

Table S1

	Liver			Brain	Ovaries	Testis	
	Plate 1	Plate 3	Plate 4	Plate 2	Plate 1	Plate 1	Plate 3
Total # reads	191,244	775,896	701,974	722,086	119,700	97,568	444,172
# Reads used in assembly	86,232	68,329	48,677	60,406	35,295	39,507	59,425
# Contigs containing reads	8,177	8,564	6,260	9,858	7,085	7,260	10,764

Table S2

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Liver to Brain			Liver to Gonads		
GO Term	FDR	# Sequences	GO Term	FDR	# Sequences
ATP binding	5.31E-24	184	ATP binding	1.75E-62	184
zinc ion binding	5.93E-20	154	zinc ion binding	4.37E-52	154
transcription factor complex	3.91E-19	148	transcription factor complex	5.31E-50	148
electron carrier activity	8.53E-18	251	structural constituent of ribosome	2.39E-39	117
structural constituent of ribosome	5.51E-15	117	soluble fraction	1.60E-32	97
integral to plasma membrane	1.40E-14	114	microsome	8.86E-28	83
soluble fraction	2.35E-12	97	protein homodimerization activity	4.16E-27	81
response to drug	2.59E-11	89	perinuclear region of cytoplasm	4.73E-23	69
electron transport	8.49E-11	85	GTP binding	1.05E-20	62
translational elongation	1.13E-10	84	electron carrier activity	6.56E-20	251
viral transcription	1.13E-10	84	oxygen binding	6.72E-20	93
microsome	1.53E-10	83	ubiquitin-protein ligase activity	5.56E-14	42
protein homodimerization activity	2.75E-10	81	GTPase activity	5.56E-14	42
Golgi membrane	3.71E-10	80	NADH dehydrogenase (ubiquinone) activity	2.58E-13	40
oxygen binding	1.97E-09	93	sequence-specific DNA binding	5.52E-13	39
endocrine pancreas development	3.01E-09	73	drug binding	5.52E-13	39
transcription factor binding	4.04E-09	72	double-stranded DNA binding	1.19E-12	38
translational termination	4.04E-09	72	mitochondrial respiratory chain complex I	2.55E-12	37
perinuclear region of cytoplasm	9.92E-09	69	transcription coactivator activity	2.55E-12	37
protein complex binding	3.24E-08	65	catalytic step 2 spliceosome	5.49E-12	36
response to metal ion	3.24E-08	65	heme binding	1.18E-11	35
nuclear mRNA splicing, via spliceosome	5.71E-08	63	microtubule	1.18E-11	35
negative regulation of cell proliferation	5.71E-08	63	apical plasma membrane	1.18E-11	35
cellular membrane organization	5.71E-08	63	nuclear speck	1.18E-11	35
aging	7.64E-08	62	unfolded protein binding	1.17E-10	32
GTP binding	7.64E-08	62	cytosolic small ribosomal subunit	1.17E-10	32
sodium ion transport	1.86E-07	59	protein heterodimerization activity	1.17E-10	32
anti-apoptosis	2.50E-07	58	early endosome	2.51E-10	31
protein domain specific binding	3.37E-07	57	protein C-terminus binding	2.47E-09	28
positive regulation of cell proliferation	4.54E-07	56	cytosolic large ribosomal subunit	2.47E-09	28
negative regulation of signal transduction	1.49E-06	52	basement membrane	2.40E-08	25

