



De Novo Transcriptome Assembly and Annotation of Liver and Brain Tissues of Common Brushtail Possums (*Trichosurus vulpecula*) in New Zealand: Transcriptome Diversity after Decades of Population Control

Supplementary Materials

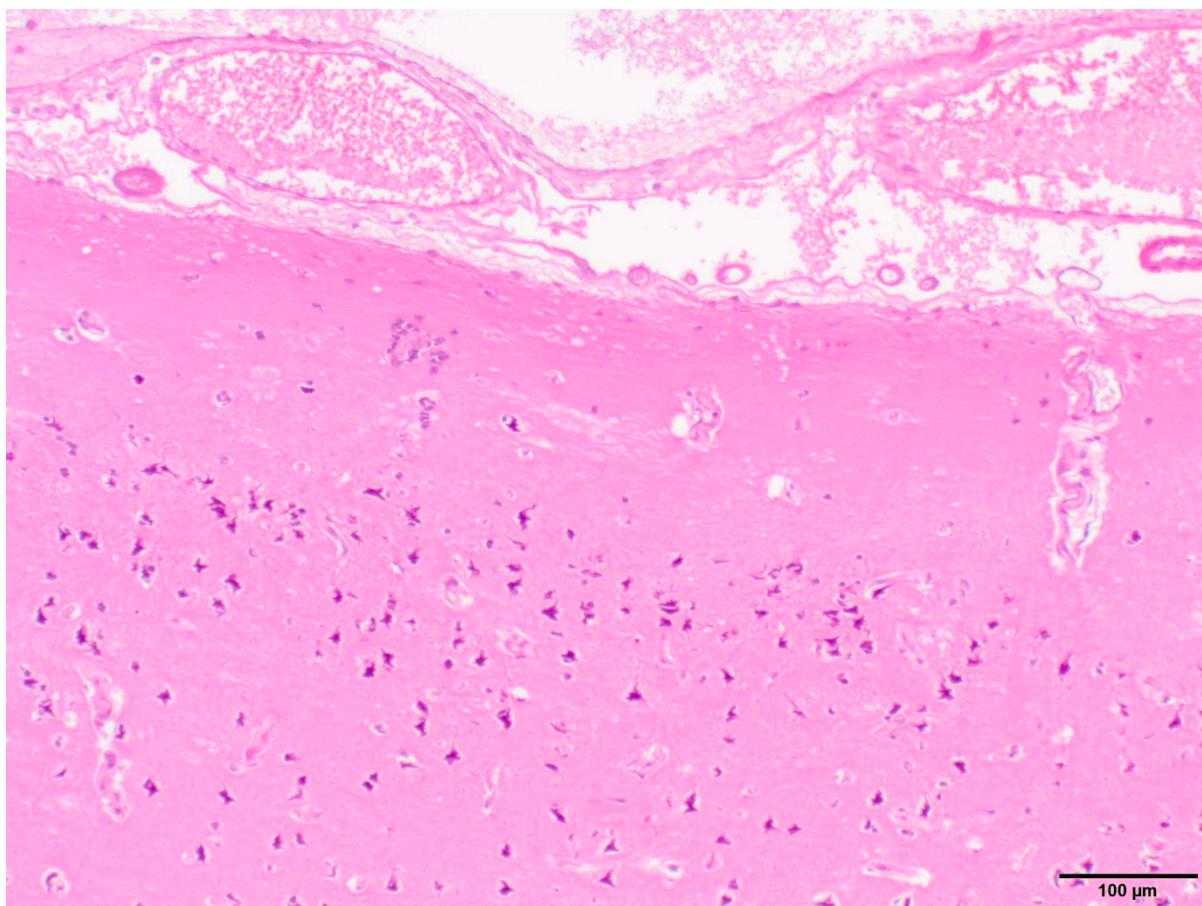


Figure S1. Mid magnification image of a brain cerebral cortex from a brushtail possum sample. The image depicts the cerebral cortex using hematoxylin and eosin staining, 100x original magnification, scale bar=100 μm .

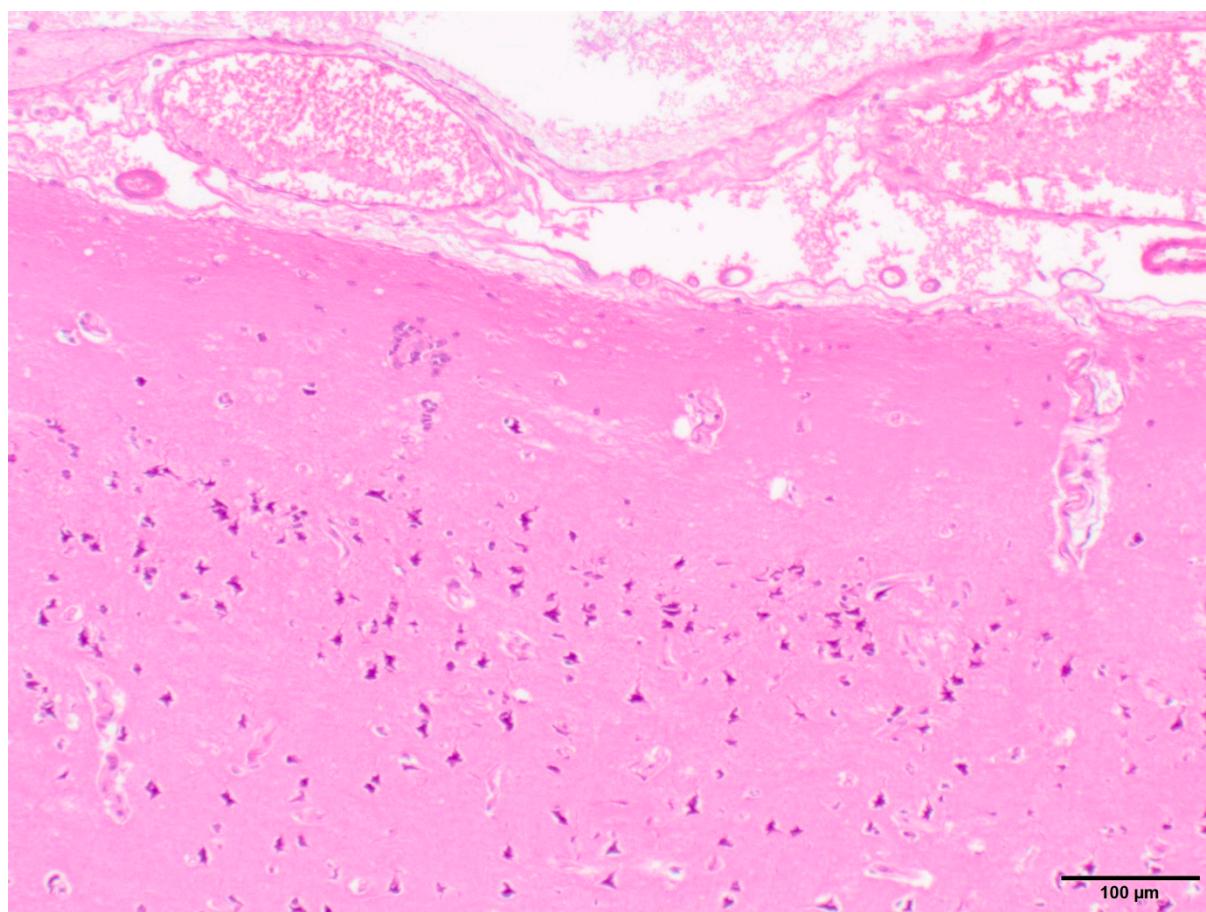


Figure S2. Mid magnification image of brain cerebral cortex from a brushtail possum sample. The image depicts the cerebral cortex using hematoxylin and eosin staining, 100x original magnification, scale bar=100 μm .

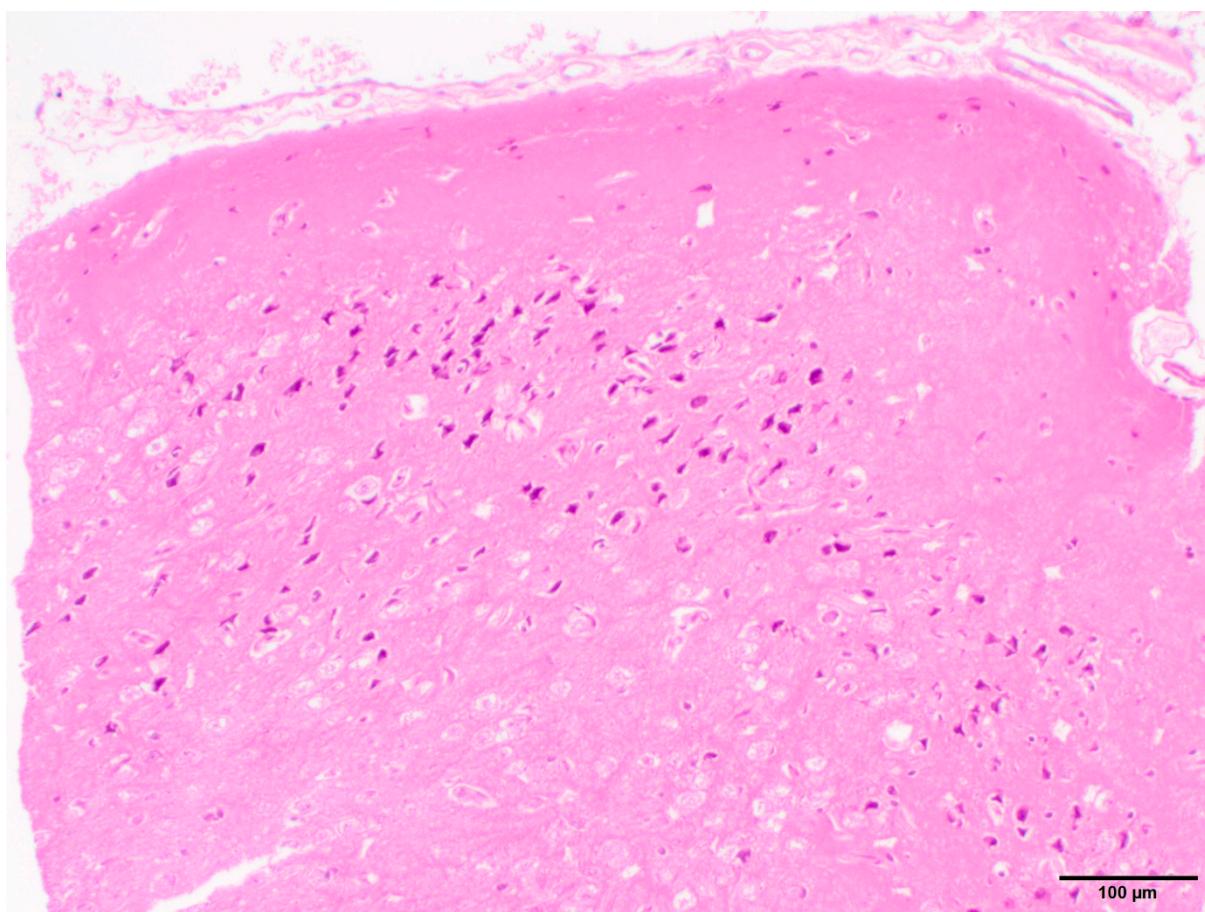


Figure S3. Mid magnification image of brain cerebral cortex from a brushtail possum sample. The image depicts the cerebral cortex using hematoxylin and eosin staining, 100x original magnification, scale bar=100 μm .

