MODIFIER|||c.653+145_653+146delGT|518|Lonrf2|protein_coding|CODING|NM_001029878|5|1)</td></tr>
<tr><td>chr1</td><td>44175792</td><td>44175792</td><td>Ercc5</td><td>GTA</td><td>G</td><td>rs233333477</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>het</td><td>intron_variant</td><td>protein_coding</td><td>NM_011729:c.2531-46_2531-45delTA</td><td>intron_variant(MODIFIER|||c.2531-46_2531-45delTA|1170|Ercc5|protein_coding|CODING|NM_011729|11|1)</td></tr>
<tr><td>chr1</td><td>45805341</td><td>45805341</td><td>Wdr75</td><td>G</td><td>GTT</td><td></td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td></td><td>intron_variant</td><td>protein_coding</td><td>NM_028599:c.496-35_496-34insTT</td><td>intron_variant(MODIFIER|||c.496-35_496-34insTT|830|Wdr75|protein_coding|CODING|NM_028599|5|1)</td></tr>
<tr><td>chr1</td><td>59107615</td><td>59107615</td><td>Tmem237</td><td>C</td><td>CCACACA</td><td></td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>het</td><td>intron_variant</td><td>protein_coding</td><td>NM_001033449:c.894-88_894-89insTGTGTG</td><td>intron_variant(MODIFIER|||c.894-88_894-89insTGTGTG|413|Tmem237|protein_coding|CODING|NM_001033449|9|1),intron_variant(MODIFIER|||c.864-88_864-89insTGTGTG|403|Tmem237|protein_coding|CODING|NM_001037812|9|1)</td></tr>
<tr><td>chr1</td><td>64937781</td><td>64937781</td><td>Plekhm3</td><td>C</td><td>CCTGCTG</td><td></td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>het</td><td>inframe_insertion</td><td>protein_coding</td><td>NM_001039493:p.Gln176_Ala177insGlnGlnGln/c.528_529insCAGCAG</td><td>inframe_insertion(MODERATE||cag/cagCAGCAG|p.Gln176_Ala177insGlnGlnGln/c.528_529insCAGCAG|761|Plekhm3|protein_coding|CODING|NM_001039493|2|1)</td></tr>
<tr><td>chr1</td><td>75529223</td><td>75529223</td><td>Stk11ip</td><td>T</td><td>TGGAGGA</td><td></td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>hom</td><td>het</td><td>inframe_insertion</td><td>protein_coding</td><td>NM_027886:p.Leu512_Glu513insLeuGluGlu/c.1536_1537insGGAGGA</td><td>inframe_insertion(MODERATE||ctg/ctGGAGGAg|p.Leu512_Glu513insLeuGluGlu/c.1536_1537insGGAGGA|1072|Stk11ip|protein_coding|CODING|NM_027886|14|1)</td></tr>
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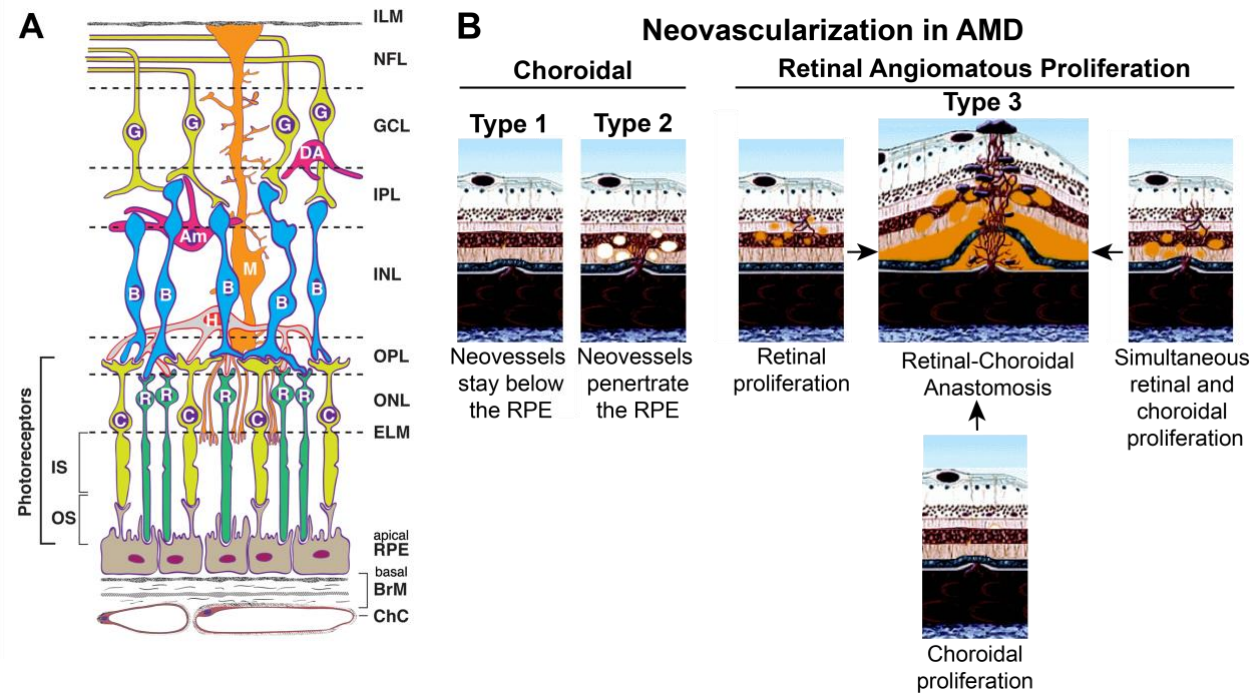