chromatin	2.01E-06	51	serine-type endopeptidase activity	2.40E-08	25
endosome membrane	3.62E-06	49	external side of plasma membrane	5.11E-08	24
positive regulation of transcription from RNA polymerase II promoter	8.79E-06	46	mRNA binding	5.11E-08	24
DNA repair	8.79E-06	46	translation initiation factor activity	5.11E-08	24
response to organic cyclic compound	8.79E-06	46	chaperone binding	1.09E-07	23
in utero embryonic development	8.79E-06	46	heparin binding	1.09E-07	23
cell division	1.58E-05	44	magnesium ion binding	1.09E-07	23
response to glucocorticoid stimulus	2.12E-05	43	tubulin complex	2.31E-07	22
ubiquinone biosynthetic process	2.12E-05	43	endoplasmic reticulum lumen	4.93E-07	21
ubiquitin-protein ligase activity	2.82E-05	42	centrosome	4.93E-07	21
GTPase activity	2.82E-05	42	flavin adenine dinucleotide binding	1.04E-06	20
mitosis	2.82E-05	42	nuclear membrane	1.04E-06	20
fatty acid biosynthetic process	2.82E-05	42	lysosomal membrane	1.04E-06	20
G-protein coupled receptor signaling pathway	2.82E-05	42	phosphatidylinositol binding	2.21E-06	19
regulation of cellular localization	3.74E-05	41	cytochrome-c oxidase activity	2.21E-06	19
sensory perception	3.74E-05	41	transcription corepressor activity	2.21E-06	19
mitochondrial electron transport, NADH to ubiquinone	3.74E-05	41	coated pit	2.21E-06	19
ATP catabolic process	3.74E-05	41	protease binding	2.21E-06	19
actin cytoskeleton	3.74E-05	41	respiratory chain complex IV	2.21E-06	19
response to hypoxia	3.74E-05	41	ubiquitin protein ligase binding	4.69E-06	18
xenobiotic metabolic process	3.74E-05	41	mitochondrial large ribosomal subunit	4.69E-06	18
positive regulation of cellular component organization	5.01E-05	40	melanosome	4.69E-06	18
post-translational protein modification	5.01E-05	40	microtubule binding	9.89E-06	17
NADH dehydrogenase (ubiquinone) activity	5.01E-05	40	calmodulin binding	9.89E-06	17
neuronal cell body	5.01E-05	40	pyridoxal phosphate binding	9.89E-06	17
sequence-specific DNA binding	6.65E-05	39	rRNA binding	9.89E-06	17
isomerase activity	6.65E-05	39	small nuclear ribonucleoprotein complex	9.89E-06	17
drug binding	6.65E-05	39	hydro-lyase activity	2.08E-05	16
peptide binding	6.65E-05	39	aromatase activity	2.08E-05	16
DNA replication	6.65E-05	39	immunoglobulin complex	2.08E-05	16
S phase of mitotic cell cycle	6.65E-05	39	trans-Golgi network	2.08E-05	16
secondary metabolic process	7.00E-05	167	metalloendopeptidase activity	2.08E-05	16

response to toxin	8.90E-05	38	heat shock protein binding	2.08E-05	16
			oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, NADH or NADPH as one donor, and incorporation of one atom of oxygen	4.33E-05	15
double-stranded DNA binding	8.90E-05	38			
mitochondrial respiratory chain complex I	1.18E-04	37	copper ion binding	4.33E-05	15
late endosome	1.18E-04	37	alcohol sulfotransferase activity	4.33E-05	15
transcription coactivator activity	1.18E-04	37	ribosome binding	4.33E-05	15
cellular amino acid biosynthetic process	1.18E-04	37	platelet alpha granule lumen	4.33E-05	15
			S-adenosylmethionine- dependent		
spermatogenesis	1.18E-04	37	methyltransferase activity	4.33E-05	15
axon guidance	1.58E-04	36	ruffle	4.33E-05	15
catalytic step 2					
spliceosome	1.58E-04	36	mitochondrial nucleoid	4.33E-05	15
platelet activation	1.58E-04	36	monosaccharide binding	4.33E-05	15
			sodium ion transmembrane transporter activity	8.98E-05	14
protein kinase binding	1.58E-04	36	fatty acid binding	8.98E-05	14
dendrite	1.58E-04	36			
anaphase-promoting complex-dependent proteasomal ubiquitin- dependent protein catabolic process	1.58E-04	36	collagen	8.98E-05	14
steroid biosynthetic process	1.58E-04	36	nucleosome	8.98E-05	14
positive regulation of cell differentiation	1.58E-04	36	integral to endoplasmic reticulum membrane	8.98E-05	14
heme binding	2.10E-04	35	late endosome membrane	8.98E-05	14
transmembrane signaling receptor activity	2.10E-04	35	growth factor binding	8.98E-05	14
negative regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle	2.10E-04	35	transcriptional repressor complex	8.98E-05	14
			bile-salt sulfotransferase activity	8.98E-05	14
microtubule	2.10E-04	35			
negative regulation of endopeptidase activity	2.10E-04	35	thiolester hydrolase activity	1.84E-04	13
apical plasma membrane	2.10E-04	35	3'-phosphoadenosine 5'- phosphosulfate binding	1.84E-04	13
integral to organelle membrane	2.10E-04	35	aminoacyl-tRNA ligase activity	1.84E-04	13
nuclear speck	2.10E-04	35	NAD binding	1.84E-04	13
negative regulation of transport	2.78E-04	34	N-acetyltransferase activity	1.84E-04	13
protein			very-low-density lipoprotein particle	1.84E-04	13
homooligomerization	2.78E-04	34			
positive regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle	2.78E-04	34	lamellipodium	1.84E-04	13