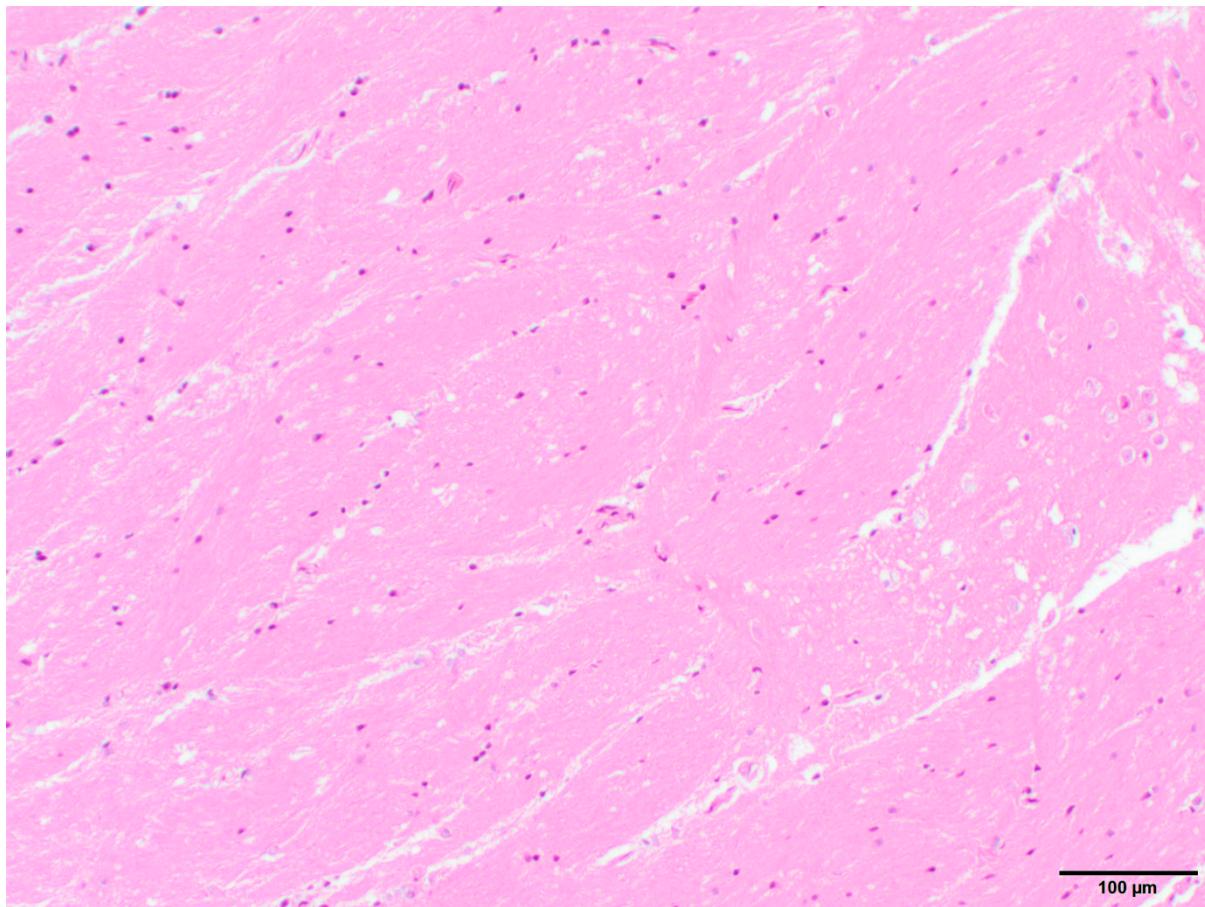


Figure S4. Mid magnification image of brain cerebral cortex from brushtail possum sample. The image depicts white matter with scattered glial cells using hematoxylin and eosin staining, 100x original magnification, scale bar=100 μm .

Table S1. The gene content of the brushtail possum's liver and brain cerebral cortex transcriptomes compared to the core-mammalian BUSCOs.

Transcriptome Name	Liver	Brain
Complete BUSCOs	3290	2446
Complete and single-copy BUSCOs	2898	2163
Complete and duplicated BUSCOs	392	283
Fragmented BUSCOs	844	988
Missing BUSCOs	5092	5792
Total BUSCO groups searched	9226	9226

Complete—contig lengths matched to the BUSCO profile; duplicated—contigs found more than once in orthology annotation; fragmented—partially covered; missing—no matches that passed orthology classification tests.

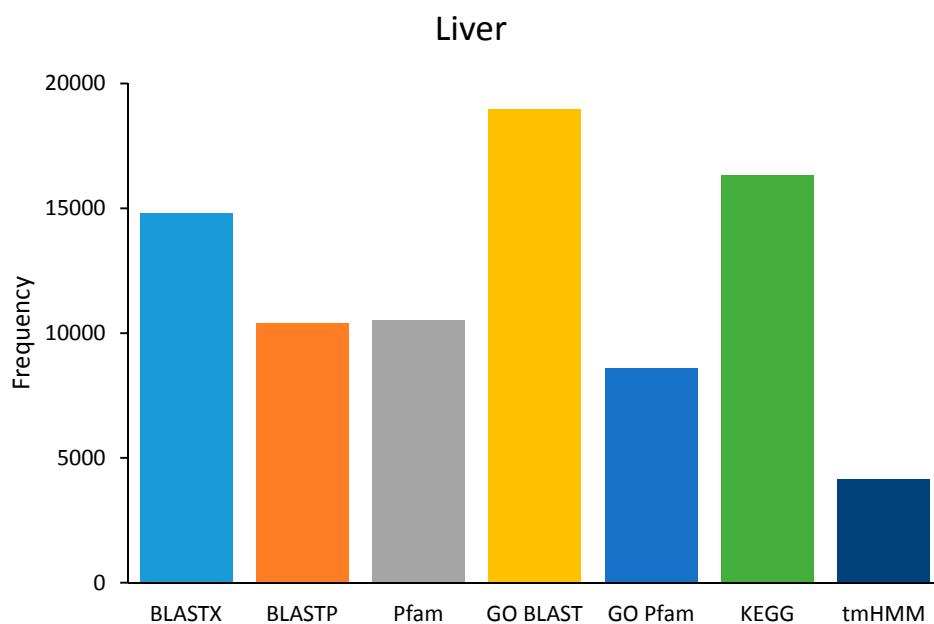


Figure S5. Number of liver transcripts that returned significant matches in different databases.

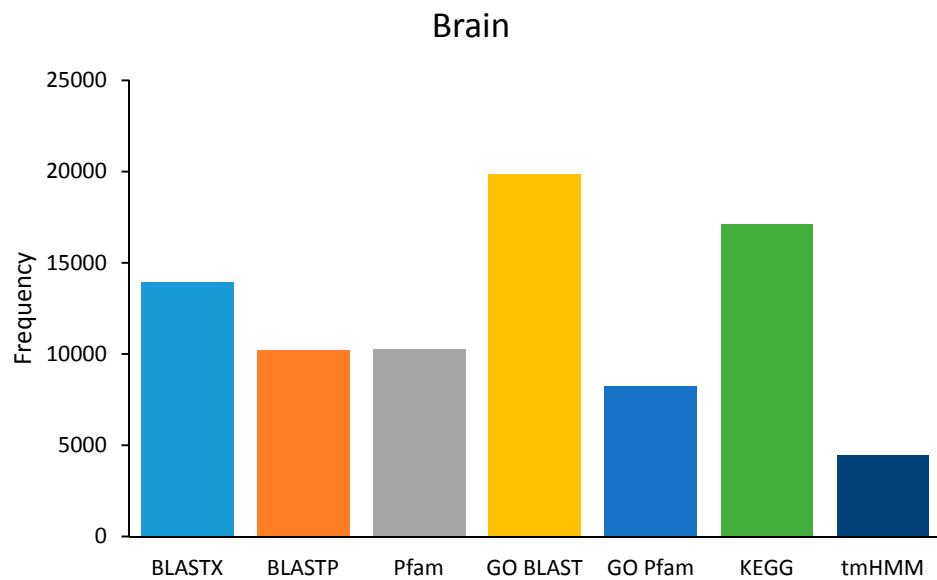


Figure S6. Number of brain cerebral cortex transcripts that returned significant matches in different databases.

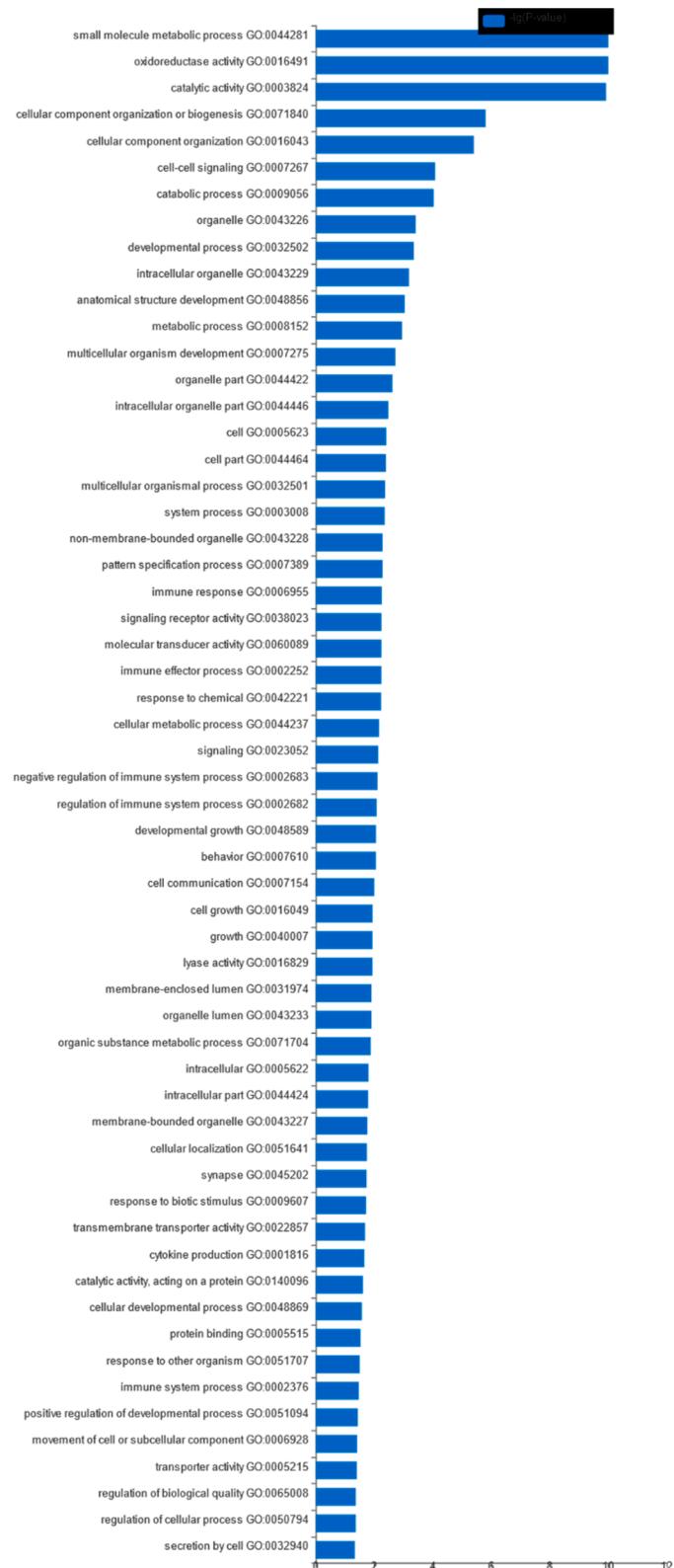


Figure S7. The Gene Ontology terms of the top 5% highly expressed transcripts that differ significantly (χ^2 test p -value <0.05) between the liver and brain cerebral cortex cells.

