Supplemental table 4: List of canonical pathways significantly represented by genes regulated with aging

A- Anterior Pituitary

Ingenuity Canonical Pathways	-log(p-value)	Ratio	Genes
Complement System	2,48	0,188	*C1qc,Serping1,C4b,C1qb,C1qa,Cfb*
Antigen Presentation Pathway	2,30	0,179	*Hla-Drb1,Cd74,Hla-Dqa1,Hla-Dra,Tapbp*
Chemokine Signaling	2,85	0,147	*Ccl11,Camk1g,Fos,Jun,Camk2b,Camk1,Ccl13,Camk2d,Calm1,Plcg2*
Glutathione Metabolism	2,12	0,137	*Gpx4,Glrx,Gpx2,Gstm5,Ggct,Gstz1,Gstp1*
Growth Hormone Signaling	2,59	0,134	*Prkcz,Igf1,Igf2,Fos,Prkcq,Slc2a4,Rps6ka1,Plcg2,Igfbp3*
Melatonin Signaling	2,40	0,132	*Prkcz,Camk2b,Map2k3,Map2k6,Prkcq,Camk2d,Calm1,Plch2,Plcg2*
Glioma Signaling	3,02	0,122	*Prkcz,Camk1g,Igf1,Igf2,Camk2b,Camk1,Ccnd1,Prkcq,Camk2d,Calm1, Cdkn2c,Plcg2*
Neuropathic Pain Signaling In Dorsal Horn Neurons	2,55	0,118	*Prkcz,Kcnq2,Camk1g,Fos,Camk2b,Camk1,Gria4,Prkcq,Camk2d,Plch2,Ntrk2,Plcg2*
B Cell Development	1,52	0,115	*Hla-Drb1,Hla-Dqa1,Hla-Dra*
Calcium-induced T Lymphocyte Apoptosis	1,42	0,107	*Prkcz,Hla-Drb1,Prkcq,Calm1,Hla-Dqa1,Hla-Dra*
Aryl Hydrocarbon Receptor Signaling	2,49	0,102	*Aldh18a1,Gstm5,Hspb7,Aldh1a2,Ccnd1,Ccnd2,Aldh16a1,Pola1,Gstp1, Aldh1l2,Aip,Fos,Jun,Nfix*
Glycerolipid Metabolism	1,70	0,099	*Ppap2c,Pnpla2,Aldh1a2,Ppapdc1b,Dgka,Adh5,Dgkb,Dgkz,Ppap2b*
Phospholipid Degradation	1,77	0,099	*Ppap2c,Ppapdc1b,Dgka,Dgkb,Plch2,Dgkz,Plcg2,Ppap2b*
Cdc42 Signaling	2,41	0,092	*Prkcz,Apc2,Myl9,Fos,Jun,Hla-Drb1,Cdc42bpa, Exoc7,Hla-Dqa1,Diaph1,Hla-Dra,Exoc2*
14-3-3-mediated Signaling	1,57	0,090	*Prkcz,Tubb3,Fos,Jun,Tubb6,Prkcq,Rps6ka1,Plch2, Plcg2,Snca*
Glycerophospholipid Metabolism	1,55	0,084	*Chka,Ppap2c,Ppapdc1b,Dgka,Dgkb,Plch2,Dgkz,Plcg2,Chpt1,Ppap2b*
p38 MAPK Signaling	1,30	0,081	*Tradd,Hspb7,Mapkapk3,H3f3c,Map2k3,Map2k6,Eef2k,Mapkapk5*
PKCθ Signaling in T Lymphocytes	1,41	0,074	*Fos,Jun,Hla-Drb1,Camk2b,Prkcq,Camk2d,Hla-Dqa1,Plcg2,Hla-Dra*
Xenobiotic Metabolism Signaling	1,90	0,074	*Aldh18a1,Ces1c,Abcc3,Gstm5,Aldh1a2,Camk2b,Map2k6,Aldh16a1,Camk2d,Ppm1j,Gstp1,Prkcz,Aldh1l2,Aip,Camk1g,Camk1,Map2k3,Prkcq,Fmo5*

B- Hypothalamus

Ingenuity Canonical Pathways	-log(p-value)	Ratio	Molecules
Complement System	7,01	0,22	*C1QC,CFH,C3,C4B,C2,C1QB,C1QA*
Antigen Presentation Pathway	4,98	0,18	*B2m,Hla-C,Psmb9,Psmb8,Tap2*
Lipid Antigen Presentation by CD1	2,06	0,15	*Fcer1g,B2m*
Interferon Signaling	3,46	0,14	*Irf9,Stat1,Psmb8,Ifit3*
Primary Immunodeficiency Signaling	3,46	0,10	*Cd4,Ptprc,Tap2,Blnk*
Role of JAK1, JAK2 and TYK2 in Interferon Signaling	1,59	0,09	*Ptpn6,Stat1*
Natural Killer Cell Signaling	4,13	0,08	*Fcer1g,Ptpn6,Rras2,Tyrobp,Fcgr3a,Fcgr2a,Rac2*
Dendritic Cell Maturation	5,76	0,07	*Fcer1g,Fcgr2b,B2m,Hla-C,Stat1,Tyrobp,Icam1,Col1a1,Fcgr3a,Fcgr2a*
Linoleic Acid Metabolism	3,08	0,07	*Cyp51a1,Fads1,Cyp2d6,Cyp4f8,Fads2*

Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	3,11	0,07	*C1qc,C3,C1qb,Clec7a,C1qa*
OX40 Signaling Pathway	2,69	0,07	*Fcer1g,B2m,Hla-C,Cd4*
Allograft Rejection Signaling	2,11	0,06	*Fcer1g,B2m,Hla-C*
Autoimmune Thyroid Disease Signaling	1,31	0,06	*Fcer1g,Hla-C*
Communication between Innate and Adaptive Immune Cells	2,44	0,06	*Fcer1g,B2m,Hla-C,Cd4*
TREM1 Signaling	1,93	0,06	*Fcgr2b,Tyrobp,Icam1*
FcγRIIB Signaling in B Lymphocytes	1,93	0,06	*Fcgr2b,Rras2,Blnk*
Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells	1,93	0,06	*Fcer1g,B2m,Hla-C*
Activation of IRF by Cytosolic Pattern Recognition Receptors	1,62	0,06	*Irf9,Stat1,Ifit2*
Caveolar-mediated Endocytosis Signaling	2,12	0,06	*Cd48,B2m,Hla-C,Alb*
Glioma Invasiveness Signaling	1,60	0,06	*F2r,Rras2,Timp4*
Glutamate Receptor Signaling	1,49	0,05	*Slc1a2,Grm2,Slc1a6*
B Cell Receptor Signaling	2,98	0,05	*Ptpn6,Fcgr2b,Rras2,Ptprc,Fcgr2a,Rac2,Blnk*
JAK/Stat Signaling	1,44	0,05	*Ptpn6,Rras2,Stat1*
GM-CSF Signaling	1,42	0,05	*Rras2,Stat1,Hck*
Virus Entry via Endocytic Pathways	1,78	0,05	*Rras2,B2m,Hla-C,Rac2*
Systemic Lupus Erythematosus Signaling	3,47	0,05	*Fcer1g,Ptpn6,Fcgr2b,Rras2,Hla-C,Ptprc,Fcgr3a,Fcgr2a*
Role of JAK1 and JAK3 in γc Cytokine Signaling	1,51	0,05	*Rras2,Stat1,Blnk*
Antiproliferative Role of Somatostatin Receptor 2	1,42	0,05	*Ptpn6,Rras2,Sst*
Fcγ Receptor-mediated Phagocytosis in Macrophages and Monocytes	1,65	0,05	*Fcgr3a,Fcgr2a,Hck,Rac2*
Growth Hormone Signaling	1,37	0,04	*Ptpn6,Stat1,Igfbp3*
LXR/RXR Activation	2,04	0,04	*C3,C4B (Includes Others),HMGCR,ALB,SCD*
Acute Phase Response Signaling	2,46	0,04	*Rras2,Cp,C3,Serpina3,C4b,Alb*
Role of NFAT in Regulation of the Immune Response	2,61	0,04	*Fcer1g,Fcgr2b,Rras2,Cd4,Fcgr3a,Fcgr2a,Blnk*
Metabolism of Xenobiotics by Cytochrome P450	1,64	0,04	*Cyp51a1,Cyp2d6,Cyp4f8,Gsta1*
PI3K Signaling in B Lymphocytes	1,77	0,04	*Fcgr2b,Rras2,C3,Ptprc,Blnk*
Hepatic Fibrosis / Hepatic Stellate Cell Activation	1,64	0,04	*Ednrb,Stat1,Icam1,Col1a1,Igfbp3*
CD28 Signaling in T Helper Cells	1,48	0,04	*Fcer1g,Ptpn6,Cd4,Ptprc*
Germ Cell-Sertoli Cell Junction Signaling	1,56	0,03	*Mllt4,Rras2,Iqgap1,Pls1,Rac2*
PKCθ Signaling in T Lymphocytes	1,49	0,03	*Fcer1g,Rras2,Cd4,Rac2*
Wnt/β-catenin Signaling	1,40	0,03	*Fzd2,Gja1,Sox4,Wnt4,Nlk*
Cdc42 Signaling	1,38	0,03	*Fcer1g,B2m,Hla-C,Iqgap1*
Protein Ubiquitination Pathway	1,63	0,03	*Hspb1,B2m,Hla-C,Psmb9,Psmb8,Ube2l6,Tap2*
ERK/MAPK Signaling	1,30	0,03	*Hspb1,Rras2,Stat1,Dusp6,Rac2*