lipoprotein metabolic process	2.78E-04	34	mitochondrial small ribosomal subunit	1.84E-04	13
ribonucleoprotein complex assembly	2.78E-04	34	carboxylesterase activity	1.84E-04	13
positive regulation of cell migration	2.78E-04	34	microtubule motor activity	1.84E-04	13
rRNA transcription	2.78E-04	34	transcription activator activity	1.84E-04	13
acyl-carrier-protein biosynthetic process	4.98E-04	32	Ras GTPase activator activity	1.84E-04	13
unfolded protein binding	4.98E-04	32	U12-type spliceosomal complex	3.87E-04	12
proteasome complex	4.98E-04	32	protein kinase regulator activity	3.87E-04	12
cytosolic small ribosomal subunit	4.98E-04	32	single-stranded DNA binding	3.87E-04	12
mitochondrial outer membrane	4.98E-04	32	peptidyl-prolyl cis-trans isomerase activity	3.87E-04	12
metal ion transmembrane transporter activity	4.98E-04	32	GDP binding	3.87E-04	12
regulation of translational initiation	4.98E-04	32	RNA-directed DNA polymerase activity	3.87E-04	12
protein heterodimerization activity	4.98E-04	32	Ras GTPase binding	3.87E-04	12
protein serine/threonine kinase activity	4.98E-04	32	cullin-RING ubiquitin ligase complex	7.97E-04	11
interspecies interaction between organisms	5.38E-04	92	protein tyrosine kinase activity	7.97E-04	11
nucleotidyltransferase activity	6.65E-04	31	oxidoreductase activity, acting on single donors with incorporation of molecular oxygen, incorporation of two atoms of oxygen	7.97E-04	11
endopeptidase inhibitor activity	6.65E-04	31	serine-type endopeptidase inhibitor activity	7.97E-04	11
regulation of inflammatory response	6.65E-04	31	lipoprotein particle receptor binding	7.97E-04	11
gluconeogenesis	6.65E-04	31	synaptosome	7.97E-04	11
early endosome	6.65E-04	31	protein serine/threonine phosphatase complex	7.97E-04	11
basolateral plasma membrane	6.65E-04	31	4 iron, 4 sulfur cluster binding	7.97E-04	11
M/G1 transition of mitotic cell cycle	6.65E-04	31	mitochondrial intermembrane space	7.97E-04	11
negative regulation of cell differentiation	6.65E-04	31	rough endoplasmic reticulum	7.97E-04	11
methyltransferase activity	8.94E-04	30	proteasome core complex	7.97E-04	11
insulin receptor signaling pathway	8.94E-04	30	eukaryotic translation initiation factor 3 complex	7.97E-04	11
regulation of cell morphogenesis	8.94E-04	30	steroid hormone receptor activity	7.97E-04	11
transmembrane receptor protein serine/threonine kinase signaling pathway	8.94E-04	30	focal adhesion	7.97E-04	11
regulation of secretion	1.18E-03	29	threonine-type endopeptidase activity	7.97E-04	11
DNA damage response, signal transduction by p53 class mediator resulting in cell cycle arrest	1.18E-03	29	nuclear matrix	7.97E-04	11

