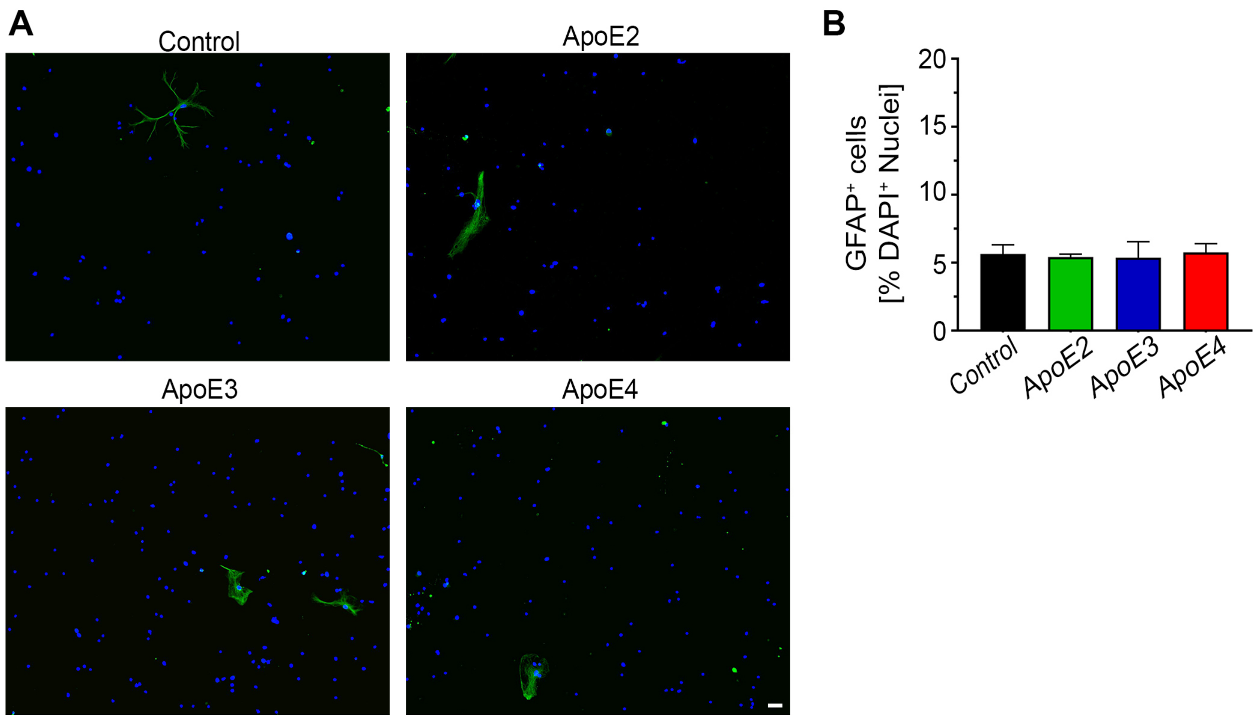
SUPPLEMENTARY MATERIALS

Supplementary Figure 1



Supplementary Figure 1. Monitoring astrocytic contaminations in dissociated neuronal cultures. **A.** Representative microphotographs of 17 DIV hippocampal primary neuronal cultures grown in the presence of control media (from *Apoe*$^{-/-}$ astrocytes) or indicated apoE lipoproteins, which were stained against GFAP and counterstained with DAPI. **B.** Shown is analysis of the number of GFAP-labeled cells against all cells in the culture, which nuclei were labeled with DAPI. Contamination of dissociated neuronal cultures by native astrocytes is in the range of 5.5% and does not vary across treatment conditions. Values represent mean + SEM from three cultures independently established per each treatment condition. **B** p = 0.98 (ANOVA). Scale bar 50 μm in **A**.

Supplementary Table 1. List of transcription factors differentially enriched in primary hippocampal neurons by apoE2, apoE3, or apoE4 lipoproteins. Transcription factors involved in KEGG pathways are highlithed in red. Fold change vs. control neurons grown in the apoE absence. NE - not expressed in the control neurons. *t*-test *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$ vs. control neurons.

Gene	Encoded Protein Name	ApoE2	ApoE3	ApoE4	Function
Ascl2	Achaete-scute family bhlh transcription factor 2	6.6****	7.3****		Neurodevelopment
Cebpb	CCAAT/enhancer-binding protein beta (Kfoury and		2.2*		Synaptic plasticity
Cebpd	CCAAT Enhancer Binding Protein Delta		2.7*		Immune/inflammatory responses
Egr2	E3 SUMO-Protein Transferase ERG2		-2.3*		Myelin formation and maintenance
Elf4	E74-like factor 4 (Kosti et al., 2020)		3.8*	20.9****	Cell cycle
Elk3	ETS Transcription Factor ELK3		2.6*		ERK signaling
Hmga2	High mobility group AT-hook 2		12.2**	3.9*	Cell cycle
Lhx4	LIM/homeobox protein Lhx4		2.5**		Neurodevelopment
Litaf	Lipopolysaccharide-induced tumor necrosis factor-alpha		3.1*		Endosomal/lysosomal pathway
Tcf7	Transcription factor 7		2.9*		Hippo signaling pathway
Tead2	Transcriptional enhancer factor TEF-2		2.7*		Hippo signaling pathway
Tead4	Transcriptional enhancer factor TEF-4		2.5*	2.9**	Hippo signaling pathway
Vdr	Vitamin D3 receptor (Gezen-Ak et al., 2011)	3.0*	6.0***	4.9***	AD pathogenesis
Ets1	E26 avian leukemia oncogene 1, 5' domain			2.6*	Neurodevelopment
Mybl2	Myeloblastosis oncogene-like 2 (Musa et al., 2017)			3.8*	Cell cycle
Elk4	ETS Transcription Factor ELK4			3.5****	ERK pathway and apoptosis
Six4	Sine oculis-related homeobox 4			4.9****	Neurodevelopment
E2f2	E2F transcription factor 2			12.5****	Cell cycle
Runx1	RUNX Family Transcription Factor 1 (Fukui et al., 2018)			2.6*	Reduction of dendritic complexity
Pax3	Paired box 3 (Lin et al., 2016)			NE**	Neurodevelopment
Tead1	TEA domain family member 1			2.3**	Hippo signaling pathway
Gli3	GLI-Kruppel family member GLI3			2.6*	Neurodevelopment
Hoxa3	Homeobox A3			21.1**	Neurodevelopment
E2f7	E2F transcription factor 7			8.0****	Cell cycle
Six3	Sine oculis-related homeobox 3			2.8*	Neurodevelopment
Creb3l3	CAMP Responsive Element Binding Protein 3 Like 3			-2.9*	Endoplasmic reticulum stress response
Klf5	Kruppel Like Factor 5 (Yanagi et al., 2008)			2.1**	Synaptic plasticity
Prrx1	Paired Related Homeobox 1 (Shimozaki et al., 2013)			2.2*	Neuronal cell linage determination/self-
Mafg	MAF BZIP Transcription Factor G (Katsuoka et al., 2003)			2.0****	Glycine signaling

Supplementary Table 2. List of KEGG pathways and individual genes of KEGG pathways, which are differentially enriched by apoE2, apoE3, or apoE4 lipoprotein treatment in primary hippocampal neurons. Fold change vs. control neurons grown in the apoE absence. NE - not expressed in apoE treatment. *t*-test **p* < 0.05, ***p* < 0.01, ****p* < 0.001, *****p* < 0.0001 vs. control neurons.

