

Supplemental table 5: List of genes regulated by aging in the hypothalamus

Gene Symbol	Gene Title	RefSeq Transcript ID	Fold change	Gene Ontology Biological Process
Up-regulated				
<i>C3</i>	complement component 3	NM_016994	5,39	positive regulation of type IIa hypersensitivity
<i>C4-2 /// C4b</i>	complement component 4, gene 2 /// complement component 4B (Chido blood group)	NM_001002805 /// NM_031504	3,58	inflammatory response
<i>RT1-A2 /// RT1-A3 /// RT1-EC2</i>	RT1 class Ia, locus A2 /// RT1 class I, locus A3 /// RT1 class Ib, locus EC2	NM_001008829 /// NM_001008830 /// NM_012645	3,47	positive regulation of T cell mediated cytotoxicity
<i>Psmb8</i>	proteasome (prosome, macropain) subunit, beta type 8 (large multifunctional pept	NM_080767	2,54	antigen processing and presentation
<i>Gpnmb</i>	glycoprotein (transmembrane) nmb	NM_133298	2,52	osteoblast differentiation
<i>Fcgr2a /// Fcgr2b</i>	Fc fragment of IgG, low affinity IIa, receptor (CD32) /// Fc fragment of IgG, lo	NM_053843 /// NM_175756	2,50	antibody-dependent cellular cytotoxicity
<i>Bst2</i>	bone marrow stromal cell antigen 2	NM_198134	2,37	positive regulation of I-kappaB kinase/NF-kappaB cascade
<i>Rsad2</i>	radical S-adenosyl methionine domain containing 2	NM_138881	2,12	ossification
<i>Psmb9</i>	proteasome (prosome, macropain) subunit, beta type 9 (large multifunctional pept	NM_012708	2,11	antigen processing and presentation
<i>Fcgr3a</i>	Fc fragment of IgG, low affinity IIIa, receptor	NM_207603	2,00	NK T cell proliferation
<i>Cp</i>	ceruloplasmin	NM_012532	1,96	liver development
<i>Lgals3bp</i>	lectin, galactoside-binding, soluble, 3 binding protein	NM_139096	1,95	cell adhesion
<i>Emr1</i>	EGF-like module containing, mucin-like, hormone receptor-like 1	NM_001007557	1,95	signal transduction
<i>Igfbp3</i>	insulin-like growth factor binding protein 3	NM_012588	1,90	regulation of cell growth
<i>Icam1</i>	intercellular adhesion molecule 1	NM_012967	1,89	ovarian follicle development
<i>Anxa4</i>	annexin A4	NM_024155	1,86	exocytosis
<i>RT1-CE12</i>	RT1 class I, locus CE12	NM_001008835	1,85	antigen processing and presentation of peptide antigen via MHC class
<i>Hspb1</i>	heat shock protein 1	NM_031970	1,85	anti-apoptosis
<i>C1qa</i>	complement component 1, q subcomponent, A chain	NM_001008515	1,84	complement activation, classical pathway
<i>Lcp1</i>	lymphocyte cytosolic protein 1	NM_001012044	1,82	T cell activation involved in immune response
<i>Gbp2</i>	guanylate binding protein 2	NM_133624	1,77	
<i>Pqlc3</i>	PQ loop repeat containing 3	NM_001034952	1,76	
<i>Aif1</i>	allograft inflammatory factor 1	NM_017196	1,76	positive regulation of protein phosphorylation
<i>Dusp6</i>	Dual specificity phosphatase 6	NM_053883	1,75	inactivation of MAPK activity
<i>Grm2</i>	glutamate receptor, metabotropic 2	NM_001105711	1,73	signal transduction
<i>Cd4</i>	Cd4 molecule	NM_012705	1,71	cytokine production
<i>Acer2</i>	alkaline ceramidase 2	NM_001107943	1,70	negative regulation of cell-matrix adhesion