Table S2. Definition and number of total KEGG metabolic pathways predicted in the brushtail possum liver transcriptome.

Liver Metabolic Pathways	Number of Pathways
Global and overview maps	
01100 Metabolic pathways	506
01110 Biosynthesis of secondary metabolites	143
01120 Microbial metabolism in diverse environments	83
01130 Biosynthesis of antibiotics	100
01200 Carbon metabolism	55
01210 2-Oxocarboxylic acid metabolism	7
01212 Fatty acid metabolism	23
01230 Biosynthesis of amino acids	27
01220 Degradation of aromatic compounds	2
Carbohydrate metabolism	
00010 Glycolysis / Gluconeogenesis	26
00020 Citrate cycle	16
00030 Pentose phosphate pathway	11
00040 Pentose and glucuronate interconversions	11
00051 Fructose and mannose metabolism	10
00052 Galactose metabolism	11
00053 Ascorbate and aldarate metabolism	6
00500 Starch and sucrose metabolism	13
00520 Amino sugar and nucleotide sugar metabolism	21
00620 Pyruvate metabolism	24
00630 Glyoxylate and dicarboxylate metabolism	20
00640 Propanoate metabolism	22
00650 Butanoate metabolism	11
00562 Inositol phosphate metabolism	17
Energy metabolism	
00190 Oxidative phosphorylation	50
00710 Carbon fixation in photosynthetic organisms	10
00720 Carbon fixation pathways in prokaryotes	6
00680 Methane metabolism	11
00910 Nitrogen metabolism	4
00920 Sulfur metabolism	4
Lipid metabolism	
00061 Fatty acid biosynthesis	7
00062 Fatty acid elongation	7
00071 Fatty acid degradation	20
00072 Synthesis and degradation of ketone bodies	4
00100 Steroid biosynthesis	11
00120 Primary bile acid biosynthesis	12
00140 Steroid hormone biosynthesis	20
00561 Glycerolipid metabolism	20
00564 Glycerophospholipid metabolism	25
00565 Ether lipid metabolism	10
00600 Sphingolipid metabolism	9
00590 Arachidonic acid metabolism	13
00591 Linoleic acid metabolism	8
00592 alpha-Linolenic acid metabolism	2
01040 Biosynthesis of unsaturated fatty acids	9

Liver Metabolic Pathways	Number of Pathways
Nucleotide metabolism	
00230 Purine metabolism	36
00240 Pyrimidine metabolism	16
Amino acid metabolism	
00250 Alanine, aspartate and glutamate metabolism	9
00260 Glycine, serine and threonine metabolism	21
00270 Cysteine and methionine metabolism	23
00280 Valine, leucine and isoleucine degradation	26
00300 Lysine biosynthesis	1
00310 Lysine degradation	26
00220 Arginine biosynthesis	7
00330 Arginine and proline metabolism	18
00340 Histidine metabolism	7
00350 Tyrosine metabolism	13
00360 Phenylalanine metabolism	9
00380 Tryptophan metabolism	22
00400 Phenylalanine, tyrosine and tryptophan biosynthesis	3
Metabolism of other amino acids	
00410 beta-Alanine metabolism	16
00430 Taurine and hypotaurine metabolism	3
00440 Phosphonate and phosphinate metabolism	3
00450 Selenocompound metabolism	5
00460 Cyanoamino acid metabolism	2
00471 D-Glutamine and D-glutamate metabolism	1
00472 D-Arginine and D-ornithine metabolism	1
00480 Glutathione metabolism	13
Glycan biosynthesis and metabolism	
00510 N-Glycan biosynthesis	20
00513 Various types of N-glycan biosynthesis	14
00512 Mucin type O-glycan biosynthesis	4
00515 Mannose type O-glycan biosynthesis	2
00514 Other types of O-glycan biosynthesis	3
00532 Glycosaminoglycan biosynthesis - chondroitin sulfate / dermatan sulfate	3
00534 Glycosaminoglycan biosynthesis - heparan sulfate / heparin	7
00533 Glycosaminoglycan biosynthesis - keratan sulfate	3
00531 Glycosaminoglycan degradation	7
00563 Glycosylphosphatidylinositol	10
00601 Glycosphingolipid biosynthesis - lacto and neolacto series	5
00603 Glycosphingolipid biosynthesis - globo and isogloblo series	3
00604 Glycosphingolipid biosynthesis - ganglio series	5
00511 Other glycan degradation	5
Metabolism of cofactors and vitamins	
00730 Thiamine metabolism	3
00740 Riboflavin metabolism	4
00750 Vitamin B6 metabolism	3
00760 Nicotinate and nicotinamide metabolism	15
00770 Pantothenate and CoA biosynthesis	6
00780 Biotin metabolism	3
00785 Lipoic acid metabolism	1

Liver Metabolic Pathways	Number of Pathways
00790 Folate biosynthesis	14
00670 One carbon pool by folate	9
00830 Retinol metabolism	23
00860 Porphyrin and chlorophyll metabolism	13
00130 Ubiquinone and other terpenoid-quinone biosynthesis	7
Metabolism of terpenoids and polyketides	
00900 Terpenoid backbone biosynthesis	9
00909 Sesquiterpenoid and triterpenoid biosynthesis	2
00981 Insect hormone biosynthesis	1
00903 Limonene and pinene degradation	1
00281 Geraniol degradation	1
01051 Biosynthesis of ansamycins	1
00523 Polyketide sugar unit biosynthesis	1
01055 Biosynthesis of vancomycin group antibiotics	1
Biosynthesis of other secondary metabolites	
00940 Phenylpropanoid biosynthesis	1
00944 Flavone and flavonol biosynthesis	1
00901 Indole alkaloid biosynthesis	1
00950 Isoquinoline alkaloid biosynthesis	4
00960 Tropane, piperidine and pyridine alkaloid biosynthesis	2
00232 Caffeine metabolism	3
00965 Betalain biosynthesis	2
00311 Penicillin and cephalosporin biosynthesis	1
00521 Streptomycin biosynthesis	4
00524 Neomycin, kanamycin and gentamicin biosynthesis	1
00525 Acarbose and validamycin biosynthesis	1
00401 Novobiocin biosynthesis	1
00254 Aflatoxin biosynthesis	2
Xenobiotics biodegradation and metabolism	
00362 Benzoate degradation	1
00627 Aminobenzoate degradation	3
00364 Fluorobenzoate degradation	1
00625 Chloroalkane and chloroalkene degradation	3
00361 Chlorocyclohexane and chlorobenzene degradation	1
00623 Toluene degradation	1
00633 Nitrotoluene degradation	1
00643 Styrene degradation	2
00930 Caprolactam degradation	4
00626 Naphthalene degradation	1
00980 Metabolism of xenobiotics by cytochrome P450	17
00982 Drug metabolism - cytochrome P450	14
00983 Drug metabolism - other enzymes	20
Genetic Information Processing	
Transcription	
03020 RNA polymerase	8
03022 Basal transcription factors	14
03040 Spliceosome	36
Translation	
03010 Ribosome	70
00970 Aminoacyl-tRNA biosynthesis	14

Liver Metabolic Pathways	Number of Pathways
03013 RNA transport	54
03015 mRNA surveillance pathway	25
03008 Ribosome biogenesis in eukaryotes	34
Folding, sorting and degradation	
03060 Protein export	11
04141 Protein processing in endoplasmic reticulum	78
04130 SNARE interactions in vesicular transport	10
04120 Ubiquitin mediated proteolysis	46
04122 Sulfur relay system	3
03050 Proteasome	26
03018 RNA degradation	24
Replication and repair	
03030 DNA replication	9
03410 Base excision repair	7
03420 Nucleotide excision repair	13
03430 Mismatch repair	5
03440 Homologous recombination	8
03450 Non-homologous end-joining	4
03460 Fanconi anemia pathway	9
Environmental Information Processing	
Membrane transport	
02010 ABC transporters	13
03070 Bacterial secretion system	1
Signal transduction	
02020 Two-component system	3
04014 Ras signaling pathway	44
04015 Rap1 signaling pathway	48
04010 MAPK signaling pathway	59
04013 MAPK signaling pathway - fly	20
04016 MAPK signaling pathway - plant	3
04011 MAPK signaling pathway - yeast	6
04012 ErbB signaling pathway	21
04310 Wnt signaling pathway	27
04330 Notch signaling pathway	12
04340 Hedgehog signaling pathway	3
04341 Hedgehog signaling pathway - fly	3
04350 TGF-beta signaling pathway	28
04390 Hippo signaling pathway	37
04391 Hippo signaling pathway - fly	15
04392 Hippo signaling pathway - multiple species	6
04370 VEGF signaling pathway	16
04371 Apelin signaling pathway	26
04630 JAK-STAT signaling pathway	33
04064 NF-kappa B signaling pathway	22
04668 TNF signaling pathway	23
04066 HIF-1 signaling pathway	33
04068 FoxO signaling pathway	33
04020 Calcium signaling pathway	24
04070 Phosphatidylinositol signaling system	18
04072 Phospholipase D signaling pathway	29

Liver Metabolic Pathways	Number of Pathways
04071 Sphingolipid signaling pathway	33
04024 cAMP signaling pathway	31
04022 cGMP-PKG signaling pathway	39
04151 PI3K-Akt signaling pathway	80
04152 AMPK signaling pathway	40
04150 mTOR signaling pathway	34
Signaling molecules and interaction	
04080 Neuroactive ligand-receptor interaction	20
04060 Cytokine-cytokine receptor interaction	40
04061 Viral protein interaction with cytokine and cytokine receptor	15
04512 ECM-receptor interaction	19
04514 Cell adhesion molecules	23
Cellular Processes	980
Transport and catabolism	
04144 Endocytosis	73
04145 Phagosome	46
04142 Lysosome	51
04146 Peroxisome	47
04140 Autophagy - animal	41
04138 Autophagy - yeast	16
04136 Autophagy - other	8
04137 Mitophagy - animal	18
04139 Mitophagy - yeast	10
Cell growth and death	
04110 Cell cycle	28
04111 Cell cycle - yeast	22
04112 Cell cycle - Caulobacter	2
04113 Meiosis - yeast	16
04114 Oocyte meiosis	24
04210 Apoptosis	40
04214 Apoptosis - fly	15
04215 Apoptosis - multiple species	7
04216 Ferroptosis	15
04217 Necroptosis	39
04115 p53 signaling pathway	16
04218 Cellular senescence	45
Cellular community - eukaryotes	
04510 Focal adhesion	55
04520 Adherens junction	26
04530 Tight junction	38
04540 Gap junction	13
04550 Signaling pathways regulating pluripotency of stem cells	30
Cellular community - prokaryotes	
02024 Quorum sensing	2
02026 Biofilm formation - Escherichia coli	1
Cell motility	
04810 Regulation of actin cytoskeleton	57
Organismal Systems	
Immune system	
04640 Hematopoietic cell lineage	17