Pathway Name	Gene	Encoded Protein Name	*p* value			Fold Change / *p* value		
			ApoE2	ApoE3	ApoE4	ApoE2	ApoE3	ApoE4
PI3K-AKT	*Col4a3*	Collagen, type IV, alpha 3 (Kerrisk et al., 2014, Kurshan and Shen, 2019)	0.0030	0.0012		3.9*		2.8*
	Prlr	Prolactin receptor				2.2*		
	Il7	Interleukin 7				3.7**	5.0**	
	Itga5	Integrin alpha-5 (Kerrisk et al., 2014, Kurshan and Shen, 2019)				2.5*	3.2*	2.6*
	Tnc	Tenascin C (Evers et al., 2002)				2.4*	3.8**	
	Col2a1	Collagen, type II, alpha 1 (Kerrisk et al., 2014, Kurshan and Shen, 2019)				3.4***		
	Ngfr	Tumor necrosis factor receptor superfamily member 16 (Rosch et al., 2005)				3.6**	7.7****	
	Fgf2	Fibroblast growth factor 2 (Woodbury and Ikezu, 2014)				2.2*	3.5**	3.0*
	Il2rb	Interleukin 2 receptor, beta chain (Woodbury and Ikezu, 2014)					7.0**	7.0**
	Flt1	FMS-like tyrosine kinase 1 (Woodbury and Ikezu, 2014)					2.3*	2.6**
	Osmr	Oncostatin-M-specific receptor subunit beta					3.3*	
	Col4a6	Collagen, type IV, alpha 6 (Kerrisk et al., 2014, Kurshan and Shen, 2019)					3.1*	
	Bcl2l11	Bcl-2-like protein 11					2.4****	
	Ccnd1	G1/S-specific cyclin-D1					2.2*	
	Itgav	Integrin alpha-V (Woodbury and Ikezu, 2014) (Kerrisk et al., 2014, Kurshan and Shen, 2019)					2.1*	
	Col6a1	Collagen alpha-1(VI) chain (Kerrisk et al., 2014, Kurshan and Shen, 2019)					2.5**	
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5 (Gross and Bassell, 2014)					2.6*	
	Pdgfd	Platelet-derived growth factor D (Woodbury and Ikezu, 2014)					3.1*	
	Spp1	Osteopontin					3.7*	

	Ptger3	Prostaglandin E receptor 3			2.1****		
	Glra1	Glycine receptor subunit alpha-1 (Becker et al., 2006, Horvath et al., 2014)			16.6***	7.9*	
	Prlr	Prolactin receptor			2.2*		
	P2ry2	P2Y purinoceptor 2 (Peterson et al., 2010)			3.0**	5.2***	2.9**
	Tacr1	NK-1 Receptor			2.7**	4.9****	
	Trhr	Thyrotropin-releasing hormone receptor (Daimon et al., 2013)			2.1****	2.2****	
	Bdkrb2	B2 bradykinin receptor			2.1*	3.0**	
	P2ry6	P2Y purinoceptor 6				2.4*	
Neuroactive ligand receptor	*Agtr1b*	Type-1B angiotensin II receptor; Receptor for angiotensin II (Guimond and Gallo-Payet, 2012)	0.0047	0.0230		3.6*	
	Drd2	D(2) dopamine receptor (Linden et al., 2018)				6.8****	
	Glra3	Glycine receptor subunit alpha-3 (McCracken et al., 2017)				3.4***	
	F2rl1	Coagulation factor II (thrombin) receptor-like 1			3.3*	3.9**	
	Ptgfr	Prostaglandin F Receptor				2.2*	
	Sstr5	Somatostatin receptor type 5 (Kailey et al., 2012)			NE*		
	Brs3	Bombesin receptor subtype-3 (Xiao et al., 2017)			NE*		
	Npffr1	Neuropeptide FF receptor 1 (Lin et al., 2017)			-2.1*		
	Glp1r	Glucagon-like peptide 1 receptor (Bliss and Lomo, 1973, Gilman et al., 2003, Abbas et al., 2009)			-3.0*		
	Col4a3	Collagen, type IV, alpha 3			3.9*		2.8*
	Itga5	Integrin alpha-5 (Kerrisk et al., 2014)			2.5*	3.2*	2.6*
	Tnc	Tenascin C			2.4*	3.8**	
	Col2a1	Collagen, type II, alpha 1			3.4***		
	Cd44	CD44 antigen (Skupien et al., 2014, Roszkowska et al., 2016)				2.9*	
ECM-receptor interaction	*Itgav*	Integrin alpha-V	0.0120	0.0072		2.1*	
	Col6a1	Collagen alpha-1(VI) chain				2.5**	
	Col4a6	Collagen, type IV, alpha 6				3.1*	
	Spp1	Osteopontin				3.7*	
	Osmr	Oncostatin-M-specific receptor subunit beta				3.3*	
	Socs3	Suppressor of cytokine signaling 3				3.5**	

	Ctf1	Cardiotrophin-1				3.0*	
	Il21r	Interleukin-21 receptor				4.0*	
	Il19	Interleukin-19				11.0**	
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5				2.6*	
	Il13ra1	Interleukin-13 receptor subunit alpha-1				2.4***	
Calcium signaling	*Ptger3*	Prostaglandin E receptor 3	0.0180		2.1****		
	Adcy7	Adenylate cyclase 7 (Sheng et al., 2013)			2.7****		
	Tacr1	Substance-P receptor			2.7**	4.9****	
	Trhr	Thyrotropin-releasing hormone receptor			2.1****	2.2****	
	Bdkrb2	B2 bradykinin receptor			2.1*	3.0**	
Inflamatory regulation of RTP channels	*Adcy7*	Adenylate cyclase 7 (Sheng et al., 2013)	0.0329		2.1****		
	Bdkrb2	B2 bradykinin receptor			2.1*	3.0**	
	P2ry2	P2Y purinoceptor 2 (Peterson et al., 2010)			3.0**	5.2***	2.9**
	Trpa1	Transient receptor potential cation channel, subfamily A, member 1			3.8*		
Cytokine-cytokine receptor interaction	*Il11*	Interlukin 11	0.045	0.0001	4.2*		
	Il12rb1	Interleukin 12 receptor, beta 1			3.3*		
	Il7	Interleukin 7			3.7**	5.0**	
	Ngfr	Tumor necrosis factor receptor superfamily member 16			3.6**	7.7****	
	Prlr	Prolactin receptor			2.2*		
	Bmp2	Bone morphogenetic protein 2				2.7*	
	Ctf1	Cardiotrophin-1				3.0*	
	Clcf1	Cardiotrophin-like cytokine factor 1 (Zou et al., 2009)				4.3*	
	Ccl6	C-C motif chemokine 6			2.5*		
	Il1r1	Interleukin-1 receptor type 1				3.0*	3.0*
	Il13ra1	Interleukin-13 receptor subunit alpha-1				2.4***	
	Il18rap	Interleukin-18 receptor accessory protein				6.2*	5.5*
	Il19	Interleukin-19				11.0**	
	Il2rb	Interleukin 2 receptor, beta chain				7.0**	7.0**