cholesterol metabolic process	1.18E-03	29	fatty-acyl-CoA binding	7.97E-04	11
rRNA processing	1.18E-03	29	DNA-directed RNA polymerase II, holoenzyme	7.97E-04	11
endosomal transport	1.18E-03	29	eukaryotic cell surface binding	1.64E-03	10
cell leading edge oxidoreductase activity, acting on the CH-OH group of donors, NAD or NADP as acceptor	1.18E-03	29	calcium-dependent protein binding	1.64E-03	10
heart development	1.57E-03	28	NADP binding	1.64E-03	10
protein C-terminus binding	1.57E-03	28	inorganic anion transmembrane transporter activity	1.64E-03	10
embryonic morphogenesis	1.57E-03	28	low-density lipoprotein particle	1.64E-03	10
regulation of cell adhesion	1.57E-03	28	spherical high-density lipoprotein particle	1.64E-03	10
cytosolic large ribosomal subunit	1.57E-03	28	transcription regulatory region DNA binding	1.64E-03	10
regulation of cellular amino acid metabolic process	1.57E-03	28	nuclear chromatin	1.64E-03	10
response to radiation	1.57E-03	28	replication fork	1.64E-03	10
response to ethanol	1.57E-03	28	integrin complex	1.64E-03	10
cytokine-mediated signaling pathway	1.57E-03	28	peroxisomal matrix	1.64E-03	10
microtubule cytoskeleton organization	1.57E-03	28	caveola	1.64E-03	10
mitochondrial transport	1.57E-03	28	translation elongation factor activity	1.64E-03	10
amino acid transport	1.57E-03	28	glutathione transferase activity	1.64E-03	10
drug metabolic process	2.08E-03	27	chylomicron	1.64E-03	10
acute-phase response	2.08E-03	27	ubiquitin binding	1.64E-03	10
response to virus	2.08E-03	27	phosphatidylinositol-4,5-bisphosphate 5-phosphatase activity	1.64E-03	10
dicarboxylic acid metabolic process	2.08E-03	27	myosin complex	1.64E-03	10
activation of protein kinase activity	2.08E-03	27	leading edge membrane	1.64E-03	10
purine nucleobase metabolic process	2.08E-03	27	Cajal body	3.34E-03	9
protein N-linked glycosylation via asparagine	2.08E-03	27	hydrolase activity, acting on carbon-nitrogen (but not peptide) bonds, in linear amides	3.34E-03	9
axon	2.08E-03	27	cysteine-type endopeptidase inhibitor activity	3.34E-03	9
transferase activity, transferring hexosyl groups	2.76E-03	26	carboxy-lyase activity	3.34E-03	9
reactive oxygen species metabolic process	2.76E-03	26	cytokine receptor activity	3.34E-03	9
steroid binding	2.76E-03	26	divalent inorganic cation transmembrane transporter activity	3.34E-03	9
microtubule associated	2.76E-03	26	phosphoprotein binding	3.34E-03	9
			chemokine activity	3.34E-03	9

microtubule associated complex	2.76E-03	26	chemokine activity	3.34E-03	9
regulation of GTPase activity	2.76E-03	26	G-protein coupled receptor activity	3.34E-03	9
sphingolipid metabolic process	2.76E-03	26	growth factor activity	3.34E-03	9
liver development	2.76E-03	26	solute:cation symporter activity	3.34E-03	9
negative regulation of transcription from RNA polymerase II promoter	2.76E-03	26	N-methyltransferase activity	3.34E-03	9
ubiquitin ligase complex	2.76E-03	26	collagen binding	3.34E-03	9
water-soluble vitamin metabolic process	2.76E-03	26	manganese ion binding	3.34E-03	9
response to acid	3.65E-03	25	nuclear pore	3.34E-03	9
androgen metabolic process	3.65E-03	25	cholesterol binding	3.34E-03	9
clathrin-coated vesicle	3.65E-03	25	extrinsic to plasma membrane	3.34E-03	9
basement membrane	3.65E-03	25	mitochondrial outer membrane translocase complex	3.34E-03	9
signal release	3.65E-03	25	protein phosphatase binding	3.34E-03	9
lung development	3.65E-03	25	Golgi cisterna membrane	3.34E-03	9
regulation of transmembrane transport	3.65E-03	25	kinesin complex	3.34E-03	9
regulation of lipid biosynthetic process	3.65E-03	25	actin filament	3.34E-03	9
membrane raft	3.65E-03	25	aminopeptidase activity	3.34E-03	9
serine-type endopeptidase activity	3.65E-03	25	growth cone	3.34E-03	9
cell-cell adhesion	3.65E-03	25	midbody	3.34E-03	9
tryptophan metabolic process	3.65E-03	25	DNA-directed RNA polymerase activity	3.34E-03	9
triglyceride metabolic process	3.65E-03	25	axon part	3.34E-03	9
nerve growth factor receptor signaling pathway	3.65E-03	25	stress fiber	3.34E-03	9
receptor-mediated endocytosis	3.65E-03	25	lipase inhibitor activity	3.34E-03	9
cytokine receptor binding	3.65E-03	25	glycoprotein binding	3.34E-03	9
leukocyte differentiation	4.81E-03	24	oxidoreductase activity, acting on the aldehyde or oxo group of donors, NAD or NADP as acceptor	3.34E-03	9
cell surface binding	4.81E-03	24	transferase activity, transferring pentosyl groups	6.79E-03	8
striated muscle tissue development	4.81E-03	24	brush border membrane	6.79E-03	8
external side of plasma membrane	4.81E-03	24	intramolecular oxidoreductase activity, transposing C=C bonds	6.79E-03	8
methylation	4.81E-03	24	beta-tubulin binding	6.79E-03	8
cellular response to reactive oxygen species	4.81E-03	24	synaptic vesicle	6.79E-03	8
pyrimidine nucleobase metabolic process	4.81E-03	24	ER to Golgi transport	6.79E-03	8
protein transporter activity	4.81E-03	24	vesicle membrane	6.79E-03	8
			ubiquinol-cytochrome-c reductase activity	6.79E-03	8