Liver Metabolic Pathways	Number of Pathways
04610 Complement and coagulation cascades	43
04611 Platelet activation	31
04620 Toll-like receptor signaling pathway	29
04624 Toll and Imd signaling pathway	11
04621 NOD-like receptor signaling pathway	42
04622 RIG-I-like receptor signaling pathway	15
04623 Cytosolic DNA-sensing pathway	14
04625 C-type lectin receptor signaling pathway	25
04650 Natural killer cell mediated cytotoxicity	22
04612 Antigen processing and presentation	12
04660 T cell receptor signaling pathway	23
04658 Th1 and Th2 cell differentiation	21
04659 Th17 cell differentiation	27
04657 IL-17 signaling pathway	16
04662 B cell receptor signaling pathway	27
04664 Fc epsilon RI signaling pathway	17
04666 Fc gamma R-mediated phagocytosis	22
04670 Leukocyte transendothelial migration	30
04672 Intestinal immune network for IgA production	6
04062 Chemokine signaling pathway	37
Endocrine system	
04911 Insulin secretion	11
04910 Insulin signaling pathway	42
04922 Glucagon signaling pathway	34
04923 Regulation of lipolysis in adipocytes	8
04920 Adipocytokine signaling pathway	24
03320 PPAR signaling pathway	25
04929 GnRH secretion	11
04912 GnRH signaling pathway	15
04913 Ovarian steroidogenesis	12
04915 Estrogen signaling pathway	24
04914 Progesterone-mediated oocyte maturation	16
04917 Prolactin signaling pathway	17
04921 Oxytocin signaling pathway	26
04926 Relaxin signaling pathway	25
04935 Growth hormone synthesis, secretion and action	27
04918 Thyroid hormone synthesis	15
04919 Thyroid hormone signaling pathway	35
04928 Parathyroid hormone synthesis, secretion and action	16
04916 Melanogenesis	15
04924 Renin secretion	11
04614 Renin-angiotensin system	7
04925 Aldosterone synthesis and secretion	15
04927 Cortisol synthesis and secretion	12
Circulatory system	
04260 Cardiac muscle contraction	12
04261 Adrenergic signaling in cardiomyocytes	19
04270 Vascular smooth muscle contraction	22
Digestive system	
04970 Salivary secretion	14

Liver Metabolic Pathways	Number of Pathways
04971 Gastric acid secretion	12
04972 Pancreatic secretion	17
04976 Bile secretion	22
04973 Carbohydrate digestion and absorption	5
04974 Protein digestion and absorption	13
04975 Fat digestion and absorption	10
04979 Cholesterol metabolism	20
04977 Vitamin digestion and absorption	7
04978 Mineral absorption	9
Excretory system	
04962 Vasopressin-regulated water reabsorption	12
04960 Aldosterone-regulated sodium reabsorption	7
04961 Endocrine and other factor-regulated calcium reabsorption	10
04964 Proximal tubule bicarbonate reclamation	8
04966 Collecting duct acid secretion	9
Nervous system	
04724 Glutamatergic synapse	11
04727 GABAergic synapse	7
04725 Cholinergic synapse	12
04728 Dopaminergic synapse	19
04726 Serotonergic synapse	15
04720 Long-term potentiation	16
04730 Long-term depression	11
04723 Retrograde endocannabinoid signaling	27
04721 Synaptic vesicle cycle	14
04722 Neurotrophin signaling pathway	28
Sensory system	
04744 Phototransduction	1
04745 Phototransduction - fly	5
04740 Olfactory transduction	1
04742 Taste transduction	2
04750 Inflammatory mediator regulation of TRP channels	14
Development and regeneration	
04320 Dorso-ventral axis formation	6
04360 Axon guidance	32
04361 Axon regeneration	20
04380 Osteoclast differentiation	31
Aging	
04211 Longevity regulating pathway	26
04212 Longevity regulating pathway - worm	24
04213 Longevity regulating pathway - multiple species	18
Environmental adaptation	
04710 Circadian rhythm	9
04713 Circadian entrainment	6
04711 Circadian rhythm - fly	2
04714 Thermogenesis	71
04626 Plant-pathogen interaction	6

Table S3. Definition and number of total KEGG metabolic pathways predicted in the brushtail possum brain cerebral cortex transcriptome.

Brain Metabolic Pathways	Number of Pathways
Global and overview maps	
01100 Metabolic pathways	301
01110 Biosynthesis of secondary metabolites	89
01120 Microbial metabolism in diverse environments	45
01130 Biosynthesis of antibiotics	60
01200 Carbon metabolism	33
01210 2-Oxocarboxylic acid metabolism	7
01212 Fatty acid metabolism	22
01230 Biosynthesis of amino acids	18
01220 Degradation of aromatic compounds	2
Carbohydrate metabolism	
00010 Glycolysis / Gluconeogenesis	15
00020 Citrate cycle	14
00030 Pentose phosphate pathway	5
00040 Pentose and glucuronate interconversions	4
00051 Fructose and mannose metabolism	3
00052 Galactose metabolism	4
00053 Ascorbate and aldarate metabolism	3
00500 Starch and sucrose metabolism	8
00520 Amino sugar and nucleotide sugar metabolism	9
00620 Pyruvate metabolism	11
00630 Glyoxylate and dicarboxylate metabolism	6
00640 Propanoate metabolism	8
00650 Butanoate metabolism	8
00562 Inositol phosphate metabolism	14
Energy metabolism	
00190 Oxidative phosphorylation	41
00710 Carbon fixation in photosynthetic organisms	8
00720 Carbon fixation pathways in prokaryotes	4
00680 Methane metabolism	5
00910 Nitrogen metabolism	2
00920 Sulfur metabolism	3
Lipid metabolism	
00061 Fatty acid biosynthesis	4
00062 Fatty acid elongation	10
00071 Fatty acid degradation	14
00072 Synthesis and degradation of ketone bodies	1
00073 Cutin, suberine and wax biosynthesis	1
00100 Steroid biosynthesis	3
00120 Primary bile acid biosynthesis	4
00140 Steroid hormone biosynthesis	3
00561 Glycerolipid metabolism	11
00564 Glycerophospholipid metabolism	19
00565 Ether lipid metabolism	10
00600 Sphingolipid metabolism	12
00590 Arachidonic acid metabolism	5
00591 Linoleic acid metabolism	1
00592 alpha-Linolenic acid metabolism	1
01040 Biosynthesis of unsaturated fatty acids	9

Brain Metabolic Pathways	Number of Pathways
Nucleotide metabolism	
00230 Purine metabolism	28
00240 Pyrimidine metabolism	5
Amino acid metabolism	
00250 Alanine, aspartate and glutamate metabolism	10
00260 Glycine, serine and threonine metabolism	5
00270 Cysteine and methionine metabolism	12
00280 Valine, leucine and isoleucine degradation	16
00300 Lysine biosynthesis	1
00310 Lysine degradation	16
00220 Arginine biosynthesis	7
00330 Arginine and proline metabolism	15
00340 Histidine metabolism	2
00350 Tyrosine metabolism	5
00360 Phenylalanine metabolism	4
00380 Tryptophan metabolism	8
00400 Phenylalanine, tyrosine and tryptophan biosynthesis	2
Metabolism of other amino acids	
00410 beta-Alanine metabolism	7
00430 Taurine and hypotaurine metabolism	1
00440 Phosphonate and phosphinate metabolism	2
00450 Selenocompound metabolism	4
00460 Cyanoamino acid metabolism	1
00471 D-Glutamine and D-glutamate metabolism	1
00480 Glutathione metabolism	7
Glycan biosynthesis and metabolism	
00510 N-Glycan biosynthesis	14
00513 Various types of N-glycan biosynthesis	11
00512 Mucin type O-glycan biosynthesis	2
00515 Mannose type O-glycan biosynthesis	7
00514 Other types of O-glycan biosynthesis	3
00532 Glycosaminoglycan biosynthesis - chondroitin sulfate / dermatan sulfate	1
00534 Glycosaminoglycan biosynthesis - heparan sulfate / heparin	10
00533 Glycosaminoglycan biosynthesis - keratan sulfate	3
00531 Glycosaminoglycan degradation	4
00563 Glycosylphosphatidylinositol	9
00601 Glycosphingolipid biosynthesis - lacto and neolacto series	4
00603 Glycosphingolipid biosynthesis - globo and isogloblo series	2
00604 Glycosphingolipid biosynthesis - ganglio series	7
00511 Other glycan degradation	7
Metabolism of cofactors and vitamins	
00730 Thiamine metabolism	3
00740 Riboflavin metabolism	1
00750 Vitamin B6 metabolism	2
00760 Nicotinate and nicotinamide metabolism	5
00770 Pantothenate and CoA biosynthesis	1
00785 Lipoic acid metabolism	1
00790 Folate biosynthesis	4
00670 One carbon pool by folate	3
00830 Retinol metabolism	5
00860 Porphyrin and chlorophyll metabolism	4

Brain Metabolic Pathways	Number of Pathways
00130 Ubiquinone and other terpenoid-quinone biosynthesis	3
Metabolism of terpenoids and polyketides	
00900 Terpenoid backbone biosynthesis	4
00981 Insect hormone biosynthesis	1
00903 Limonene and pinene degradation	1
01051 Biosynthesis of ansamycins	1
Biosynthesis of other secondary metabolites	
00940 Phenylpropanoid biosynthesis	1
00950 Isoquinoline alkaloid biosynthesis	3
00960 Tropane, piperidine and pyridine alkaloid biosynthesis	2
00261 Monobactam biosynthesis	1
00521 Streptomycin biosynthesis	1
00524 Neomycin, kanamycin and gentamicin biosynthesis	1
Xenobiotics biodegradation and metabolism	
00362 Benzoate degradation	1
00627 Aminobenzoate degradation	4
00364 Fluorobenzoate degradation	1
00625 Chloroalkane and chloroalkene degradation	2
00361 Chlorocyclohexane and chlorobenzene degradation	1
00623 Toluene degradation	1
00930 Caprolactam degradation	4
00626 Naphthalene degradation	1
00980 Metabolism of xenobiotics by cytochrome P450	5
00982 Drug metabolism - cytochrome P450	4
00983 Drug metabolism - other enzymes	6
Genetic Information Processing	
Transcription	
03020 RNA polymerase	3
03022 Basal transcription factors	10
03040 Spliceosome	30
Translation	
03010 Ribosome	55
00970 Aminoacyl-tRNA biosynthesis	13
03013 RNA transport	48
03015 mRNA surveillance pathway	21
03008 Ribosome biogenesis in eukaryotes	17
Folding, sorting and degradation	
03060 Protein export	10
04141 Protein processing in endoplasmic reticulum	53
04130 SNARE interactions in vesicular transport	8
04120 Ubiquitin mediated proteolysis	35
03050 Proteasome	14
03018 RNA degradation	15
Replication and repair	
03030 DNA replication	4
03410 Base excision repair	4
03420 Nucleotide excision repair	10
03430 Mismatch repair	4
03440 Homologous recombination	2
03450 Non-homologous end-joining	1