	Il21r	Interleukin-21 receptor					4.0*	
	Lif	LIF Interleukin 6 Family Cytokine					2.4*	
	Osmr	Oncostatin-M-specific receptor subunit beta					3.3*	
	Tnfsf12	Tumor necrosis factor ligand superfamily member 12					3.0*	
	Prlr	Prolactin receptor				2.2*		
	Il7	Interleukin 7				3.7**	5.0**	
	Il11	Interlukin 11					4.2*	
	Lif	LIF Interleukin 6 Family Cytokine					2.4*	
	Il2rb	Interleukin 2 receptor, beta chain					7.0**	7.0**
JAK-STAT	*Ccnd1*	G1/S-specific cyclin-D1	0.0468	0.0001			2.2*	
	Socs3	Suppressor of cytokine signaling 3					3.5**	
	Ctf1	Cardiotrophin-1					3.0*	
	Il21r	Interleukin-21 receptor					4.0*	
	Il19	Interleukin-19					11.0**	
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5					2.6*	
	Il13ra1	Interleukin-13 receptor subunit alpha-1					2.4***	
	Bdkrb2	B2 bradykinin receptor				2.1*	3.0**	
	Col4a3	Collagen, type IV, alpha 3				3.9*		2.8*
	Fgf2	Fibroblast growth factor 2				2.2*	3.5**	3.0*
	Wnt5b	Protein Wnt-5b				2.5***	2.5**	
	Agtr1b	Type-1B angiotensin II receptor; Receptor for angiotensin II					3.6*	
	Bmp2	Bone morphogenetic protein 2					2.7*	
Patways in cancer	*Casp8*	Caspase-8		0.0099	0.036		3.2**	
	Col4a6	Collagen, type IV, alpha 6 (Kerrisk et al., 2014, Kurshan and Shen, 2019)					3.1*	
	Ccnd1	G1/S-specific cyclin-D1					2.2*	
	Cdkn2b	Cyclin-dependent kinase 4 inhibitor B (Tawarayama et al., 2019)					2.5*	
	Egln3	Prolyl hydroxylase EGLN3					2.2**	
	Fzd10	Frizzled-10					2.9*	

	Itgav	Integrin alpha-V			2.1*	
	Mmp1a	Interstitial collagenase A			33.7**	15.0*
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5			2.6*	
	Pml	Promyelocytic leukemia protein			2.4*	
	Tcf7	Transcription factor 7			2.5*	
	Agtr1b	Type-1B angiotensin II receptor; Receptor for angiotensin II			3.6*	
	Bmp2	Bone morphogenetic protein 2			2.7*	
	Casp8	Caspase-8			3.2**	
	Col4a6	Collagen, type IV, alpha 6			3.1*	
	Fgf2	Fibroblast growth factor 2		2.2*	3.5**	3.0*
	Wnt5b	Protein Wnt-5b		2.5***	2.5**	
	Cbl	Casitas B-lineage lymphoma				2.1***
	E2f2	E2F transcription factor 2				12.5****
	Gli3	GLI-Kruppel family member GLI3				2.6*
	Cdk6	Cyclin-dependent kinase 6				3.8****
	Erbb2	Erb-b2 receptor tyrosine kinase 2				2.5*
	Runx1	Runt-related transcription factor 1				2.6*
	Wnt10b	Wingless-type MMTV integration site family, member 10B				3.0*
TNF signaling	*Bcl3*	B-cell lymphoma 3 protein homolog	0.0001		2.3*	
	Cebpb	CCAAT/enhancer-binding protein beta			2.2*	
	Casp8	Caspase-8			3.2**	
	Lif	Leukemia inhibitory factor			2.4*	2.1*
	Mmp3	Stromelysin-1 (Sedaghat et al., 2012)			4.6*	
	Mapk13	Mitogen-activated protein kinase 13			3.1*	
	Map3k8	Mitogen-activated protein kinase kinase kinase 8			2.7**	
	Nod2	Nucleotide-binding oligomerization domain containing 2			8.3*	9.0*
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5			2.6*	
	Sele	E-selectin			3.1*	
	Socs3	Suppressor of cytokine signaling 3			3.5**	

Proteo-glycans in cancer	*Cd44*	CD44 antigen	0.0002			2.9*	
	Cav1	Caveolin-1				2.3*	
	Cav2	Caveolin-2				2.0*	
	Ccnd1	G1/S-specific cyclin-D1				2.2*	
	Fgf2	Fibroblast growth factor 2			2.2*	3.5**	3.0*
	Fzd10	Frizzled-10				2.9*	
	Hbegf	Proheparin-binding EGF-like growth factor				2.4*	
	Itga5	Integrin alpha-5			2.5*	3.2*	2.6*
	Mapk13	Mitogen-activated protein kinase 13				3.1*	
	Msn	Moesin				2.7*	
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5				2.6*	
	Rras	Ras-related protein R-Ras				2.2*	
	Wnt5b	Protein Wnt-5b			2.5***	2.5**	
Hippo signaling	*Fzd10*	Frizzled-10	0.0001	0.0003		2.9*	
	Tcf7	Transcription factor 7				2.5*	
	Bmp2	Bone morphogenetic protein 2				2.7*	
	Ccnd1	G1/S-specific cyclin-D1				2.2*	
	Wnt5b	Protein Wnt-5b			2.5***	2.5**	
	Ctgf	Connective tissue growth factor			2.8*	4.1*	4.7*
	Id1	Inhibitor of DNA binding 1				5.0**	3.2*
	Tead4	Transcriptional enhancer factor TEF-4 (Lavado et al., 2018)				2.5*	2.9**
	Tead2	Transcriptional enhancer factor TEF-2 (Lavado et al., 2018)				2.7*	
	Wwtr1	WW domain-containing transcription regulator protein				3.0*	2.1*
	Snai2	Snail family zinc finger 2			3.0*	3.4*	3.2*
	Bmp8a	Bone morphogenetic protein 8A				7.5*	
	Ajuba	Ajuba LIM protein (Lavado et al., 2018)					4.0**
	Wnt10b	Wingless-type MMTV integration site family, member 10B					3.0*
	Mob1a	MOB kinase activator 1A					2.1**

	Tead1	TEA domain family member 1				2.3**	
	Limd1	LIM domains containing 1					2.3**
	Amotl1	Angiomotin-like 1 (Rojek et al., 2019)					2.6**
	Meis1	Homeobox protein Meis1				2.1*	
	Bmp2	Bone morphogenetic protein 2				2.7*	
	Fgf2	Fibroblast growth factor 2			2.2*	3.5**	3.0*
	Fzd10	Frizzled-10				2.9*	
	Id1	Inhibitor of DNA binding 1				5.0**	3.2*
	Id3	DNA-binding protein inhibitor ID-3				6.3****	4.9***
	Lif	Leukemia inhibitory factor				2.4*	2.1*
Pluripotency of stem cells	*Mapk13*	Mitogen-activated protein kinase 13	0.0004	0.0049		3.1*	
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5				2.6*	
	Wnt5b	Protein Wnt-5b			2.5***	2.5**	
	Zfhx3	Zinc finger homeobox protein 3				2.8*	4.1***
	Rest	RE1-silencing transcription factor					2.4*
	Wnt10b	Wingless-type MMTV integration site family, member 10B					3.0*
	Zfhx3	Zinc finger homeobox protein 3				2.8*	4.1***
	Cav2	Caveolin-2 (Stern and Mermelstein, 2010)				2.0*	
	Cav1	Caveolin-1 (Stern and Mermelstein, 2010)				2.3*	
	Ccnd1	G1/S-specific cyclin-D1				2.2*	
	Flt1	FMS-like tyrosine kinase 1				2.3*	2.6**
	Itga5	Integrin alpha-5			2.5*	3.2*	2.6*
	Itgav	Integrin alpha-V				2.1*	
Focal adhesion	*Tnc*	Tenascin C	0.0007		2.4*	3.8**	
	Mylk2	Myosin light chain kinase 2, skeletal/cardiac muscle				12.1*	
	Col6a1	Collagen alpha-1(VI) chain				2.5**	
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5				2.6*	
	Pdgfd	Platelet-derived growth factor D				3.1*	
	Col4a6	Collagen, type IV, alpha 6				3.1*	
	Spp1	Osteopontin				3.7*	