translation initiation factor activity	4.81E-03	24	oligosaccharyltransferase complex	6.79E-03	8
response to hydrogen peroxide	4.81E-03	24	protein transmembrane transporter activity	6.79E-03	8
ribonucleoprotein complex binding	4.81E-03	24	aldo-keto reductase (NADP) activity	6.79E-03	8
monocarboxylic acid binding	4.81E-03	24	vitamin D3 25-hydroxylase activity	6.79E-03	8
actin filament organization	4.81E-03	24	proteasome regulatory particle	6.79E-03	8
protein processing	4.81E-03	24	polysome	6.79E-03	8
receptor complex	4.81E-03	24	toxin binding	6.79E-03	8
epithelial cell differentiation	4.81E-03	24	steroid hormone receptor binding	6.79E-03	8
small GTPase regulator activity	4.81E-03	24	cysteine-type endopeptidase activity	6.79E-03	8
carboxylic ester hydrolase activity	4.81E-03	24	hydrogen-exporting ATPase activity, phosphorylative mechanism	6.79E-03	8
chaperone binding	6.40E-03	23	RNA polymerase II distal enhancer sequence-specific DNA binding transcription factor activity	6.79E-03	8
regulation of sequence-specific DNA binding	6.40E-03	23	double-stranded RNA binding	6.79E-03	8
transcription factor activity	6.40E-03	23	postsynaptic density MHC class I protein complex	6.79E-03	8
regulation of binding	6.40E-03	23			
muscle organ development	6.40E-03	23			
positive regulation of response to external stimulus	6.40E-03	23	protein binding, bridging histone deacetylase complex	6.79E-03	8
heparin binding	6.40E-03	23	histone acetyltransferase complex	6.79E-03	8
glycolysis	6.40E-03	23			
regulation of Ras protein	6.40E-03	23	endoribonuclease activity	6.79E-03	8
signal transduction	6.40E-03	23	exonuclease activity	6.79E-03	8
spindle	6.40E-03	23	protein kinase C binding	6.79E-03	8
cell-cell junction	6.40E-03	23	ribonucleoprotein granule oxidoreductase activity, acting on the CH-CH group of donors, NAD or NADP as acceptor	6.79E-03	8
glycine metabolic process	6.40E-03	23	integrin binding	1.36E-02	7
cholesterol efflux	6.40E-03	23			
protein import into nucleus	6.40E-03	23	NF-kappaB binding	1.36E-02	7
defense response to bacterium	6.40E-03	23	structural constituent of cytoskeleton	1.36E-02	7
terpenoid metabolic process	6.40E-03	23	protein disulfide oxidoreductase activity	1.36E-02	7
amino acid binding	6.40E-03	23	cation channel activity	1.36E-02	7
magnesium ion binding	6.40E-03	23			
regulation of neuron differentiation	8.39E-03	22	cofactor transporter activity	1.36E-02	7
platelet degranulation	8.39E-03	22	SMAD binding	1.36E-02	7
response to unfolded protein	8.39E-03	22	sterol transporter activity	1.36E-02	7
embryonic organ development	8.39E-03	22	COPI vesicle coat	1.36E-02	7