Brain Metabolic Pathways	Number of Pathways
03460 Fanconi anemia pathway	7
Environmental Information Processing	
Membrane transport	
02010 ABC transporters	9
03070 Bacterial secretion system	1
Signal transduction	
02020 Two-component system	4
04014 Ras signaling pathway	52
04015 Rap1 signaling pathway	55
04010 MAPK signaling pathway	56
04013 MAPK signaling pathway - fly	21
04016 MAPK signaling pathway - plant	3
04011 MAPK signaling pathway - yeast	7
04012 ErbB signaling pathway	22
04310 Wnt signaling pathway	19
04330 Notch signaling pathway	8
04340 Hedgehog signaling pathway	4
04341 Hedgehog signaling pathway - fly	2
04350 TGF-beta signaling pathway	13
04390 Hippo signaling pathway	23
04391 Hippo signaling pathway - fly	13
04392 Hippo signaling pathway - multiple species	2
04370 VEGF signaling pathway	12
04371 Apelin signaling pathway	36
04630 JAK-STAT signaling pathway	18
04064 NF-kappa B signaling pathway	5
04668 TNF signaling pathway	15
04066 HIF-1 signaling pathway	27
04068 FoxO signaling pathway	29
04020 Calcium signaling pathway	32
04070 Phosphatidylinositol signaling system	20
04072 Phospholipase D signaling pathway	37
04071 Sphingolipid signaling pathway	30
04024 cAMP signaling pathway	45
04022 cGMP-PKG signaling pathway	36
04151 PI3K-Akt signaling pathway	63
04152 AMPK signaling pathway	27
04150 mTOR signaling pathway	29
Signaling molecules and interaction	
04080 Neuroactive ligand-receptor interaction	24
04060 Cytokine-cytokine receptor interaction	15
04061 Viral protein interaction with cytokine and cytokine receptor	8
04512 ECM-receptor interaction	10
04514 Cell adhesion molecules	22
Cellular Processes	
Transport and catabolism	
04144 Endocytosis	71
04145 Phagosome	32
04142 Lysosome	35
04146 Peroxisome	21
04140 Autophagy - animal	41

Brain Metabolic Pathways	Number of Pathways
04138 Autophagy - yeast	20
04136 Autophagy - other	13
04137 Mitophagy - animal	19
04139 Mitophagy - yeast	10
Cell growth and death	
04110 Cell cycle	16
04111 Cell cycle - yeast	10
04113 Meiosis - yeast	9
04114 Oocyte meiosis	22
04210 Apoptosis	25
04214 Apoptosis - fly	13
04215 Apoptosis - multiple species	4
04216 Ferroptosis	9
04217 Necroptosis	21
04115 p53 signaling pathway	11
04218 Cellular senescence	33
Cellular community - eukaryotes	
04510 Focal adhesion	42
04520 Adherens junction	24
04530 Tight junction	36
04540 Gap junction	20
04550 Signaling pathways regulating pluripotency of stem cells	22
Cellular community - prokaryotes	
02024 Quorum sensing	3
02026 Biofilm formation - Escherichia coli	1
Cell motility	
04810 Regulation of actin cytoskeleton	46
Organismal Systems	
Immune system	
04640 Hematopoietic cell lineage	10
04610 Complement and coagulation cascades	10
04611 Platelet activation	26
04620 Toll-like receptor signaling pathway	12
04624 Toll and Imd signaling pathway	4
04621 NOD-like receptor signaling pathway	24
04622 RIG-I-like receptor signaling pathway	6
04623 Cytosolic DNA-sensing pathway	5
04625 C-type lectin receptor signaling pathway	16
04650 Natural killer cell mediated cytotoxicity	16
04612 Antigen processing and presentation	8
04660 T cell receptor signaling pathway	16
04658 Th1 and Th2 cell differentiation	8
04659 Th17 cell differentiation	13
04657 IL-17 signaling pathway	8
04662 B cell receptor signaling pathway	13
04664 Fc epsilon RI signaling pathway	15
04666 Fc gamma R-mediated phagocytosis	20
04670 Leukocyte transendothelial migration	21
04672 Intestinal immune network for IgA production	1
04062 Chemokine signaling pathway	34
Endocrine system	

Brain Metabolic Pathways	Number of Pathways
04911 Insulin secretion	19
04910 Insulin signaling pathway	30
04922 Glucagon signaling pathway	23
04923 Regulation of lipolysis in adipocytes	13
04920 Adipocytokine signaling pathway	12
03320 PPAR signaling pathway	13
04929 GnRH secretion	15
04912 GnRH signaling pathway	23
04913 Ovarian steroidogenesis	6
04915 Estrogen signaling pathway	30
04914 Progesterone-mediated oocyte maturation	18
04917 Prolactin signaling pathway	11
04921 Oxytocin signaling pathway	32
04926 Relaxin signaling pathway	28
04935 Growth hormone synthesis, secretion and action	30
04918 Thyroid hormone synthesis	18
04919 Thyroid hormone signaling pathway	32
04928 Parathyroid hormone synthesis, secretion and action	18
04916 Melanogenesis	19
04924 Renin secretion	14
04614 Renin-angiotensin system	5
04925 Aldosterone synthesis and secretion	21
04927 Cortisol synthesis and secretion	15
Circulatory system	
04260 Cardiac muscle contraction	21
04261 Adrenergic signaling in cardiomyocytes	30
04270 Vascular smooth muscle contraction	24
Digestive system	
04970 Salivary secretion	18
04971 Gastric acid secretion	20
04972 Pancreatic secretion	21
04976 Bile secretion	18
04973 Carbohydrate digestion and absorption	9
04974 Protein digestion and absorption	4
04975 Fat digestion and absorption	5
04979 Cholesterol metabolism	12
04977 Vitamin digestion and absorption	2
04978 Mineral absorption	8
Excretory system	
04962 Vasopressin-regulated water reabsorption	11
04960 Aldosterone-regulated sodium reabsorption	11
04961 Endocrine and other factor-regulated calcium reabsorption	15
04964 Proximal tubule bicarbonate reclamation	5
04966 Collecting duct acid secretion	7
Nervous system	
04724 Glutamatergic synapse	31
04727 GABAergic synapse	24
04725 Cholinergic synapse	25
04728 Dopaminergic synapse	32
04726 Serotonergic synapse	18
04720 Long-term potentiation	21

Brain Metabolic Pathways	Number of Pathways
04730 Long-term depression	16
04723 Retrograde endocannabinoid signaling	41
04721 Synaptic vesicle cycle	19
04722 Neurotrophin signaling pathway	28
Sensory system	
04744 Phototransduction	1
04745 Phototransduction - fly	5
04740 Olfactory transduction	6
04742 Taste transduction	8
04750 Inflammatory mediator regulation of TRP channels	19
Development and regeneration	
04320 Dorso-ventral axis formation	7
04360 Axon guidance	34
04361 Axon regeneration	23
04380 Osteoclast differentiation	23
Aging	
04211 Longevity regulating pathway	26
04212 Longevity regulating pathway - worm	22
04213 Longevity regulating pathway - multiple species	17
Environmental adaptation	
04710 Circadian rhythm	5
04713 Circadian entrainment	27
04711 Circadian rhythm - fly	2
04712 Circadian rhythm - plant	1
04714 Thermogenesis	62
04626 Plant-pathogen interaction	6

Table S4. Liver synonymous/non-synonymous amino acid substitution.

Number of occurrences	Codon change	Amino acid change	Non-synonymous
648	GAC_GAT	D	D
630	AAC_AAT	N	N
582	GAT_GAC	D	D
552	GAA_GAG	E	E
549	ACA_ACG	T	T
519	AAT_AAC	N	N
483	ATT_ATC	I	I
480	TAC_TAT	Y	Y
465	CAC_CAT	H	H
459	CCA_CCG	P	P
456	GCA_GCG	A	A
426	TCC_TCT	S	S
426	GAG_GAA	E	E
426	AAA_AAG	K	K
405	ACC_ACT	T	T
393	ACT_ACC	T	T
390	GCC_GCT	A	A
381	CTG_TTG	L	L
378	GCG_GCA	A	A
378	CCG_CCA	P	P
378	AAG_AAA	K	K
375	ACG ACA	T	T

Number of occurrences	Codon change	Amino acid change	Non-synonymous	
372	CAT_CAC	H	H	FALSE
372	CAA_CAG	Q	Q	FALSE
363	TAT_TAC	Y	Y	FALSE
360	TTG_CTG	L	L	FALSE
360	CTG_CTA	L	L	FALSE
357	ATC_ATT	I	I	FALSE
342	CAG_CAA	Q	Q	FALSE
339	GTC_GTA	V	V	FALSE
318	GGT_GGC	G	G	FALSE
315	TCA_TCG	S	S	FALSE
300	GCT_GCC	A	A	FALSE
288	GCC_GGT	G	G	FALSE
285	TCG_TCA	S	S	FALSE
285	GTT_GTC	V	V	FALSE
276	AGC_AGT	S	S	FALSE
273	CTA_CTG	L	L	FALSE
261	TTT_TTC	F	F	FALSE
261	CCC_CCT	P	P	FALSE
252	CTC_CTT	L	L	FALSE
249	GGG_GGA	G	G	FALSE
231	TTC_TTT	F	F	FALSE
231	CCT_CCC	P	P	FALSE
225	TGC_TGT	C	C	FALSE
198	TTG_TTA	L	L	FALSE
198	CTT_CTC	L	L	FALSE
195	GTC_GTT	V	V	FALSE
192	GGA_GGG	G	G	FALSE
186	TCT_TCC	S	S	FALSE
183	AGT_AGC	S	S	FALSE
180	TGT_TGC	C	C	FALSE
171	GTA_GTG	V	V	FALSE
168	AGA_AGG	R	R	FALSE
153	GTG_GTT	V	V	FALSE
144	AGG_AGA	R	R	FALSE
141	GCC_GCA	A	A	FALSE
120	GCC_GGA	G	G	FALSE
114	ACA_ACT	T	T	FALSE
105	TTA_TTG	L	L	FALSE
99	CTC_CTG	L	L	FALSE
96	CTG_CTC	L	L	FALSE
96	ATC_ATA	I	I	FALSE
96	ACG_ACT	T	T	FALSE
93	CGT_CGC	R	R	FALSE
90	CGC_CGT	R	R	FALSE
90	CCC_CCA	P	P	FALSE
87	GGC_GGG	G	G	FALSE
84	ACC ACA	T	T	FALSE
81	GGA_GGC	G	G	FALSE
81	GCG_GCT	A	A	FALSE
81	CTG_CTT	L	L	FALSE
81	CTA_TTA	L	L	FALSE