Transcription misregulation in cancer	*Cebpb*	CCAAT/enhancer-binding protein beta	0.0049	0.0006		2.2*	
	Flt1	FMS-like tyrosine kinase 1				2.3*	2.6**
	Meis1	Homeobox protein Meis1				2.1*	
	Hhex	Hematopoietically-expressed homeobox protein Hhex				12.1*	11.4*
	Hmga2	High mobility group AT-hook 2				12.2**	3.9*
	Hpgd	15-hydroxyprostaglandin dehydrogenase [NAD(+)]			2.5***		
	Il2rb	Interleukin 2 receptor, beta chain				7.0**	7.0**
	Mmp3	Stromelysin-1 (Sedaghat et al., 2012)				4.6*	
	Ngfr	Tumor necrosis factor receptor superfamily member 16			3.6**	7.7****	
	Pml	Promyelocytic leukemia protein				2.4*	
	Aff1	AF4/FMR2 family member 1					3.26****
	Elk4	ETS Transcription Factor ELK4					3.5****
	Hist1h3g	Histone cluster 1, h3g					2.6*
	Il2rb	Interleukin 2 receptor, beta chain				7.0**	7.0**
	Runx1	RUNX Family Transcription Factor 1					2.6*
	Six4	Sine oculis-related homeobox 4					4.9****
TGF-beta signaling	*Smad6*	MAD homolog 6	0.0061			3.7*	
	Bmp2	Bone morphogenetic protein 2				2.7*	
	Bmp8a	Bone morphogenetic protein 8A				7.5*	
	Cdkn2b	Cyclin-dependent kinase 4 inhibitor B				2.5*	
	Id1	Inhibitor of DNA binding 1				5.0**	3.2*
	Id3	DNA-binding protein inhibitor ID-3				6.3****	4.9***
	Ltbp1	Latent-transforming growth factor beta-binding protein 1				3.2**	2.0*
Regulation of actin cytoskeleton	*Arpc1b*	Actin-related protein 2/3 complex subunit 1B (Chou and Wang, 2016)	0.0086			2.8*	
	Itga5	Integrin alpha-5			2.5*	3.2*	2.6*
	Itgav	Integrin alpha-V				2.1*	
	Mylk2	Myosin light chain kinase 2				12.0*	
	Rras	Ras-related protein R-Ras (Iwasawa et al., 2012)				2.2*	

	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5				2.6*	
	Pdgfd	Platelet-derived growth factor D				3.1*	
	Msn	Moesin				2.7*	
	Bdkrb2	B2 bradykinin receptor			2.1*	3.0**	
	Fgf2	Fibroblast growth factor 2			2.2*	3.5**	3.0*
	Fgd3	FYVE, rhogef and PH domain-containing protein 3				2.4*	
Bacterial invasion of epithelial cells	*Arpc1b*	Actin-related protein 2/3 complex subunit 1B	0.018			2.8*	
	Cav1	Caveolin-1				2.3*	
	Cav2	Caveolin-2				2.0*	
	Itga5	Integrin alpha-5			2.5*	3.2*	2.6*
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5				2.6*	
	Rhog	Rho-related GTP-binding protein rhog				2.2*	
Rap1 signaling	*Flt1*	FMS-like tyrosine kinase 1	0.024			2.3*	2.6**
	Angpt2	Angiopoietin-2				2.8*	
	Drd2	D(2) dopamine receptor				6.8****	
	Fgf2	Fibroblast growth factor 2			2.2*	3.5**	3.0*
	Id1	Inhibitor of DNA binding 1				5.0**	3.2*
	Mapk13	Mitogen-activated protein kinase 13				3.1*	
	Ngfr	Tumor necrosis factor receptor superfamily member 16			3.6**	7.7****	
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5				2.6*	
	Rras	Ras-related protein R-Ras				2.2*	
MicroRNAs in cancer	*Bmf*	Bcl-2-modifying factor	0.043	0.038		3.0*	4.0***
	Bcl2l11	Bcl-2-like protein 11				2.4****	
	Cd44	CD44 antigen				2.9*	
	Cdc25c	M-phase inducer phosphatase 3				2.3*	
	Ccnd1	G1/S-specific cyclin-D1				2.2*	
	Hmga2	High mobility group AT-hook 2			12.2**	3.9*	
	Itga5	Integrin alpha-5			2.5*	3.2*	2.6*
	Notch3	Neurogenic locus notch homolog protein 3				2.5*	

	Serpinb5	Serine (or cysteine) peptidase inhibitor, clade B, member 5			2.6*	3.4*	
	Tnc	Tenascin C			2.4*	3.8**	
	Vim	Vimentin				2.7*	
	E2f2	E2F transcription factor 2					12.5****
	Cdca5	Cell division cycle associated 5					4.2**
	Cdk6	Cyclin-dependent kinase 6					3.8****
	Erbb2	Erb-b2 receptor tyrosine kinase 2					2.5*
	Igf2bp1	Insulin-like growth factor 2 mrna binding protein 1					55.4****
Toll-like receptor	*Casp8*	Caspase-8	0.047			3.2**	
	Mapk13	Mitogen-activated protein kinase 13				3.1*	
	Map3k8	Mitogen-activated protein kinase kinase kinase 8				2.7**	
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5				2.6*	
	Spp1	Osteopontin				3.7*	
	Tlr7	Toll-like receptor 7				4.3***	2.7*
Measles	*Fcgr2b*	Low affinity immunoglobulin gamma Fc region receptor II	0.05			2.5***	
	Ccnd1	G1/S-specific cyclin-D1				2.2*	
	Il2rb	Interleukin 2 receptor, beta chain				7.0**	7.0**
	Msn	Moesin				2.7*	
	Pik3r5	Phosphoinositide 3-kinase regulatory subunit 5				2.6*	
	Tacr1	NK-1 Receptor			2.7**	4.9****	
	Tlr7	Toll-like receptor 7				4.3***	2.7*
HTLV-1 infection	*Bub1b*	Mitotic checkpoint serine/threonine-protein kinase BUB1 beta		0.0041		2.5*	4.1***
	Ets1	E26 avian leukemia oncogene 1, 5' domain					2.6*
	E2f2	E2F transcription factor 2					12.5****
	Elk4	ETS Transcription Factor ELK4					3.5****
	H2-Q6	Histocompatibility 2, Q region locus 6				2.1*	2.4*
	H2-T23	Histocompatibility 2, T region locus 23					2.3*
	H2-T24	Histocompatibility 2, T region locus 24					3.8****
	Il1r1	Interleukin-1 receptor type 1				3.0*	

	Il2rb	Interleukin 2 receptor, beta chain		7.0**	7.0**
	Wnt10b	Wingless-type MMTV integration site family, member 10B			3.0*
Glycerolipid metabolism	*Mboat1*	membrane bound O-acyltransferase domain containing 1 (Tabe et al., 2016)	0.0280		2.9*
	Dgkk	Diacylglycerol kinase kappa (Kim et al., 2010)			2.1*
	Agpat2	1-acylglycerol-3-phosphate O-acyltransferase 2 (lysophosphatidic acid acyltransferase, beta)			2.1*
	Plpp2	phospholipid phosphatase 2 (Kim et al., 2010)			4.2***
Viral carcino-genesis	*Cdk6*	Cyclin-dependent kinase 6	0.0490		3.8****
	H2-Q6	Histocompatibility 2, Q region locus 6		2.1*	2.4*
	H2-T23	Histocompatibility 2, T region locus 23			2.3*
	H2-T24	Histocompatibility 2, T region locus 24			3.8****
	Hist1h2bh	Histone cluster 1, h2bh			2.0*
	Hist1h2bk	Histone cluster 1, h2bk			2.2*
	Hist1h4m	Histone cluster 1, h4m			11.6****
Chronic myeloid leukemia	*Cbl*	Casitas B-lineage lymphoma	0.0490		2.1***
	E2f2	E2F transcription factor 2			12.5****
	Cdk6	Cyclin-dependent kinase 6			3.8****
	Runx1	RUNX Family Transcription Factor 1			2.6*

Supplementary Table 3. List of genes not included in KEGG pathways, which are differentially enriched by apoE2, apoE3, or apoE4 lipoprotein treatment in primary hippocampal neurons. Fold change vs. control neurons grown in the apoE absence. NE - not expressed in the control neurons. *t*-test **p* < 0.05, ***p* < 0.01, ****p* < 0.001, *****p* < 0.0001 vs. control neurons.