<i>Cyp27a1</i>	cytochrome P450, family 27, subfamily a, polypeptide 1	NM_178847	1,68	steroid catabolic process
<i>Crym</i>	crystallin, mu	NM_053955	1,68	negative regulation of transcription from RNA polymerase II promoter
<i>C2</i>	complement component 2	NM_172222	1,67	proteolysis
<i>Cenpj</i>	centromere protein J	NM_001107265	1,66	centriole replication
<i>Cml3</i>	camello-like 3	XM_001074100 /// XM_575585	1,64	gastrulation with mouth forming second

<i>Ms4a6b</i>	membrane-spanning 4-domains, subfamily A, member 6B	NM_001006975	1,63	
<i>Tyrobp</i>	Tyrosine protein tyrosine kinase binding protein	NM_212525	1,63	intracellular signaling pathway
<i>RT1-EC2</i>	RT1 class Ib, locus EC2	NM_012645	1,63	antigen processing and presentation of peptide antigen via MHC class
<i>Ctsz</i>	cathepsin Z	NM_183330	1,63	proteolysis
<i>Cfh</i>	complement factor H	NM_130409	1,62	complement activation
<i>Plek</i>	pleckstrin	NM_001025750	1,62	hemopoietic progenitor cell differentiation
<i>Rab27a</i>	RAB27A, member RAS oncogene family	NM_017317	1,61	protein targeting
<i>Fam189a2</i>	family with sequence similarity 189, member A2	XM_001078764 /// XM_219909	1,61	
<i>Smagp</i>	small trans-membrane and glycosylated protein	NM_182817	1,61	
<i>Fcgr1g</i>	Fc fragment of IgE, high affinity I, receptor for; gamma polypeptide	NM_001131001	1,60	positive regulation of type IIa hypersensitivity
<i>C1qc</i>	complement component 1, q subcomponent, C chain	NM_001008524	1,59	complement activation, classical pathway
<i>Pycard</i>	PYD and CARD domain containing	NM_172322	1,58	proteolysis
<i>Pcdhb9</i>	protocadherin beta 9	NM_001109390	1,56	cell adhesion
<i>Ifit3</i>	interferon-induced protein with tetratricopeptide repeats 3	NM_001007694	1,55	
<i>Pbld</i>	phenazine biosynthesis-like protein domain containing	NM_138530	1,54	biosynthetic process
<i>Tspo</i>	translocator protein	NM_012515	1,53	steroid biosynthetic process
<i>Tmc4</i>	transmembrane channel-like 4	NM_001034104	1,52	
<i>Stat1 /// Stat4</i>	signal transducer and activator of transcription 1 /// signal transducer and act	NM_001012226 /// NM_001034164 /// NM_032612	1,52	transcription
<i>Tmem176a</i>	transmembrane protein 176A	NM_001039008	1,51	
<i>Adpgk</i>	ADP-dependent glucokinase	NM_001100723	1,50	carbohydrate metabolic process
<i>Aadat</i>	aminoadipate aminotransferase	NM_017193	1,49	2-oxoglutarate metabolic process
<i>Ube2l6</i>	ubiquitin-conjugating enzyme E2L 6	NM_001024755	1,49	modification-dependent protein catabolic process
<i>Cd53</i>	Cd53 molecule	NM_012523	1,48	regulation of growth
<i>Uba7</i>	ubiquitin-like modifier activating enzyme 7	NM_001106856	1,48	protein modification process
<i>Anxa3</i>	Annexin A3	NM_012823	1,47	phagocytosis
<i>Clec7a</i>	C-type lectin domain family 7, member a	NM_001173386 /// XM_001067977 /// XM_578404	1,47	response to yeast
<i>Serpina3n</i>	serine (or cysteine) peptidase inhibitor, clade A, member 3N	NM_031531	1,47	inflammatory response