Number of occurrences	Codon change	Amino acid change	Non-synonymous	
81	ACG_ACC	T	T	FALSE
78	TCC_TCA	S	S	FALSE
78	GTC_GTG	V	V	FALSE
75	CCC_CCG	P	P	FALSE
72	TTA_CTA	L	L	FALSE
72	CCG_CCT	P	P	FALSE
69	GTG_GTC	V	V	FALSE
66	GGG_GGT	G	G	FALSE
63	CTC_CTA	L	L	FALSE
60	TCC_TCG	S	S	FALSE
57	TCA_TCT	S	S	FALSE
57	GGG_GGC	G	G	FALSE
51	GTT_GTG	V	V	FALSE
48	GTT_GTA	V	V	FALSE
48	ACC_ACG	T	T	FALSE
45	GGA_GGT	G	G	FALSE
45	GCC_GCG	A	A	FALSE
45	CGG_CGA	R	R	FALSE
42	GTC_GTA	V	V	FALSE
42	CTT_CTG	L	L	FALSE
42	CCA_CCT	P	P	FALSE
39	GCA_GCT	A	A	FALSE
39	CGA_CGG	R	R	FALSE
39	ACT ACA	T	T	FALSE
39	ACA_ACC	T	T	FALSE
36	GCT_GCA	A	A	FALSE
36	CGA_CGT	R	R	FALSE
33	TCG_TCC	S	S	FALSE
33	CGA_AGA	R	R	FALSE
30	CGG_AGG	R	R	FALSE
30	CGC_CGG	R	R	FALSE
30	ATT_ATA	I	I	FALSE
27	GCT_GCG	A	A	FALSE
27	CTT_CTA	L	L	FALSE
27	ATA_ATT	I	I	FALSE
24	GGT_GGA	G	G	FALSE
24	CGT_CGA	R	R	FALSE
24	CGG_CGC	R	R	FALSE
24	CCG_CCC	P	P	FALSE
24	AGA_CGA	R	R	FALSE
21	GCG_GCC	A	A	FALSE
21	CCA_CCC	P	P	FALSE
18	TCT_TCA	S	S	FALSE
18	TCG_TCT	S	S	FALSE
15	TCA_TCC	S	S	FALSE
15	GTA_GTT	V	V	FALSE
15	GGT_GGG	G	G	FALSE
15	CGG_CGT	R	R	FALSE
15	CGA_CGC	R	R	FALSE
15	CCT_CCG	P	P	FALSE
12	GCA_GCC	A	A	FALSE

Number of occurrences	Codon change	Amino acid change	Non-synonymous
12	CTA_CTT	L	L
12	CTA_CTC	L	L
12	CGC_CGA	R	R
12	ACT_ACG	T	T
9	TCT_TCG	S	S
9	N/A_N/A	L	L
9	GTA_GTC	V	V
9	CGT_CGG	R	R
9	CCT_CCA	P	P
9	ATC_GTC	A	A
9	ATA_ATC	I	I
6	TTC_CTC	E	E
6	N/A_N/A	V	V
6	N/A_N/A	Q	Q
6	GGT_AGT	T	T
6	GCT_ACT	S	S
6	AGG_CGG	R	R
3	N/A_N/A	T	T
3	N/A_N/A	R	R
3	N/A_N/A	N	N
3	N/A_N/A	I	I
3	N/A_N/A	E	E
3	N/A_N/A	A	A
3	CCA_CCG	T	T
3	AAG_AAA	G	G
285	GTT_ATT	V	I
234	ACG_ATG	T	M
225	GTC_ATC	V	I
192	ATG_ACG	M	T
174	AGT_AAT	S	N
159	AAT_AGT	N	S
153	GTA_ATA	V	I
153	CAA_CGA	Q	R
141	ATC_GTC	I	V
135	ATT_GTT	I	V
132	GTG_ATG	V	M
132	ATG_GTG	M	V
126	ATA_GTA	I	V
117	GAT_AAT	D	N
117	ACT_GCT	T	A
117	ACA_GCA	T	A
114	GCC_ACC	A	T
108	GCA ACA	A	T
108	CAT_CGT	H	R
108	ATG_ATA	M	I
108	AAT_GAT	N	D
102	AGA_AAA	R	K
99	GTG_GCG	V	A
96	CGT_CAT	R	H
96	CAG_CGG	Q	R
96	ATA ACA	I	T

Number of occurrences	Codon change	Amino acid change	Non-synonymous	
93	CGG_CAG	R	Q	TRUE
90	GAG_GAC	E	D	TRUE
90	ACC_AGC	T	S	TRUE
90	AAA_GAA	K	E	TRUE
87	CTT_TTT	L	F	TRUE
87	CAC_CGC	H	R	TRUE
87	AAG_AGG	K	R	TRUE
87	AAC_ACC	N	T	TRUE
84	CCT_GCT	P	A	TRUE
81	GTC_GCC	V	A	TRUE
81	CAT_TAT	H	Y	TRUE
81	AAA_AGA	K	R	TRUE
78	GAA_GGA	E	G	TRUE
75	GCT_ACT	A	T	TRUE
75	GCA_GTA	A	V	TRUE
75	GAG_AAG	E	K	TRUE
75	ATT_ACT	I	T	TRUE
75	ACC_GCC	T	A	TRUE
75	ACA_ATA	T	I	TRUE
72	GGT_AGT	G	S	TRUE
72	GAG_GAT	E	D	TRUE
72	ACC_AAC	T	N	TRUE
66	CTG_ATG	L	M	TRUE
66	ACT_ATT	T	I	TRUE
66	AAG_AAT	K	N	TRUE
63	TCT_TTT	S	F	TRUE
63	GGG_AGG	G	R	TRUE
63	GAC_GAA	D	E	TRUE
60	GCG_GTG	A	V	TRUE
60	GAA_AAA	E	K	TRUE
57	TGG_CGG	W	R	TRUE
57	TCG_TTG	S	L	TRUE
54	GCT_GTT	A	V	TRUE
54	CTC_TTC	L	F	TRUE
54	CCG_CTG	P	L	TRUE
54	AGG_AAG	R	K	TRUE
54	AAC_GAC	N	D	TRUE
51	TCA_TTA	S	L	TRUE
51	GCC_CCC	A	P	TRUE
51	GAC_AAC	D	N	TRUE
51	CTG_CAG	L	Q	TRUE
51	CGA_CAA	R	Q	TRUE
51	CCT_CTT	P	L	TRUE
51	AGT_ACT	S	T	TRUE
48	TTT_CTT	F	L	TRUE
48	GGA_AGA	G	R	TRUE
48	GCC_TCC	A	S	TRUE
48	CTG_CCG	L	P	TRUE
48	ATA_ATG	I	M	TRUE
48	ACC_ATC	T	I	TRUE
48	ACA_AGA	T	R	TRUE

Number of occurrences	Codon change	Amino acid change	Non-synonymous	
45	TTG_TCG	L	S	TRUE
45	TCA ACA	S	T	TRUE
45	GGA_GAA	G	E	TRUE
45	GCT_TCT	A	S	TRUE
45	GCA_GGA	A	G	TRUE
45	CTC_ATC	L	I	TRUE
45	AGA ACA	R	T	TRUE
45	AAG_GAG	K	E	TRUE
42	GGC AGC	G	S	TRUE
42	CGT_TGT	R	C	TRUE
42	CAC_TAC	H	Y	TRUE
42	ATT_ATG	I	M	TRUE
42	AGT_GGT	S	G	TRUE
42	AGG_GGG	R	G	TRUE
42	AAA_CAA	K	Q	TRUE
39	TTC_CTC	F	L	TRUE
39	TTA_TCA	L	S	TRUE
39	TCT_CCT	S	P	TRUE
39	GCC_GTC	A	V	TRUE
39	GAG_CAG	E	Q	TRUE
39	CCT_TCT	P	S	TRUE
39	CCC_TCC	P	S	TRUE
39	ATC_ACC	I	T	TRUE
39	AGC_AAC	S	N	TRUE
36	GCC_GGC	A	G	TRUE
36	CCA_TCA	P	S	TRUE
36	CAG_GAG	Q	E	TRUE
36	CAA_GAA	Q	E	TRUE
36	AGC_ACC	S	T	TRUE
36	ACG_AGG	T	R	TRUE
33	TGT_CGT	C	R	TRUE
33	TGC_CGC	C	R	TRUE
33	TAT_TGT	Y	C	TRUE
33	TAT_CAT	Y	H	TRUE
33	TAC_TTC	Y	F	TRUE
33	TAC_CAC	Y	H	TRUE
33	GTT_TTT	V	F	TRUE
33	GTT_GCT	V	A	TRUE
33	GTC_CTC	V	L	TRUE
33	GCA_TCA	A	S	TRUE
33	CAA_AAA	Q	K	TRUE
30	TTG GTG	L	V	TRUE
30	TTG_ATG	L	M	TRUE
30	TGT_TCT	C	S	TRUE
30	TCC_ACC	S	T	TRUE
30	TCA_CCA	S	P	TRUE
30	GAG GTG	E	V	TRUE
30	CGT_CTT	R	L	TRUE
30	CGG_TGG	R	W	TRUE
30	CCA_CTA	P	L	TRUE
30	CAT_CTT	H	L	TRUE

Number of occurrences	Codon change	Amino acid change	Non-synonymous
30	CAG_CAT	Q	H
30	ATG_ATT	M	I
30	ATG_AGG	M	R
30	AAC_AGC	N	S
30	AAC_AAG	N	K
27	GCG_ACG	A	T
27	GAT_GGT	D	G
27	GAC_GAG	D	E
27	CTT_CGT	L	R
27	AAG_AAC	K	N
24	TTT_TAT	F	Y
24	TTT_GTT	F	V
24	TTA_ATA	L	I
24	TGT_TAT	C	Y
24	GAG_GCG	E	A
24	GAA_CAA	E	Q
24	CTT_ATT	L	I
24	CCC_CAC	P	H
24	CAC_CAG	H	Q
24	ATG_TTG	M	L
24	AGC_GGC	S	G
24	AGC_AGA	S	R
24	ACT_AGT	T	S
21	TTC_TCC	F	S
21	TCT_GCT	S	A
21	TCT_ACT	S	T
21	TCC_TTC	S	F
21	TCC_CCC	S	P
21	GTG_CTG	V	L
21	GGT_GAT	G	D
21	GCA_CCA	A	P
21	GAT_GAG	D	E
21	GAC_TAC	D	Y
21	GAC_GGC	D	G
21	CGC_TGC	R	C
21	CGC_CTC	R	L
21	CGC_AGC	R	S
21	CCA_CGA	P	R
21	AAT_ATT	N	I
21	AAC_ATC	N	I
21	AAA ACA	K	T
21	AAA AAT	K	N
18	TTA_TTC	L	F
18	TGG_TGC	W	C
18	TGC_AGC	C	S
18	TAT_TCT	Y	S
18	GGG GTG	G	V
18	GGG_GAG	G	E
18	GGC_GCC	G	A
18	GCT_GAT	A	D
18	GCT_CCT	A	P

Number of occurrences	Codon change	Amino acid change	Non-synonymous
18	GCG_GAG	A	E
18	GAT_GAA	D	E
18	CGT_AGT	R	S
18	CCT_CAT	P	H
18	CCC_CTC	P	L
18	ATG_CTG	M	L
18	AGG_AGT	R	S
18	AGC_AGG	S	R
18	ACT_TCT	T	S
18	AAT_AAG	N	K
15	TTC_TTG	F	L
15	TTC_TTA	F	L
15	TGG_TGT	W	C
15	TCG_CCG	S	P
15	TCC_TAC	S	Y
15	GTT_CTT	V	L
15	GCG_TCG	A	S
15	GAA_GAT	E	D
15	CTT_CCT	L	P
15	CTT_CAT	L	H
15	CTA_CCA	L	P
15	CAA_CAT	Q	H
15	ATC_CTC	I	L
15	AGA_GGA	R	G
15	ACG_AAG	T	K
15	ACC_TCC	T	S
15	AAC_AAA	N	K
12	TGG_TCG	W	S
12	TCT_TGT	S	C
12	TCG_GCG	S	A
12	TAT_TTT	Y	F
12	GGT_GTT	G	V
12	GCA_GAA	A	E
12	GAT_GCT	D	A
12	GAA_GAC	E	D
12	CTG_GTG	L	V
12	CTA_GTA	L	V
12	CTA_ATA	L	I
12	CGC_CAC	R	H
12	ATC_TTC	I	F
12	ATC_ATG	I	M
12	AGT_CGT	S	R
12	AGT_AGG	S	R
12	AGC_ATC	S	I
12	AGA_AGT	R	S
12	AGA_AGC	R	S
12	ACC_CCC	T	P
12	AAT_ACT	N	T
12	AAG_CAG	K	Q
9	TTT_TCT	F	S
9	TTG_TTT	L	F