Enriched by All Apoliporotein E Isoforms

Ontological Category	Gene	Encoded Protein Name	Fold change / p value		
			ApoE2	**ApoE3**	**ApoE4**
Cytoskeleton	*Cdc42bpg*	Serine/threonine-protein kinase MRCK gamma		2.7*	
	Rhoc	Rho-related GTP-binding protein		2.7*	
	Kank2	KN motif and ankyrin repeat domain-containing protein 2		2.6*	
	Rab29	Ras-related protein Rab-7L1		2.5*	
	Plxnb1	Plexin-B1		2.4**	
	Tec	Tyrosine-protein kinase Tec		2.4*	
	Emp2	Epithelial membrane protein 2		2.3*	
	Tes	Testin		2.2*	
	Rhoj	Rho-related GTP-binding protein rhoj (Basu and Lamprecht, 2018)		2.2*	2.1*
	Ninj1	Ninjurin 1	2.1****		
	Gas2l3	Growth arrest-specific 2 like			2.9****
	Wasf2	Wiskott-Aldrich Syndrome Protein (WASP) Family Member 2			2.2*
	Sprr1a	Cornifin-A		4.4*	
	Apbb1ip	Amyloid beta (A4) precursor protein-binding, family B, member 1 interacting protein			3.8*
	Strip2	Striatin-interacting proteins 2		-2.2**	
	Flnc	Filamin C, gamma			2.4*
	Cotl1	Coactosin-like 1	2.3****		
	Fhod3	Formin homology 2 domain containing 3	2.1**	2.4***	
	Krt6a	Keratin, type II cytoskeletal 6A	-8.5*		
	Ecm1	Extracellular matrix protein 1		2.9*	2.1*
	Syne3	Nesprin-3		2.9**	2.6**
	Gan	Giant axonal neuropathy			2.5****
Myelin maintenance	*Gldn*	Gliomedin (Feinberg et al., 2010)	4.1***	6.9****	3.5***
	Egr2	E3 SUMO-Protein Transferase ERG2		-2.3*	

	Prx	Periaxin (Raasakka et al., 2019)			2.8****
Neurodevelopment	*Ascl2*	Achaete-scute family bhlh transcription factor 2	6.6****	7.3****	
	Ctf2	Cardiotrophin 2	4.6*		
	Shox2	Short stature homeobox 2 (Scott et al., 2011)			9.6*
	Six4	Sine oculis-related homeobox 4			4.9****
	Bnc2	Basonuclin 2			4.6***
	Id3	DNA-binding protein inhibitor ID-3		6.3****	4.9***
	Gli3	GLI-Kruppel family member GLI3			2.6*
	Notch3	Neurogenic locus notch homolog protein 3		2.5*	
	Pax3	Paired box 3 (Lin et al., 2016)			NE**
	Gpr157	G protein-coupled receptor 157			2.3*
	Zfhx3	Zinc finger homeobox protein 3		2.8*	4.1***
	Ets1	E26 avian leukemia oncogene 1, 5' domain			2.6*
	Papss2	3'-phosphoadenosine 5'-phosphosulfate synthase 2	2.7*	3.7*	
	Kdr	Vascular endothelial growth factor receptor 2 (Bellon et al., 2010)	-2.3*		
	Igf2bp1	Insulin-like growth factor 2 mrna binding protein 1 (2)			55.4****
	Tll2	Tolloid-like 2	2.1*		
	Hoxa3	Homeobox A3			21.1**
	Zfp568	Zinc finger protein 568			2.8****
	Six3	Sine oculis-related homeobox 3			2.8*
	Mmp21	Matrix metallopeptidase 21			2.6*
	Prdm16	PR domain containing 16		2.2*	2.2*
	Ripply1	Protein ripply1	NE**	NE***	
	Olfml3	Olfactomedin-like protein 3		2.0*	
	Dhh	Desert hedgehog protein		2.5*	
	Phactr4	Phosphatase and actin regulator 4			2.5*
	Dmp1	Dentin matrix protein 1	3.1****		
	Lhx4	LIM/homeobox protein Lhx4		2.5**	
	Serping1	Plasma protease C1 inhibitor (Gorelik et al., 2017)		2.6*	
	Prokr1	Prokineticin receptor 1 (Ruiz-Ferrer et al., 2011)		3.5**	
Immune response	*Ly6g6e*	Lymphocyte antigen 6 complex, locus G6E (Wu et al., 2015)	7.3***	3.2*	
	Cd28	CD28 antigen	3.8*		

	Il11	Interleukin 11	3.6**	4.3*	
	Lime1	Lck-interacting transmembrane adapter 1		7.7*	
	Lypd8	Ly6/PLAUR domain-containing protein 8		7.5***	
	Tmem173	Stimulator of interferon genes protein		4.7**	2.7*
	Tlr7	Toll-like receptor 7 (Hung et al., 2018)		4.3***	2.7*
	Akr1b8	Aldose reductase-related protein 2		2.6*	
	Ptx3	Pentraxin-related protein PTX3 (Rodriguez-Grande et al., 2014)		2.5*	2.3*
	Il33	Interleukin-33		2.1*	
	Clec9a	C-type lectin domain family 9 member A	-4.8**		
	Lif	Leukemia inhibitory factor (Wright et al., 2003)		2.4*	2.1*
	Cebpd	CCAAT Enhancer Binding Protein Delta		2.7*	
	Rbp3	Retinol-binding protein 3 (Komatsu et al., 2005)		10.0*	7.9*
	Lrat	Lecithin retinol acyltransferase (O'Byrne et al., 2005)		5.7*	
	Aldh1a2	Retinal dehydrogenase 2 (Koppaka et al., 2012)		7.1***	
Retinol synthesis/metabolism	*Crabp1*	Cellular retinoic acid binding protein I (Uhrig et al., 2008)	2.7*		2.3*
	Aldh1a3	Retinal dehydrogenase 3 (Koppaka et al., 2012)	11.7**		
	Cyp26b1	Cytochrome P450 26B1(Stoney et al., 2016)	2.9*	6.4****	
	Aox2	Aldehyde oxidase 2	11.7*		
	Cyp26a1	Cytochrome P450 26A1 (Stoney et al., 2016)	2.5*	2.0**	
	Ltbp1	Latent-transforming growth factor beta-binding protein 1		3.2**	2.0*
	Ccdc80	Coiled-coil domain-containing protein 80		3.1*	
	Cdh19	Cadherin 19, type 2		2.9*	2.6
	Scarf2	Scavenger receptor class F, member 2			2.5***
	Plagl2	Pleiomorphic adenoma gene-like 2			2.1***
Cell adhesion	*Lpp*	LIM domain containing preferred translocation partner in lipoma			2.0**
	Troap	Trophinin associated protein			4.7*
	Cdh9	Cadherin-9 (Williams et al., 2011)	-2.1****	-2.3**	
	Rs1	Retinoschisin		-2.6*	
	Cdh23	Cadherin-23	-3.8****	-3.3**	
	Tmem204	Transmembrane protein 204		-4.0*	
	Cldn3	Claudin 3	9.6*		
	Zfp703	Zinc finger protein 703	2.2**	2.1**	2.7**