<i>C1qb</i>	complement component 1, q subcomponent, B chain	NM_019262	1,47	immune response
<i>Grxcr1</i>	glutaredoxin, cysteine rich 1	NM_001191935 /// XM_001077572 /// XM_573590	1,46	sensory perception of sound
<i>Alb</i>	albumin	NM_134326	1,45	transport
<i>Blnk</i>	B-cell linker	NM_001025767	1,44	intracellular signaling pathway
<i>Ptpn6</i>	protein tyrosine phosphatase, non-receptor type 6	NM_053908	1,44	negative regulation of humoral immune response mediated by circulating
<i>Rac2</i>	ras-related C3 botulinum toxin substrate 2	NM_001008384	1,44	GTP catabolic process
<i>Irf9</i>	interferon regulatory factor 9	NM_001012041	1,43	transcription
<i>Npc2</i>	Niemann-Pick disease, type C2	NM_173118	1,42	response to virus
<i>Calca</i>	calcitonin-related polypeptide alpha	NM_001033955 /// NM_001033956 /// NM_017338	1,41	endothelial cell proliferation
<i>Rnaset2</i>	ribonuclease T2	NM_001106210	1,41	
<i>Dsp</i>	desmoplakin	XM_001058477 /// XM_225259	1,41	cell-cell adhesion
<i>Lap3</i>	leucine aminopeptidase 3	NM_001011910	1,40	proteolysis

<i>RT1-CE5</i>	RT1 class I, locus CE5	NM_001008843 /// NM_001033986	1,40	antigen processing and presentation of peptide antigen via MHC class
<i>Csf1r</i>	colony stimulating factor 1 receptor	NM_001029901	1,40	protein phosphorylation
<i>Tap2</i>	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)	NM_032056	1,40	positive regulation of T cell mediated cytotoxicity
<i>Tnfaip8l2</i>	tumor necrosis factor, alpha-induced protein 8-like 2	NM_001014039	1,40	innate immune response
<i>Laptm5</i>	lysosomal protein transmembrane 5	NM_053538	1,39	transport
<i>Casp4</i>	caspase 4, apoptosis-related cysteine peptidase	NM_053736	1,39	proteolysis
<i>S100a9</i>	S100 calcium binding protein A9	NM_053587	1,38	chronic inflammatory response
<i>Cidea</i>	cell death-inducing DFFA-like effector a	NM_001170467	1,37	temperature homeostasis
<i>Ephx1</i>	epoxide hydrolase 1, microsomal	NM_001034090 /// NM_012844	1,37	cellular aromatic compound metabolic process
<i>Ptprc</i>	protein tyrosine phosphatase, receptor type, C	NM_001109887 /// NM_001109888 /// NM_001109889 /// NM_001109890 /// NM_138507	1,37	activation of MAPK activity
<i>Gldc</i>	glycine dehydrogenase (decarboxylating)	NM_001107583	1,37	cellular amino acid metabolic process
<i>Anxa11</i>	annexin A11	NM_001011918	1,36	phagocytosis
<i>Hck</i>	hemopoietic cell kinase	NM_013185	1,36	protein phosphorylation
<i>Unc93b1</i>	unc-93 homolog B1 (C. elegans)	NM_001108513	1,36	toll-like receptor signaling pathway
<i>Gadd45b</i>	growth arrest and DNA-damage-inducible, beta	NM_001008321	1,36	activation of MAPKK activity
<i>Ifit2</i>	interferon-induced protein with tetratricopeptide repeats 2	NM_001024753	1,36	cellular response to interferon-alpha
<i>Cd37</i>	CD37 molecule	NM_017124	1,36	positive regulation of immunoglobulin production
<i>Ctse</i>	cathepsin E	NM_012938	1,35	proteolysis
<i>Cyb5r2</i>	cytochrome b5 reductase 2	NM_001014244	1,35	steroid biosynthetic process