secondary active transmembrane transporter activity	8.39E-03	22	PDZ domain binding	1.36E-02	7
estrogen metabolic process	8.39E-03	22	intercellular canaliculus	1.36E-02	7
pyruvate metabolic process	8.39E-03	22	histone methyltransferase complex	1.36E-02	7
regulation of proteolysis	8.39E-03	22	acetylglucosaminyltransferase activity	1.36E-02	7
peroxisomal part	8.39E-03	22	spindle pole	1.36E-02	7
vesicle organization	8.39E-03	22	transaminase activity	1.36E-02	7
regulation of membrane potential	8.39E-03	22	integral to mitochondrial membrane	1.36E-02	7
glycerolipid biosynthetic process	8.39E-03	22	hemoglobin complex	1.36E-02	7
cell cortex	8.39E-03	22	histone binding	1.36E-02	7
organic anion transport	8.39E-03	22	damaged DNA binding	1.36E-02	7
polysaccharide metabolic process	8.39E-03	22	cytoplasmic dynein complex	1.36E-02	7
morphogenesis of an epithelium	8.39E-03	22	intermediate filament	1.36E-02	7
phospholipid biosynthetic process	8.39E-03	22	growth factor receptor binding	1.36E-02	7
lysine catabolic process	8.39E-03	22	organic anion transmembrane transporter activity	1.36E-02	7
tubulin complex	8.39E-03	22	gated channel activity	1.36E-02	7
L-serine metabolic process	8.39E-03	22	RNA helicase activity	1.36E-02	7
fatty acid beta-oxidation	8.39E-03	22	single-stranded RNA binding	1.36E-02	7
regulation of lipase activity	8.39E-03	22	microvillus	1.36E-02	7
regulation of fatty acid metabolic process	8.39E-03	22	endoplasmic reticulum-Golgi intermediate compartment membrane	1.36E-02	7
GTPase activator activity	8.39E-03	22	proton-transporting V-type ATPase complex	1.36E-02	7
regulation of epithelial cell proliferation	1.11E-02	21	proton-transporting two-sector ATPase complex, catalytic domain	1.36E-02	7
response to activity	1.11E-02	21	steroid dehydrogenase activity	1.36E-02	7
cellular aldehyde metabolic process	1.11E-02	21	hydrogen ion transporting ATP synthase activity, rotational mechanism	1.36E-02	7
transport vesicle	1.11E-02	21	proton-transporting ATPase activity, rotational mechanism	1.36E-02	7
gland development	1.11E-02	21	secretory granule membrane	1.36E-02	7
endoplasmic reticulum lumen	1.11E-02	21	mannosyl-oligosaccharide	1.36E-02	7
endoplasmic reticulum-Golgi intermediate compartment	1.11E-02	21	mannosidase activity	1.36E-02	7
centrosome	1.11E-02	21	tRNA binding	1.36E-02	7
tube morphogenesis	1.11E-02	21	complement binding	1.36E-02	7
protein dephosphorylation	1.11E-02	21	dolichyl-diphosphooligosaccharide-protein glycotransferase activity	1.36E-02	7
			signal sequence binding	1.36E-02	7

threonine metabolic process	1.11E-02	21	phospholipase activity	1.36E-02	7
glutathione metabolic process	1.11E-02	21	thiamine pyrophosphate binding	2.65E-02	6
cellular calcium ion homeostasis	1.11E-02	21	SH3 domain binding	2.65E-02	6
cellular iron ion homeostasis	1.11E-02	21	hormone activity	2.65E-02	6
regulation of MAPK cascade	1.46E-02	20	actin filament binding	2.65E-02	6
phagocytosis	1.46E-02	20	receptor signaling protein serine/threonine kinase activity	2.65E-02	6
flavin adenine dinucleotide binding	1.46E-02	20	protein serine/threonine phosphatase activity	2.65E-02	6
regulation of angiogenesis	1.46E-02	20	protein tyrosine phosphatase activity	2.65E-02	6
			oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, 2-oxoglutarate as one donor, and incorporation of one atom each of oxygen into both donors	2.65E-02	6
female pregnancy	1.46E-02	20	phosphotransferase activity, phosphate group as acceptor	2.65E-02	6
positive regulation of lipid metabolic process	1.46E-02	20	testosterone 6-beta-hydroxylase activity	2.65E-02	6
high-density lipoprotein particle	1.46E-02	20	methyl indole-3-acetate esterase activity	2.65E-02	6
developmental growth myeloid cell differentiation	1.46E-02	20	methyl salicylate esterase activity	2.65E-02	6
			methyl jasmonate esterase activity	2.65E-02	6
hormone transport	1.46E-02	20	ATPase binding	2.65E-02	6
bile acid metabolic process	1.46E-02	20	ADP binding	2.65E-02	6
regulation of endocytosis	1.46E-02	20	thyroid hormone receptor activity	2.65E-02	6
tricarboxylic acid cycle	1.46E-02	20	racemase and epimerase activity, acting on carbohydrates and derivatives	2.65E-02	6
endocytic vesicle response to estradiol stimulus	1.46E-02	20	intramolecular transferase activity	2.65E-02	6
regulation of cholesterol transport	1.46E-02	20	ligase activity, forming carbon-carbon bonds	2.65E-02	6
regulation of protein catabolic process	1.46E-02	20	RS domain binding	2.65E-02	6
mitochondrial electron transport, cytochrome c to oxygen	1.46E-02	20	iron ion transmembrane transporter activity	2.65E-02	6
nuclear membrane	1.46E-02	20	L-serine transmembrane transporter activity	2.65E-02	6
synapse part	1.46E-02	20	cleavage furrow intermediate-density lipoprotein particle	2.65E-02	6
lysosomal membrane	1.46E-02	20	extracellular matrix binding	2.65E-02	6
Golgi stack	1.46E-02	20	drug transmembrane	2.65E-02	6
gonad development	1.46E-02	20			