	Has2	Hyaluronan synthase 2			3.1*
	Ibsp	Bone sialoprotein 2	-2.3*		
	Mcam	Cell surface glycoprotein MUC18		2.4*	
	Ptpn14	Tyrosine-protein phosphatase non-receptor type 14		2.3*	6.4****
	Lrrn4	Leucine-rich repeat neuronal protein 4 (Bando et al., 2013)		-3.0*	
	Fxyd5	FXYD domain-containing ion transport regulator 5 (Tokhtaeva et al., 2016)		2.5*	
	F3	Tissue factor (Chen et al., 2018)		2.8*	
	Cthrc1	Collagen triple helix repeat-containing protein 1		2.4*	
	Loxl4	Loxl4 (Velez et al., 2020)		2.2*	2.7*
	Col13a1	Collagen alpha-1(XIII) chain (Hubert et al., 2009)	-2.5**		
	Col15a1	Collagen alpha-1(XV) chain (Bretaud et al., 2020)	-3.0*		
	Col19a1	Collagen alpha-1(XIX) chain (Su et al., 2010)		-2.3***	
	Mmp1a	Interstitial collagenase A		33.7**	15.0*
	P4ha3	Prolyl 4-hydroxylase subunit alpha-3 (Knapp and Klann, 2002, Salim, 2017)		3.0*	
	Ddr2	Discoidin domain receptor family, member 2			3.1***
Oxidative stress	*Prkd3*	Protein kinase D3			2.4*
	Tgm1	Transglutaminase 1, K polypeptide (Basso et al., 2012)	2.5**	4.5**	4.1*
	Ass1	Argininosuccinate synthase 1 (Heneka et al., 2001)		2.7*	
	Cox4i2	Cytochrome c oxidase subunit IV isoform 2	10.2**		8.9*
	Trim30a	Tripartite motif-containing 30A			2.8*
	Acoxl	Acyl-Coenzyme A oxidase-like Protein kinase D3	NE*		
	Gpx3	Glutathione Peroxidase 3 (Buchser et al., 2012)		3.8**	
	Ncf1	Neutrophil NADPH Oxidase Factor 1 (Brennan et al., 2009)	-2.0*		
Wnt signaling	*Mdfi*	Myod family inhibitor (Chen et al., 2020)		3.2*	
	Sfrp2	Secreted frizzled-related protein 2		3.0*	
	Tpbg	Trophoblast glycoprotein		2.6*	
	Wisp1	WNT1 inducible signaling pathway protein 1 (Maiese, 2014)			2.8*
	Sostdc1	Sclerostin domain containing 1	3.6****		
	Wif1	Wnt inhibitory factor 1	2.3*		
	Nkd1	Protein naked cuticle homolog 1		2.4**	
	Tmem88	Transmembrane protein 88	-2.1*		

	Gpc3	Glypican-3 (Capurro et al., 2014)	-2.9**	-2.9*	
	Mfrp	Membrane frizzled-related protein			2.2*
	Wnt9b	Protein Wnt-9b (Inestrosa and Varela-Nallar, 2014, McLeod and Salinas, 2018)	-2.6*		
	Wnt7a	Protein Wnt-7a (Inestrosa and Varela-Nallar, 2014, McLeod and Salinas, 2018)	-2.0**		
	Gm5415	Predicted gene 5415	-4.2*		
Related to neurological diseases or vision defects	*Vdr*	Vitamin D3 receptor (Gezen-Ak et al., 2011)	3.0*	6.0***	4.9***
	Sh3pxd2a	SH3 and PX domain-containing protein 2A (Saini and Courtneidge, 2018)		2.0**	2.5****
	Dysf	Dysferlin (Galvin et al., 2006)		3.3*	2.9*
	Trib3	Tribbles pseudokinase 3 (Zhang et al., 2019)			2.5*
	Apol9a	Apolipoprotein L 9a (Thekkinghat et al., 2019)			3.3*
	Fbxl7	F-box/LRR-repeat protein 7 (Tosto et al., 2015)	-2.5**		
	Nod2	Nucleotide-binding oligomerization domain containing 2 (28, 29)		8.3*	9.0*
	Mafg	MAF BZIP Transcription Factor G (Katsuoka et al., 2003)			2.0****
	Aoah	Acyloxyacyl hydrolase (Aguiniga et al., 2019)	11.8**	15.5*	14.5*
	Ush1g	Usher syndrome type-1G protein homolog (Weil et al., 2003)	-8.2*		
	Ush2a	Usher syndrome 2A (Weil et al., 2003)		5.8*	7.4**
	Otos	Otospiralin (Delprat et al., 2002)	4.3*	3.2*	
Excitatory signaling	*Slc7a11*	Cystine/Glutamate Transporter (XCR) (Bridges et al., 2012)		2.3*	2.9*
	Spata13	Spermatogenesis-associated protein 13		2.1***	
	Slc30a3	Zinc transporter 3 (Qian and Noebels, 2005, Martel et al., 2010)	-2.4*	-4.1*	
	Pmepa1	Protein TMEPAI (Maag et al., 2015)	2.8****	2.2*	
	Hipk2	Homeodomain interacting protein kinase 2 (Lee et al., 2016, Shang et al., 2018)			4.2****
Survival	*Slc5a3*	Sodium/myo-inositol cotransporter (Miller et al., 1993, Berry et al., 1999, Watanabe et al., 2012, Dai et al., 2016)		2.1*	
	Ngb	Neuroglobin (Sun et al., 2001, Burmester and Hankeln, 2009)		-2.5*	
	Ifi202b	Interferon-activable protein 202 (Xin et al., 2006)	2.3*	3.1*	
	Axl	AXL receptor tyrosine kinase (Axelrod and Pienta, 2014)		2.5*	2.3*
	Prokr2	Prokineticin receptor 2	2.3***	2.0***	
	Otos	Otospiralin	4.3*	3.2*	
	Chp2	Calcineurin B homologous protein 2 (Pang et al., 2002)		2.8**	