<i>Pygl</i>	phosphorylase, glycogen, liver	NM_022268	1,35	carbohydrate metabolic process
<i>Aqp1</i>	aquaporin 1	NM_012778	1,35	glomerular filtration
<i>Gsta3</i>	glutathione S-transferase A3	NM_031509	1,35	glutathione metabolic process
<i>Zfp36</i>	zinc finger protein 36	NM_133290	1,35	nuclear-transcribed mRNA catabolic process, deadenylation-dependent
<i>B2m</i>	beta-2 microglobulin	NM_012512	1,35	positive regulation of T cell mediated cytotoxicity
<i>Six4</i>	SIX homeobox 4	NM_001106739	1,35	regulation of transcription, DNA-dependent
<i>Slfn8</i>	schlafen 8	NM_001013970	1,34	
<i>Pls1</i>	Plastin 1 (I isoform)	NM_001108178	1,34	
<i>Cd48</i>	Cd48 molecule	NM_139103	1,34	signal transduction
<i>Cdh23</i>	cadherin 23 (otocadherin)	NM_053644	1,33	cell adhesion
<i>Fcn1</i>	ficolin (collagen/fibrinogen domain containing) 1	NM_031348	1,33	signal transduction
<i>Ctss</i>	cathepsin S	NM_017320	1,33	proteolysis
<i>Kitlg</i>	KIT ligand	NM_021843 /// NM_021844	1,33	ovarian follicle development
<i>Sash3</i>	SAM and SH3 domain containing 3	NM_001134992	1,32	positive regulation of immunoglobulin production
<i>Iqgap1</i>	IQ motif containing GTPase activating protein 1	NM_001108489	1,32	signal transduction
<i>Abca8a</i>	ATP-binding cassette, sub-family A (ABC1), member 8a	XM_001081603 /// XM_221100	1,32	
<i>Dctd</i>	dCMP deaminase	NM_001013882 /// NM_001161512	1,32	nucleotide biosynthetic process
<i>Sp110</i>	SP110 nuclear body protein	NM_001034137	1,32	transcription
<i>Dlk1</i>	delta-like 1 homolog (Drosophila)	NM_053744	1,32	embryo development
<i>Abcg3l1</i>	ATP-binding cassette, sub-family G (WHITE), member 3-like 1	NM_001004076	1,32	
<i>Cmtm7</i>	CKLF-like MARVEL transmembrane domain containing 7	NM_001109300	1,31	
<i>Arhgdib</i>	Rho, GDP dissociation inhibitor (GDI) beta	NM_001009600	1,31	

<i>Wnk1</i>	WNK lysine deficient protein kinase 1	NM_001002823 /// NM_053794	1,30	positive regulation of systemic arterial blood pressure
<i>Klhl6</i>	kelch-like 6 (Drosophila)	NM_001105867	1,30	germinal center formation
<i>Plagl1</i>	pleiomorphic adenoma gene-like 1	NM_012760	1,30	positive regulation of transcription from RNA polymerase II promoter

Down-regulated

<i>Ghrh</i>	growth hormone releasing hormone	NM_031577	-1,99	G-protein signaling, coupled to cAMP nucleotide second messenger
<i>S100g</i>	S100 calcium binding protein G	NM_012521	-1,82	
<i>Cd38</i>	CD38 molecule	NM_013127	-1,79	response to hypoxia
<i>Nts</i>	neurotensin	NM_001102381	-1,76	regulation of blood vessel size
<i>Ccnd2</i>	cyclin D2	NM_022267	-1,72	G1/S transition of mitotic cell cycle
<i>Pnlip</i>	pancreatic lipase	NM_013161	-1,63	lipid metabolic process
<i>Scd1</i>	stearoyl-Coenzyme A desaturase 1	NM_139192	-1,57	lipid metabolic process
<i>Mtmr1</i>	myotubularin related protein 1	NM_001191725 /// XM_001059230 /// XM_228644	-1,56	dephosphorylation
<i>Wnt4</i>	wingless-type MMTV integration site family, member 4	NM_053402	-1,55	metanephros development