Figure S1. The retina and age-related macular degeneration. A, chorioretinal cells and layers. Taken from Zheng *et al*. 2012, PLos One, and modified. Cells (from bottom to top): RPE, retinal pigment epithelium (nurse cells to the photoreceptors); C, cone photoreceptor; R, rod photoreceptor; H, horizontal cell (interneuron); B, bipolar cell (interneuron); M, Müller cell (radial glial cell); Am, amacrine cell (interneuron); DA, displaced amacrine cell (interneuron); G, ganglion cell (output neuron). Müller cells (M) extend almost the width of the retina; their apical processes form the ELM, and their foot processes partially form the ILM. Layers (from bottom to top): ChC, choriocapillaris (capillary bed for the RPE and photoreceptors); BrM, Bruch's membrane (vessel wall and RPE substratum); ELM, external limiting membrane (junctional complexes); ONL, outer nuclear layer; OPL, outer plexiform layer (synapses); INL, inner nuclear layer; IPL, inner plexiform layer; GCL, ganglion cell layer; NFL, nerve fiber layer (ganglion cell axons); ILM, inner limiting membrane. Non-photoreceptor layers of the retina are supplied by the retinal circulation (not shown). Graphics by D. Fisher; inspired by Figure 4-2 of Ryan SJ, editor. **B**, Schematic representation of neovascularization in age-related macular degeneration (AMD). Taken with permission from Yannuzzi et al. 2008, Retina, and modified. See main text for details.

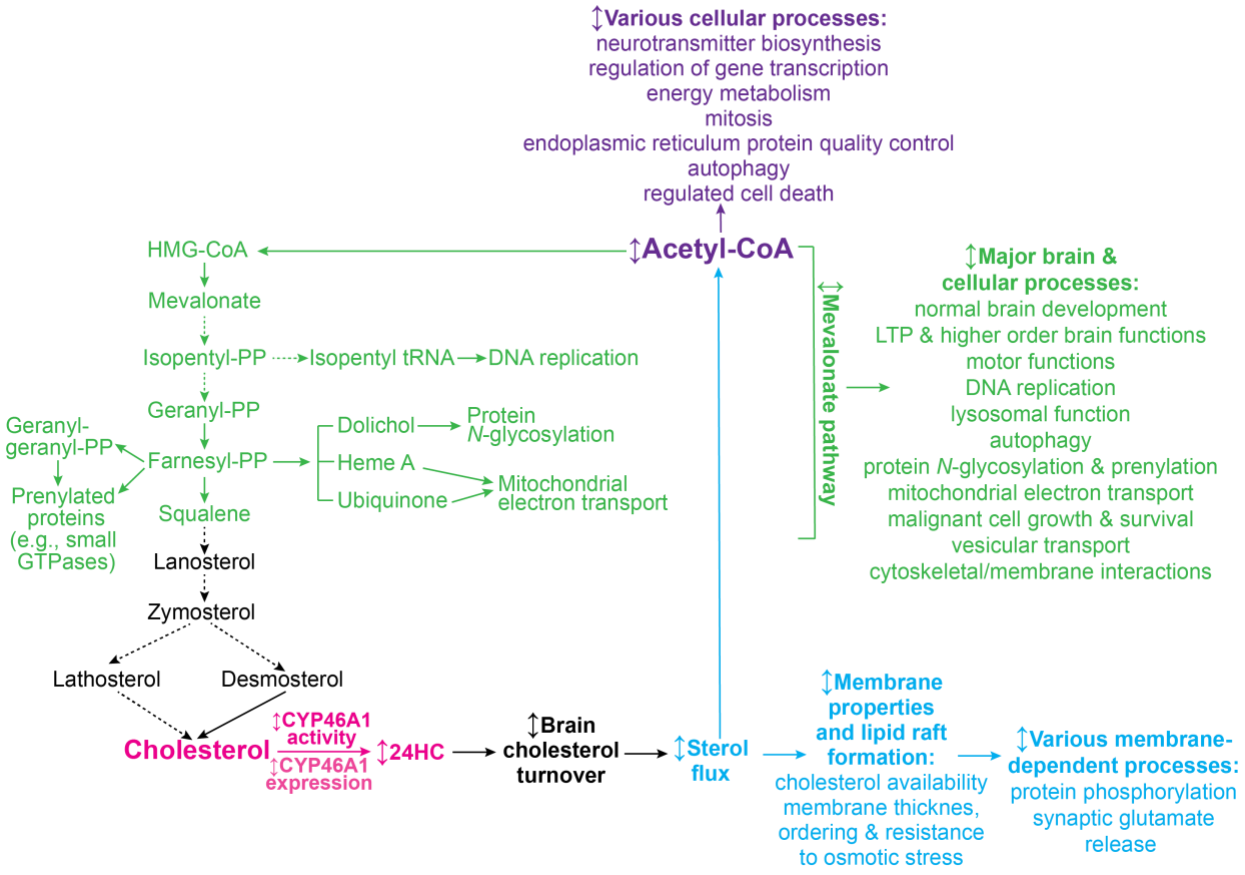

Figure S2. Schematic representation of the three primary processes (the unifying mechanisms) that can integrate a variety of CYP46A1 targeting effects. These are mevalonate pathway (green), sterol flux (blue), and acetyl-CoA production (violet). See main text for details. The initial event, CYP46A1-mediated cholesterol 24-hydroxylation, is colored in magenta. Dashed arrows indicate multiple steps; ↕: the up-down arrow indicates modulation (increase or decrease); HMG: 3-hydroxy-3-methylglutaryl; PP, pyrophosphate. Taken from Pikuleva, 2021, *Explor Neuroprot Ther*.