	Il1rl1	Interleukin-1 receptor-like 1		2.6*	2.8*
	Cmklr1	Chemerin Chemokine-Like Receptor 1 (Peng et al., 2015)		3.3**	
	Ier3	Radiation-inducible immediate-early gene IEX-1 (Arlt and Schafer, 2011)		2.6*	
	Pde7b	Camp-specific 3’,5’-cyclic phosphodiesterase 7B (Morales-Garcia et al., 2011, Gordon et al., 2016)	-2.1**	-2.7****	-2.1*
	Lgals1	Galectin-1 (Starossom et al., 2012)		3.0*	
	Nxnl2	Nucleoredoxin-like protein 2 (Jaillard et al., 2012)		NE*	
Energy / glucose metabolism	*Gck*	Glucokinase (De Backer et al., 2016, Matschinsky and Wilson, 2019)	-2.2***	-2.1**	
	Medag	Mesenteric estrogen dependent adipogenesis (Zhang et al., 2012)		3.2*	
	Pomc	Pro-opiomelanocortin-alpha (Toda et al., 2017)	2.3*	2.5*	2.8*
Inhibition of neurite growth	*Rgma*	Repulsive guidance molecule A (Isaksen et al., 2020)		2.2*	
	Timp1	Tissue inhibitor of metalloproteinase 1 (Ould-yahoui et al., 2009)	2.9*	4.2**	
	Rhog	Rho-related GTP-binding protein rhog (Franke et al., 2012)		2.2*	
	Hhex	Hematopoietically-expressed homeobox protein Hhex (Simpson et al., 2015)		12.1*	11.4*
Promotion of neurite growth	*Gpr6*	G-protein coupled receptor 6 (Tanaka et al., 2007)		-2.4**	
	Cdh6	Cadherin-6 (Guaiquil et al., 2014, Duan et al., 2018)		2.2*	
	Esm1	Endothelial cell-specific molecule 1		4.6*	
	Kdr	Vascular endothelial growth factor receptor 2 (Luck et al., 2019)	-2.3*		
	Sulf1	Sulfatase 1 (Kalus et al., 2009)	2.0*	2.3*	
	Fpr2	Formyl peptide receptor 2			NE*
Excitatory inhibition	*Gad1-ps*	Glutamate decarboxylase 1, pseudogene (Tao et al., 2018)	3.4*	4.9*	
	Gal	Galanin (Anselmi et al., 2009)	2.9*	4.7**	
	Necab1	N-terminal EF-hand calcium binding protein 1 (Sugita et al., 2002, Lewerenz et al., 2013, Andero et al., 2014, Zhang et al., 2015)	2.1**		
	Gpr39	G protein-coupled receptor 39 (Gilad et al., 2015)			13.2*
	Tac2	Tachykinin-2		3.5*	
	Ano1	Anoctamin-1		4.7**	
	Runx3	Runt related transcription factor 3 (Levanon et al., 2002)	12.0*	30.0**	
Ion channels/transporters	*Atp6v0a4*	V-type proton atpase 116 kda subunit A isoform 4 (Bodzeta et al., 2017, Fassio et al., 2018)		3.5*	
	Clcnkb	Chloride channel protein clc-Kb (Rahmati et al., 2018)		NE*	

	Kcnj8	ATP-sensitive inward rectifier potassium channel 8 (Bajgar et al., 2001, Sun and Feng, 2013)	4.3*	7.6**	
	Gjb6	Connexin 30 (Koulakoff et al., 2008, Pannasch et al., 2014)		5.1*	
	Trpm1	Transient receptor potential cation channel, subfamily M, member 1 (Shen et al., 2012)		3.9*	6.3*
	Kctd4	Potassium Channel Tetramerization Domain Containing 4 (Liu et al., 2013)		-2.2*	
	Kcnmb2	Calcium-activated potassium channel subunit beta-2 (Yu et al., 2018)		-2.3**	
	Trpm3	Transient receptor potential cation channel, subfamily M, member 3 (Zamudio-Bulcock et al., 2011)		-2.3*	
	Slc5a12	Sodium-coupled monocarboxylate transporter 2 (Ganapathy et al., 2008, Riske et al., 2017)	-5.9*		
	Slco1a4	Solute carrier organic anion transporter family member 1A4		3.4*	
	Scn7a	Sodium channel protein		3.1***	
	Piezo2	Piezo-type mechanosensitive ion channel component 2 (Song et al., 2019, Wang and Hamill, 2020)	2.3*		
Endosomes/lysosomes	*Ly75*	Lymphocyte antigen 75		4.5**	3.2*
	Litaf	Lipopolysaccharide-induced tumor necrosis factor-alpha factor homolog (Lee et al., 2011, Lee et al., 2012)		3.1*	
	Ston1	Stonin 1 (Breusegem and Seaman, 2014)			2.4*
	Ifitm1	Interferon-induced transmembrane protein 1		6.5*	5.3*
	Fcgr2b	Low affinity immunoglobulin gamma Fc region receptor II (Kam et al., 2013)		2.5***	
	Asic4	Acid-sensing ion channel 4 (Schwartz et al., 2015)	-2.3**		
	Serpina3g	Serine protease inhibitor A3G		3.0****	2.2*
	Cbl	Casitas B-lineage lymphoma (Yu et al., 2012)			2.1***
	Wipf1	WAS/WASL-interacting protein family member 1 (Franco et al., 2012)		2.5*	2.2*
	Ldlrap1	Low density lipoprotein receptor adaptor protein 1 (Johnson et al., 2014, Lane-Donovan and Herz, 2017)			5.0**
Lipid metabolism	*Lipg*	Endothelial lipase (Yun et al., 2019)		-2.3**	
	Gdpd3	Lysophospholipase D GDPD3 (Lecomte et al., 2005, Wijayatunge et al., 2018)		-3.2*	
	Pla2g2d	Group IID secretory phospholipase A2 (Sun et al., 2010)	-10.4*		
	Liph	Lipase member H (Yung et al., 2015, Roza et al., 2019)		3.5**	
	Gpr132	Probable G-protein coupled receptor 132		13.5**	

	Alox8	Polyunsaturated fatty acid lipoxygenase ALOX8			4.9**
	Alox5	Arachidonate 5-lipoxygenase		3.6*	
	Lcat	Phosphatidylcholine-sterol acyltransferase (Hirsch-Reinshagen et al., 2009)		3.2*	
	Apobr	Apolipoprotein B receptor			2.9*
	Ldlrad4	Low density lipoprotein receptor class A domain containing 4 (Chong et al., 2017)	2.0****		
	Angptl4	Angiopoietin-related protein 4 (Bluher, 2015, Vienberg et al., 2015)		5.0**	4.8*
Cell cycle	*Usp44*	Ubiquitin specific peptidase 44			9.6****
	Prm1	Protamine 1			5.3**
	Cdca5	Cell division cycle associated 5			4.2**
	Kif14	Kinesin family member 14			3.1***
	Aspm	Abnormal spindle-like microcephaly-associated protein homolog			3.0**
	Foxm1	Forkhead box M1			2.6**
	Cdca2	Cell division cycle associated 2			2.5*
	Eme1	Essential meiotic structure-specific endonuclease 1			2.4*
	Nek2	NIMA (never in mitosis gene a)-related expressed kinase 2			2.3***
	Foxn3	Forkhead box N3 (Grassi et al., 2017)			2.1***
	Top2a	Topoisomerase (DNA) II alpha	3.5****		
	Dmc1	Meiotic recombination protein DMC1/LIM15 homolog		-3.2*	
	Meikin	Meiosis-specific kinetochore protein		-5.5*	
	Cdkn3	Cyclin-dependent kinase inhibitor 3	-2.2*		
	Insc	Protein inscuteable homolog	-2.5***		
	Cenpf	Centromere protein F			2.6***
	Rmi2	Recq-mediated			15.7****
	Mybl2	Myeloblastosis oncogene-like 2 (Musa et al., 2017)			3.8*
	Cdkn2b	Cyclin-dependent kinase 4 inhibitor B		2.5*	
	Cdc25c	M-phase inducer phosphatase 3		2.3*	
	Elf4	E74-like factor 4 (Kosti et al., 2020)		3.8*	20.9****
	E2f7	E2F transcription factor 7			8.0****
	Ect2	Ect2 oncogene			3.0*
	Ticrr	TOPBP1-interacting checkpoint and replication regulator			2.8*
	Stil	SCL-interrupting locus protein homolog		2.0*	2.8**

	Tex12	Testis expressed gene 12 (Hamer et al., 2006)	NE**	NE*	
	Cdc6	Cell division cycle 6			5.6****
	E2f2	E2F transcription factor 2 (Szpara et al., 2007, Castillo et al., 2015, Frade and Ovejero-Benito, 2015, Sharma et al., 2017)			12.5****
	Bub1b	Mitotic checkpoint serine/threonine-protein kinase BUB1 beta (Szpara et al., 2007, Frade and Ovejero-Benito, 2015, Sharma et al., 2017)		2.5*	4.1***
	Cdk6	Cyclin-dependent kinase 6 (Sharma et al., 2017)			3.8****
	Espl1	Extra spindle pole bodies 1, separase (Szpara et al., 2007, Frade and Ovejero-Benito, 2015, Sharma et al., 2017)			3.4***