<i>Col1a1</i>	collagen, type I, alpha 1	NM_053304	-1,52	skeletal system development
<i>Mfhas1</i>	malignant fibrous histiocyoma amplified sequence 1	NM_001107316	-1,52	
<i>Tlcd1</i>	TLC domain containing 1	NM_001013858	-1,51	
<i>Shisa4</i>	shisa homolog 4 (Xenopus laevis)	NM_001077826	-1,48	
<i>Col5a2</i>	collagen, type V, alpha 2	NM_053488	-1,47	skeletal system development
<i>Gal</i>	galanin prepropeptide	NM_033237	-1,46	response to stress
<i>Tm7sf2</i>	transmembrane 7 superfamily member 2	NM_001013071	-1,45	
<i>Slc7a10</i>	solute carrier family 7, (neutral amino acid transporter, y+ system) member 10	NM_053726	-1,45	amino acid transmembrane transport
<i>Fzd2</i>	frizzled homolog 2 (Drosophila)	NM_172035	-1,44	cell activation
<i>Nlk</i>	Nemo like kinase	NM_001191924 /// XM_001080888 /// XM_573152	-1,43	protein phosphorylation
<i>Pnma12</i>	PNMA-like 2	NM_001107481	-1,42	
<i>Thrsp</i>	thyroid hormone responsive	NM_012703	-1,42	
<i>Tmem100</i>	transmembrane protein 100	NM_001017479	-1,41	
<i>Hhat1</i>	hedgehog acyltransferase-like	NM_001106868	-1,41	negative regulation of N-terminal protein palmitoylation
<i>Pop5</i>	Processing of precursor 5, ribonuclease P/MRP subunit (S. cerevisiae)	NM_001105752	-1,41	tRNA processing
<i>Egr4</i>	early growth response 4	NM_019137	-1,40	transcription
<i>Nptx1</i>	neuronal pentraxin 1	NM_153735	-1,40	
<i>Bdh1</i>	3-hydroxybutyrate dehydrogenase, type 1	NM_053995	-1,40	liver development
<i>Fastkd5</i>	FAST kinase domains 5	XR_085786 /// XR_086207	-1,39	
<i>Fads2</i>	fatty acid desaturase 2	NM_031344	-1,39	lipid metabolic process
<i>Sept_11</i>	septin 11	NM_001107208	-1,39	cell cycle
<i>Ndp</i>	Norrie disease (pseudoglioma) (human)	NM_001108814	-1,38	placenta development
<i>Slc40a1</i>	solute carrier family 39 (iron-regulated transporter), member 1	NM_133315	-1,38	transport
<i>Hcrtr1</i>	hypocretin (orexin) receptor 1	NM_013064	-1,38	signal transduction
<i>Rras2</i>	related RAS viral (r-ras) oncogene homolog 2	NM_001013434	-1,38	signal transduction
<i>Scrg1</i>	stimulator of chondrogenesis 1	NM_033499	-1,37	

<i>Phkg1</i>	phosphorylase kinase, gamma 1	NM_031573	-1,37	carbohydrate metabolic process
<i>Tmem90b</i>	transmembrane protein 90B	NM_001025020	-1,36	response to biotic stimulus
<i>Syt6</i>	synaptotagmin VI	NM_022191	-1,36	transport
<i>Col4a5</i>	collagen, type IV, alpha 5	XM_001055156 /// XM_343778	-1,36	
<i>YdjC</i>	YdjC homolog (bacterial)	NM_001013863	-1,36	carbohydrate metabolic process
<i>Tbl1xr1</i>	transducin (beta)-like 1 X-linked receptor 1	NM_001108941	-1,36	negative regulation of gene-specific transcription from RNA polymerase
<i>Bbox1</i>	butyrobetaine (gamma), 2-oxoglutarate dioxygenase (gamma-butyrobetaine hydroxyla	NM_022629	-1,36	carnitine biosynthetic process
<i>Cyp51</i>	cytochrome P450, family 51	NM_012941	-1,35	steroid biosynthetic process
<i>Sv2b</i>	synaptic vesicle glycoprotein 2b	NM_057207	-1,35	neurotransmitter uptake