Number of occurrences	Codon change	Amino acid change	Non-synonymous	
9	TGT_TGG	C	W	TRUE
9	TGG_TTG	W	L	TRUE
9	TGC_TCC	C	S	TRUE
9	TGC_TAC	C	Y	TRUE
9	TAT_AAT	Y	N	TRUE
9	GTG_TTG	V	L	TRUE
9	GTC_TTC	V	F	TRUE
9	GTA_GTG	Y	C	TRUE
9	GTA_CTA	V	L	TRUE
9	GCC_GAC	G	D	TRUE
9	GGA_GTA	G	V	TRUE
9	GCC_GAC	A	D	TRUE
9	GAT_GTT	D	V	TRUE
9	GAG_GGG	E	G	TRUE
9	GAA_GCA	E	A	TRUE
9	CTT_GTT	L	V	TRUE
9	CTC_CCC	L	P	TRUE
9	CCG_TCG	P	S	TRUE
9	CCC_GCC	P	A	TRUE
9	CAT_CAG	H	Q	TRUE
9	CAG_AAG	Q	K	TRUE
9	ATT_AGT	I	S	TRUE
9	ATG_ATC	M	I	TRUE
9	ACA_TCA	T	S	TRUE
9	AAA_AAC	K	N	TRUE
6	TTT_TTG	F	L	TRUE
6	TTG_TTC	L	F	TRUE
6	TTC_TGC	F	C	TRUE
6	TTC_GTC	F	V	TRUE
6	TGG_GGG	W	G	TRUE
6	TCA_GCA	S	A	TRUE
6	GTT_GAT	V	D	TRUE
6	GTG_GAG	V	E	TRUE
6	GTA_GCA	V	A	TRUE
6	GTA_GAA	V	E	TRUE
6	GGT_TGT	G	C	TRUE
6	GGG_TGG	G	W	TRUE
6	GGG_GCG	G	A	TRUE
6	GGA_GCA	G	A	TRUE
6	GAT_TAT	D	Y	TRUE
6	GAT_CAT	D	H	TRUE
6	CTC_GTC	L	V	TRUE
6	CGG_CCG	R	P	TRUE
6	CGC_CCC	R	P	TRUE
6	CCA_GCA	P	A	TRUE
6	CCA_ACA	P	T	TRUE
6	CAT_CAA	H	Q	TRUE
6	CAT_AAT	H	N	TRUE
6	CAG_CTG	Q	L	TRUE
6	CAG_CAC	Q	H	TRUE
6	CAC_GAC	H	D	TRUE

Number of occurrences	Codon change	Amino acid change	Non-synonymous
6	ATG_AAG	M	K
6	ATA_CTA	I	L
6	ATA_AAA	I	K
6	ACT_ATT	S	I
6	AGG_ATG	R	M
6	ACG_GCG	T	A
6	AAT_CAT	N	H
6	AAG_ACG	K	T
6	AAC_CAC	N	H
3	TGT_TTT	C	F
3	TGT_AGT	C	S
3	TGC_TGG	C	W
3	TCT_TAT	S	Y
3	TAC_TGC	Y	C
3	N/A_N/A	T	M
3	N/A_N/A	S	T
3	N/A_N/A	R	Q
3	GTG_GGG	V	G
3	GTC_GGC	V	G
3	GTA_TTA	V	L
3	GGT_GCT	G	A
3	GGG_CGG	G	R
3	GGC_GTC	G	V
3	GGA_CGA	G	R
3	GCG_GGG	A	G
3	GCG_CCG	A	P
3	GAC_GTC	D	V
3	GAC_GCC	D	A
3	CTG_CGG	L	R
3	CTC_CAC	L	H
3	CGT_GGT	R	G
3	CGT_CCT	R	P
3	CGC_GGC	R	G
3	CGA_GGA	R	G
3	CCT_ACT	P	T
3	CCG_CAG	P	Q
3	CCG_ACG	P	T
3	CCC_CGC	P	R
3	CCA_CAA	P	Q
3	CAT_GAT	H	D
3	CAC_CTC	H	L
3	CAC_CAT	V	M
3	CAC_CAA	H	Q
3	CAA_CTA	Q	L
3	ATT_TTT	I	F
3	ATT_AAT	I	N
3	ATA_TTA	I	L
3	ATA_AGA	I	R
3	AGC_CGC	S	R
3	AGA ATA	R	I
3	ACT_CCT	T	P

Number of occurrences	Codon change	Amino acid change	Non-synonymous
3	ACT_AAT	T	N
3	ACA_AAA	T	K
3	AAT_AAA	N	K
3	AAG_ATG	K	M

Table S5. Brain synonymous/non-synonymous amino acid substitution.

Number of occurrences	Codon change	Amino acid change	Non-synonymous
105	GAC_GAT	D	D
85	CCA_CCG	P	P
80	CCG_CCA	P	P
78	GAA_GAG	E	E
75	GCA_GCG	A	A
75	GAG_GAA	E	E
74	ACG ACA	T	T
71	GCT_GCC	A	A
71	AAC_AAT	N	N
69	ATT_ATC	I	I
68	GCC_GCT	A	A
68	GAT_GAC	D	D
67	TAC_TAT	Y	Y
63	CAG_CAA	Q	Q
60	ACA_ACG	T	T
60	AAT_AAC	N	N
59	CAC_CAT	H	H
59	CAA_CAG	Q	Q
57	AAA_AAG	K	K
56	ATC_ATT	I	I
52	TCA_TCG	S	S
50	CTG_TTG	L	L
47	GGT_GGC	G	G
46	AGC_AGT	S	S
45	TAT_TAC	Y	Y
45	GTA_GTG	V	V
44	CTT_CTC	L	L
44	AGT_AGC	S	S
44	ACC_ACT	T	T
43	CAT_CAC	H	H
41	TCC_TCT	S	S
41	CCT_CCC	P	P
39	GTT_GTC	V	V
37	GCG_GCA	A	A
36	CTG_CTA	L	L
36	CCC_CCT	P	P
34	TTT_TTC	F	F
34	ACT_ACC	T	T
33	TTG_CTG	L	L
33	GGG_GGA	G	G
33	CTA_CTG	L	L
32	GGC_GGT	G	G
31	TGC_TGT	C	C
31	GGA_GGG	G	G

Number of occurrences	Codon change	Amino acid change	Non-synonymous	
28	GTC_GTT	V	V	FALSE
28	CTC_CTT	L	L	FALSE
27	GTG_GTA	V	V	FALSE
27	CGC_CGT	R	R	FALSE
25	CTG_CTT	L	L	FALSE
24	TCG_TCA	S	S	FALSE
24	AAG_AAA	K	K	FALSE
23	TTG_TTA	L	L	FALSE
23	AGA_AGG	R	R	FALSE
22	TGT_TGC	C	C	FALSE
22	TCC_TCG	S	S	FALSE
20	TTC_TTT	F	F	FALSE
19	TCT_TCC	S	S	FALSE
19	GTG_GTT	V	V	FALSE
19	CTC_CTG	L	L	FALSE
19	CTA_TTA	L	L	FALSE
18	GCA_GCT	A	A	FALSE
18	CGA_CGG	R	R	FALSE
18	CCG_CCT	P	P	FALSE
17	CGT_CGC	R	R	FALSE
17	AGG_AGA	R	R	FALSE
15	TCA_TCT	S	S	FALSE
15	CGA_AGA	R	R	FALSE
15	CCA_CCT	P	P	FALSE
14	ATC_ATA	I	I	FALSE
14	ACC ACA	T	T	FALSE
13	GGC_GGG	G	G	FALSE
13	CTC_CTA	L	L	FALSE
13	CCC_CCA	P	P	FALSE
12	CTG_CTC	L	L	FALSE
11	GTC_GTG	V	V	FALSE
11	GGA_GGC	G	G	FALSE
11	CGG_CGA	R	R	FALSE
11	CGG_AGG	R	R	FALSE
10	TTA_CTA	L	L	FALSE
10	GTC_GTA	V	V	FALSE
10	ATA_ATT	I	I	FALSE
10	ACG_ACT	T	T	FALSE
8	TTA_TTG	L	L	FALSE
8	GTG_GTC	V	V	FALSE
8	GCT_GCA	A	A	FALSE
8	CCA_CCC	P	P	FALSE
7	TCG_TCC	S	S	FALSE
7	GGG_GGT	G	G	FALSE
7	GGA_GGT	G	G	FALSE
7	GCG_GCT	A	A	FALSE
7	GCC_GCA	A	A	FALSE
7	CTT_CTA	L	L	FALSE
7	ATT_ATA	I	I	FALSE
6	TCG_TCT	S	S	FALSE
6	TCC_TCA	S	S	FALSE

Number of occurrences	Codon change	Amino acid change	Non-synonymous	
6	GTT_GTA	V	V	FALSE
6	GGC_GGA	G	G	FALSE
6	CTA_CTC	L	L	FALSE
6	CGC_CGA	R	R	FALSE
6	AGA_CGA	R	R	FALSE
6	ACT ACA	T	T	FALSE
6	ACA ACT	T	T	FALSE
5	GCG_GCC	A	A	FALSE
5	GCC_GCG	A	A	FALSE
5	CCT_CCA	P	P	FALSE
4	TCT_TCG	S	S	FALSE
4	N/A_N/A	A	A	FALSE
4	GGG_GGC	G	G	FALSE
4	GCA_GCC	A	A	FALSE
4	CGA_CGT	R	R	FALSE
4	CCG_CCC	P	P	FALSE
4	ATA_ATC	I	I	FALSE
3	TCT_TCA	S	S	FALSE
3	N/A_N/A	V	V	FALSE
3	GTA_GTT	V	V	FALSE
3	CTA_CTT	L	L	FALSE
3	CGG_CGT	R	R	FALSE
3	ACC_ACG	T	T	FALSE
2	N/A_N/A	P	P	FALSE
2	N/A_N/A	L	L	FALSE
2	GGA_AGA	R	R	FALSE
2	GCT_GCG	A	A	FALSE
2	CTT_CTG	L	L	FALSE
2	ACG_ACC	T	T	FALSE
2	AAA_AGA	E	E	FALSE
1	TCA_TCC	S	S	FALSE
1	N/A_N/A	Q	Q	FALSE
1	GTT_GTG	V	V	FALSE
1	GTA_GTC	V	V	FALSE
1	GGT_GGG	G	G	FALSE
1	GGT_GGA	G	G	FALSE
1	CTA_CAA	T	T	FALSE
1	CGG_CGC	R	R	FALSE
1	CGC_CGG	R	R	FALSE
1	CCT_CCG	P	P	FALSE
1	CCC_CCG	P	P	FALSE
1	AGG_CGG	R	R	FALSE
1	ACG_GCG	E	E	FALSE
1	AAG_GAG	E	E	FALSE
22	GTG_CTG	V	L	TRUE
22	AAA_AGA	K	R	TRUE
19	AGT_AAT	S	N	TRUE
18	GAG_CAG	E	Q	TRUE
18	AAC_GAC	N	D	TRUE
17	GTG_ATG	V	M	TRUE
17	GGT_AGT	G	S	TRUE