Enriched by apoE2$_{HDL}$ and apoE3$_{HDL}$

Ontological Category	Gene	Encoded Protein Name	ApoE2	ApoE3	ApoE4
Excitatory AMPAR signaling	*Syndig1l*	Synapse differentiation-inducing gene protein 1-like (Kalashnikova et al., 2010)	2.2***	3.6****	
	Gsg1l	Germ cell-specific gene 1-like protein (Gu et al., 2016)	-2.1**	-2.1**	
	Nptx1	Neuronal pentraxin-1 (DeGregorio-Rocasolano et al., 2001, Figueiro-Silva et al., 2015, Schaukowitch et al., 2017)	-2.4*		
	Gpc3	Glypican-3 (Gottschling et al., 2019)	-2.9**	-2.9*	
	Igsf1	Immunoglobulin superfamily member 1 (Jang et al., 2016)	-2.0**		
	Wnt7a	Protein Wnt-7a (McLeod and Salinas, 2018)	-2.1**		
Synaptic plasticity	*C1ql1*	C1q-related factor (Bolliger et al., 2011)		3.1**	
	Pml	Promyelocytic leukemia protein (Korb and Finkbeiner, 2013)		2.4*	
	Akain1	A kinase (PRKA) anchor inhibitor 1 (Zhong et al., 2009)	2.2***		
	Esm1	Endothelial cell-specific molecule 1		4.6*	
	Kdr	Vascular endothelial growth factor receptor 2	-2.3*		
	Klf5	Kruppel Like Factor 5 (Yanagi et al., 2008)		2.1**	
	Spata13	Spermatogenesis-associated protein 13 (Evans et al., 2015)		2.1***	
	Cebpb	CCAAT/enhancer-binding protein beta (Kfoury and Kapatos, 2009)		2.2*	
Neurotransmitter exocytosis	*Syt15*	Synaptotagmin XV (Fukuda, 2003)	2.8*		
	Otof	Otoferlin	-3.3*		
	Stx11	Syntaxin-11 (Johnson and Chapman, 2010, Zhou et al., 2013)		3.6*	
	Synpr	Synaptoporin (Lee et al., 2013, Andre et al., 2018)		-2.4****	

	Sytl4	Synaptotagmin-like protein 4 (Rafi et al., 2019)		2.9*	
	Slc6a2	Sodium-dependent noradrenaline transporter (Torres et al., 2003, Tully and Bolshakov, 2010)		4.6*	
	Rab27b	RAB27B, member RAS oncogene family (Rafi et al., 2019)	2.2***		
Chaperone protein	*Hspb1*	Heat shock protein beta-1 (Srivastava et al., 2012)	2.9*	4.4*	
	Hspb8	Heat shock protein beta-8 (Crippa et al., 2016)		2.9*	
	Hspb3	Heat shock protein 3 (La Padula et al., 2016)	2.8**		
	Fkbp10	Peptidyl-prolyl cis-trans isomerase FKBP10		2.4*	
	Cryaa	Crystallin, alpha A	10.6**		
Cellular growth suppression	*Rasl10a*	Ras-like protein family member 10A (Hermey et al., 2013)	-2.7**	-2.4*	
Tumor suppressor	*Vwa5a*	Von Willebrand factor A domain-containing protein 5A		2.5**	
	Ndrg1	Protein NDRG1 (Okuda et al., 2004, Okuda et al., 2008)		2.2*	

Enriched by apoE3$_{HDL}$ and apoE4$_{HDL}$.

Ontological Category	Gene	Encoded Protein Name	ApoE2	ApoE3	ApoE4
Intracellular trafficking	*Sec16b*	Protein transport protein Sec16B		2.2*	
	Scrg1	Scrapie-responsive protein 1 (Dandoy-Dron et al., 2003)		2.3*	
	Ap1m2	AP-1 complex subunit mu-2		2.4*	
	Klc3	Kinesin light chain 3 (Killian et al., 2012)		2.1**	
	Sec22c	SEC22 homolog C, vesicle trafficking protein (Wang et al., 2018)			2.1****
	Exph5	Exophilin-5 (Ostrowski et al., 2010)		2.1**	
	Sft2d2	SFT2 domain containing 2 (Breusegem and Seaman, 2014)			3.1**
	Ptpn21	Protein tyrosine phosphatase, non-receptor type 21 (Choi et al., 2014)			2.0*
Apoptosis	*Bmf*	Bcl-2-modifying factor (Moran et al., 2013, Akhter et al., 2018)		3.0*	4.0***
	Nradd	Death domain-containing membrane protein NRADD (Wang et al., 2003)		2.9*	
	Casp12	Caspase-12		2.7*	
	Casp8	Caspase-8		3.2**	
	Cideb	Cell death activator CIDE-B		2.2*	
	Zmat3	Zinc finger matrin type 3		2.3*	2.3****

	Adamtsl4	ADAMTS-like protein 4		2.6*	
	Elk4	ETS Transcription Factor ELK4		3.5****	
	Lgals1	Galectin-1		3.0*	
DNA repair	*Gpr87*	G-protein coupled receptor 87 (Zhang et al., 2009)		-16.5*	
	Brip1	BRCA1 interacting protein C-terminal helicase 1 (Greenberg, 2008)			2.7*
	Bard1	BRCA1 associated RING domain 1 (Greenberg, 2008)			2.9**

Enriched by apoE3$_{HDL}$

Ontological Category	Gene	Encoded Protein Name	ApoE2	ApoE3	ApoE4
Lysomal acidification	*Atp6v1c2*	V-type proton atpase subunit C 2		-2.9*	
Lipids synthesis	*Elovl7*	Elongation of very long chain fatty acids protein 7 (Shin et al., 2009)		2.5***	
Development and cognitive impairment	*Fbln2*	Fibulin-2 (Tang et al., 2019)		3.7*	
Calcium storage/sensing	*Casq1*	Calsequestrin-1		4.0*	
	Casr	Extracellular calcium-sensing receptor (Chen et al., 2010)		3.8***	

Enriched by apoE4$_{HDL}$

Ontological Category	Gene	Encoded Protein Name	ApoE2	ApoE3	ApoE4
Histones	*Hist1h2bk*	Histone cluster 1, h2bk (Rachdaoui et al., 2017)			2.2*
	Hist1h2bh	Histone cluster 1, h2bh (Rachdaoui et al., 2017)			2.0*
	Hist1h3g	Histone cluster 1, h3g (Rachdaoui et al., 2017)			2.6*
	Hist1h4m	Histone cluster 1, h4m (Rachdaoui et al., 2017)			11.6****
Increased in aging	*Rest*	RE1-silencing transcription factor (D'Alessandro et al., 2009, Baldelli and Meldolesi, 2015)			2.4*
Fatty acid synthesis in mitochondria	*H2-Ke6*	H2-K region expressed gene 6			4.4*
Stress Response	*Ucn2*	Urocortin 2 (Liu et al., 2015, Zheng et al., 2016)			9.1*
	Creb3l3	CAMP Responsive Element Binding Protein 3 Like 3			-2.9*
Moyamoya disease/ Ischemia	*Rnf213*	Ring finger protein 213 (Sato-Maeda et al., 2016)			2.5*

Nerve regeneration after injury	*Ankrd1*	Ankyrin repeat domain 1 (cardiac muscle) (Obara et al., 2016)	15.9****
Dysregulation synaptic plasticity	*Eif4ebp2*	Eukaryotic translation initiation factor 4E binding protein 2 (Banko et al., 2005)	8.3****

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