<i>Fxyd7</i>	FXD domain-containing ion transport regulator 7	NM_022008	-1,35	transport
<i>Slc1a2</i>	solute carrier family 1 (glial high affinity glutamate transporter), member 2	NM_001035233 /// NM_017215	-1,34	amino acid transmembrane transport
<i>Rnf182</i>	ring finger protein 182	NM_001109117	-1,34	protein ubiquitination
<i>Tmeff1</i>	transmembrane protein with EGF-like and two follistatin-like domains 1	NM_023020	-1,34	multicellular organismal development
<i>Ednrb</i>	endothelin receptor type B	NM_017333	-1,34	neural crest cell migration
<i>Asb1</i>	ankyrin repeat and SOCS box-containing 1	NM_001108232	-1,34	intracellular signaling pathway
<i>Timp4</i>	tissue inhibitor of metalloproteinase 4	NM_001109393	-1,33	central nervous system development
<i>Slc1a6</i>	solute carrier family 1 (high affinity aspartate/glutamate transporter), member	NM_032065	-1,33	amino acid transmembrane transport
<i>Gamt</i>	guanidinoacetate N-methyltransferase	NM_012793	-1,33	creatine metabolic process
<i>Nrarp</i>	Notch-regulated ankyrin repeat protein	NM_001143750	-1,33	
<i>Sst</i>	somatostatin	NM_012659	-1,33	response to acid
<i>Nkain4</i>	Na ⁺ /K ⁺ transporting ATPase interacting 4	NM_001106550	-1,32	
<i>F2r</i>	coagulation factor II (thrombin) receptor	NM_012950	-1,32	activation of MAPKK activity
<i>Pdyn</i>	prodynorphin	NM_019374	-1,32	neuropeptide signaling pathway
<i>Hmgcr</i>	3-hydroxy-3-methylglutaryl-Coenzyme A reductase	NM_013134	-1,32	steroid biosynthetic process
<i>Mpped1</i>	metallophosphoesterase domain containing 1	NM_001130569	-1,32	
<i>Cyp2d4</i>	cytochrome P450, family 2, subfamily d, polypeptide 4	NM_138515	-1,32	steroid metabolic process
<i>Cpxm1</i>	carboxypeptidase X (M14 family), member 1	NM_001106511	-1,31	proteolysis
<i>Metn</i>	meteorin, glial cell differentiation regulator	NM_001009962	-1,31	multicellular organismal development
<i>Cyp4f17</i>	cytochrome P450, family 4, subfamily f, polypeptide 17	NM_001191986 /// XM_002726858 /// XM_002729769 /// XM_576190	-1,31	
<i>Mllt4</i>	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); tran	NM_013217	-1,31	cell adhesion
<i>Acss2</i>	acyl-CoA synthetase short-chain family member 2	NM_001107793	-1,31	acetyl-CoA biosynthetic process
<i>Fads1</i>	fatty acid desaturase 1	NM_053445	-1,30	lipid metabolic process
<i>Cyp2d4</i>	cytochrome P450, family 2, subfamily d, polypeptide 4	NM_138515	-1,30	steroid metabolic process
<i>Sox4</i>	SRY (sex determining region Y)-box 4	XM_001068302 /// XM_344594	-1,30	response to hypoxia
<i>Lrrc40</i>	Leucine rich repeat containing 40	NM_001034926	-1,30	
<i>Gja1</i>	gap junction protein, alpha 1	NM_012567	-1,30	in utero embryonic development
<i>Csrp2</i>	cysteine and glycine-rich protein 2	NM_177425	-1,30	multicellular organismal development
<i>Dcx</i>	doublecortin	NM_053379	-1,30	neuron migration
<i>Htr1a</i>	5-hydroxytryptamine (serotonin) receptor 1A	NM_012585	-1,30	signal transduction

* P value = 0.029, was obtained by permutation analysis. Fold change ≥ 1.3 .