Number of occurrences	Codon change	Amino acid change	Non-synonymous
17	CAG_GAG	Q	E
17	ATT_ACT	I	T
16	TTC_CTC	F	L
16	GTG_GCG	V	A
16	AAG_GAG	K	E
15	GAA_GGA	E	G
15	CGA_CAA	R	Q
15	CAA_CGA	Q	R
15	AGA_AAA	R	K
14	TTT_TCT	F	S
14	GTA_ATA	V	I
14	GAC_GAG	D	E
14	CCT_TCT	P	S
14	ATG_GTG	M	V
13	GTT_ATT	V	I
13	GCT_ACT	A	T
13	CGC_CAC	R	H
13	AGG_GGG	R	G
13	ACG_ATG	T	M
12	TCT_TTT	S	F
12	GGA_GAA	G	E
12	AGA_GGA	R	G
12	AGA ACA	R	T
12	ACA ATA	T	I
11	TGT_TCT	C	S
11	TGT_TAT	C	Y
11	TCC_ACC	S	T
11	GAG_GGG	E	G
11	ATC_GTC	I	V
10	GTC_GAC	V	D
10	ATA ACA	I	T
10	ACT_GCT	T	A
10	AAT_AGT	N	S
9	GTC_ATC	V	I
9	GCA ACA	A	T
9	GAC_TAC	D	Y
9	CTT_CCT	L	P
9	CCT_GCT	P	A
9	CCG_CTG	P	L
9	CAC CGC	H	R
9	ATA_ATG	I	M
9	AGC AAC	S	N
9	ACC AAC	T	N
9	ACA AGA	T	R
9	AAA_GAA	K	E
8	TGC_TCC	C	S
8	TCT_CCT	S	P
8	TAT_TGT	Y	C
8	GTC_CTC	V	L
8	GGG_ AGG	G	R
8	GCC ACC	A	T

Number of occurrences	Codon change	Amino acid change	Non-synonymous
8	GAG_AAG	E	K
8	CTC_TTC	L	F
8	CCC_TCC	P	S
8	CCA_CAA	P	Q
8	CAG_CAC	Q	H
8	ATT_GTT	I	V
8	ACC_GCC	T	A
8	AAG_AGG	K	R
7	TTC_TCC	F	S
7	CAT_TAT	H	Y
7	CAA_CTA	Q	L
7	ATG_ACG	M	T
7	ATA_AGA	I	R
7	AAC_AGC	N	S
6	TCT_TGT	S	C
6	TCA_CCA	S	P
6	TAT_CAT	Y	H
6	GTT_CTT	V	L
6	GGA_AGA	G	R
6	GCG_GTG	A	V
6	GCC_GTC	A	V
6	CTC_ATC	L	I
6	CCC_CTC	P	L
6	CAG_AAG	Q	K
6	CAC_CAG	H	Q
5	TTA_ATA	L	I
5	TCT_TAT	S	Y
5	TCC_TTC	S	F
5	GGC_GAC	G	D
5	GCT_CCT	A	P
5	GAT_GTT	D	V
5	GAT_GCT	D	A
5	GAT_GAG	D	E
5	GAG_GAT	E	D
5	GAA_GAT	E	D
5	GAA_CAA	E	Q
5	CTT_ATT	L	I
5	CTC_GTC	L	V
5	CTA_CCA	L	P
5	CGA_CTA	R	L
5	CCT_ACT	P	T
5	CCA_CTA	P	L
5	CAC_CAA	H	Q
5	ATC_ACC	I	T
5	AGT_GGT	S	G
5	AGT_AGG	S	R
5	AGG_AGT	R	S
5	ACT_TCT	T	S
5	ACT_ATT	T	I
5	ACT_AGT	T	S
4	TTG_TTT	L	F

Number of occurrences	Codon change	Amino acid change	Non-synonymous
4	TTG_TCG	L	S
4	TTG_ATG	L	M
4	GTT_GCT	V	A
4	GTC_TTC	V	F
4	GTC_GCC	V	A
4	GTA_TTA	V	L
4	GTA_GCA	V	A
4	GGG_GAG	G	E
4	GCT_TCT	A	S
4	CTT_TTT	L	F
4	CTG_GTG	L	V
4	CTC_CCC	L	P
4	CGC_AGC	R	S
4	CAG_CGG	Q	R
4	ATG_ATA	M	I
4	AGT_ACT	S	T
4	AGG_AGC	R	S
4	AGG_AAG	R	K
4	AAT_GAT	N	D
4	AAA_ATA	K	I
3	TTT_CTT	F	L
3	TTC_TTG	F	L
3	TTC_GTC	F	V
3	TGT_TTT	C	F
3	TCC_CCC	S	P
3	N/A_N/A	R	H
3	N/A_N/A	K	E
3	GTT_TTT	V	F
3	GTG_GGG	V	G
3	GCA_TCA	A	S
3	GCA_GAA	A	E
3	GAG_GAC	E	D
3	GAC_AAC	D	N
3	CTG_ATG	L	M
3	CTA_GTA	L	V
3	CGT_TGT	R	C
3	CGG_TGG	R	W
3	CGG_CAG	R	Q
3	CCA ACA	P	T
3	CAT_AAT	H	N
3	CAG_CAT	Q	H
3	CAC_TAC	H	Y
3	CAA_GAA	Q	E
3	CAA_CAT	Q	H
3	ATG_ATT	M	I
3	ATG_ATC	M	I
3	ATC_TTC	I	F
3	ATA_AAA	I	K
3	AGT_AGA	S	R
3	AGC_AGG	S	R
3	AGC_AGA	S	R

Number of occurrences	Codon change	Amino acid change	Non-synonymous
3	ACG_AAG	T	K
3	ACC_ATC	T	I
3	ACA_GCA	T	A
2	TTT_TTG	F	L
2	TTG_TTC	L	F
2	TTG_GTG	L	V
2	TTA_TTT	L	F
2	TGT_AGT	C	S
2	TGG_TGC	W	C
2	TGC_CGC	C	R
2	TCT_ACT	S	T
2	TAC_TGC	Y	C
2	N/A_N/A	V	I
2	N/A_N/A	Q	P
2	GTG_TTG	V	L
2	GGT_GTT	G	V
2	GGT_GAT	G	D
2	GGC_AGC	G	S
2	GGA_GTA	G	V
2	GGA_CGA	G	R
2	GCT_GAT	A	D
2	GCG_ACG	A	T
2	GCA_GGA	A	G
2	GAT_TAT	D	Y
2	GAT_GGT	D	G
2	GAT_CAT	D	H
2	GAT_AAT	D	N
2	GAG_GAT	D	Y
2	GAC_GTC	D	V
2	GAC_GGC	D	G
2	GAA_AAA	E	K
2	CTT_GTT	L	V
2	CTT_CAT	L	H
2	CTG_CCG	L	P
2	CTG_CAG	L	Q
2	CTC_CGC	L	R
2	CTC_CAC	L	H
2	CTA_CAA	L	Q
2	CGC_TGC	R	C
2	CGC_CTC	R	L
2	CCT_CTT	P	L
2	CCC_CGC	P	R
2	CCA_TCA	P	S
2	CCA_GCA	P	A
2	CAG_TAG	T	I
2	CAC_GAC	H	D
2	CAC_CTC	H	L
2	ATT_TTT	I	F
2	ATG_AAG	M	K
2	ATA_GTA	I	V
2	AGT_ATT	S	I

Number of occurrences	Codon change	Amino acid change	Non-synonymous
2	AGA_ATA	R	I
2	ACT_CCT	T	P
2	ACG_GCG	T	A
2	ACC_TCC	T	S
2	AAT_TAT	N	Y
2	AAC_ATC	N	I
2	AAC_ACC	N	T
1	TTT_TTA	F	L
1	TTT_TGT	F	C
1	TTT_GTT	F	V
1	TTG_TGG	L	W
1	TTC_TAC	F	Y
1	TTA_TCA	L	S
1	TTA_GTA	L	V
1	TGT_CGT	C	R
1	TGG_TGT	W	C
1	TGG_CGG	W	R
1	TGC_TTC	C	F
1	TGC_AGC	C	S
1	TCT_GCT	S	A
1	TCG_TTG	S	L
1	TCG_TGG	S	W
1	TCC_TGC	S	C
1	TCC_TAC	S	Y
1	TAT_TTT	Y	F
1	TAC_TCC	Y	S
1	TAC_CAC	Y	H
1	N/A_N/A	I	V
1	N/A_N/A	F	S
1	N/A_N/A	C	Y
1	GTG_GAG	V	E
1	GTG_GAG	S	R
1	GTG_CTG	S	T
1	GTA_GAA	V	E
1	GTA_CTA	V	L
1	GGT_CGT	G	R
1	GGG_GTG	G	V
1	GGG_GCG	G	A
1	GGG_CGG	G	R
1	GGC_GTC	R	S
1	GGC_GTC	G	V
1	GGC_GCC	G	A
1	GGA_GTA	D	Y
1	GGA_GGG	E	G
1	GGA_CGA	G	A
1	GCC_TCC	A	S
1	GCC_CCC	A	P
1	GCA_GTA	A	V
1	GAG_GGG	R	G
1	GAG_GCG	E	A
1	GAG_GAC	E	Q

Number of occurrences	Codon change	Amino acid change	Non-synonymous
1	GAC_GAG	Q	E
1	GAA_GTA	E	V
1	GAA_GCA	E	A
1	CTT_CGT	L	R
1	CTA_ATA	L	I
1	CGT_CCT	R	P
1	CGT_CAT	R	H
1	CGG_GGG	R	G
1	CCT_CAT	P	H
1	CCG_TCG	P	S
1	CCG_GCG	P	A
1	CCG_CAG	P	Q
1	CCC_ACC	P	T
1	CCA_CGA	P	R
1	CAT_CTT	H	L
1	CAT_CGT	H	R
1	CAT_CCT	H	P
1	CAT_CAA	H	Q
1	CAG_CTG	Q	L
1	CAG_CCG	Q	P
1	CAG_CAC	E	Q
1	CAC_CAG	Q	E
1	CAA_CAC	Q	H
1	ATG_TTG	M	L
1	ATC_CTC	I	L
1	ATC_AGC	I	S
1	ATA_TTA	I	L
1	ATA_CTA	I	L
1	AGT_AGA	C	S
1	AGG_CGG	E	A
1	AGG_ATG	R	M
1	AGG_AGC	E	Q
1	AGC_GGC	S	G
1	AGC_AGA	P	T
1	AGA_AGC	R	S
1	ACC_CCC	T	P
1	ACA_TCA	T	S
1	ACA_AGA	Q	E
1	AAT_AAA	N	K
1	AAG_AAT	K	N
1	AAC_CAC	N	H
1	AAC_AAG	N	K
1	AAA_CAA	K	Q
1	AAA_AAG	R	G
1	AAA_AAC	K	N