gonad development	1.46E-02	20	drug transmembrane transporter activity	2.65E-02	6
anion transmembrane transporter activity	1.46E-02	20	antiporter activity	2.65E-02	6
skeletal system development	1.46E-02	20	ferric iron binding	2.65E-02	6
organelle assembly	1.46E-02	20	basal plasma membrane	2.65E-02	6
G-protein coupled receptor binding	1.46E-02	20	membrane attack complex	2.65E-02	6
isoleucine metabolic process	1.46E-02	20	vitamin D 24-hydroxylase activity	2.65E-02	6
valine metabolic process	1.46E-02	20	condensed chromosome kinetochore	2.65E-02	6
regulation of ion transport	1.46E-02	20	clathrin vesicle coat	2.65E-02	6
response to heat	1.46E-02	20	trans-Golgi network	2.65E-02	6
forebrain development	1.46E-02	20	transport vesicle	2.65E-02	6
mRNA transport	1.92E-02	19	integral to Golgi membrane	2.65E-02	6
'de novo' posttranslational protein folding	1.92E-02	19	isoprenoid binding	2.65E-02	6
complement activation	1.92E-02	19	protein phosphatase regulator activity	2.65E-02	6
striated muscle cell differentiation	1.92E-02	19	autophagic vacuole	2.65E-02	6
protein polymerization	1.92E-02	19	integral to peroxisomal membrane	2.65E-02	6
protein tetramerization	1.92E-02	19	ATP-dependent DNA helicase activity	2.65E-02	6
regulation of T cell activation	1.92E-02	19	cytokine binding	2.65E-02	6
sulfotransferase activity	1.92E-02	19	biotin carboxylase activity	2.65E-02	6
regulation of reproductive process	1.92E-02	19	sarcolemma	2.65E-02	6
phosphatidylinositol metabolic process	1.92E-02	19	ATP-dependent peptidase activity	2.65E-02	6
phosphatidylinositol binding	1.92E-02	19	beta-amyloid binding	2.65E-02	6
cellular response to lipopolysaccharide	1.92E-02	19	caffeine oxidase activity	2.65E-02	6
cellular response to vitamin	1.92E-02	19	receptor inhibitor activity	2.65E-02	6
divalent metal ion transport	1.92E-02	19	postsynaptic membrane	2.65E-02	6
cytochrome-c oxidase activity	1.92E-02	19	oxoglutarate dehydrogenase complex	2.65E-02	6
nucleosome assembly	1.92E-02	19	recycling endosome membrane	2.65E-02	6
transcription corepressor activity	1.92E-02	19	protein N-terminus binding	2.65E-02	6
coated pit	1.92E-02	19	clathrin-coated endocytic vesicle membrane	2.65E-02	6
glutamine family amino acid metabolic process	1.92E-02	19	biotin carboxylase complex	2.65E-02	6
branched chain family amino acid catabolic process	1.92E-02	19	anchored to membrane	2.65E-02	6
protease binding	1.92E-02	19	biotin binding	2.65E-02	6
response to vitamin D	1.92E-02	19	perikaryon	2.65E-02	6
respiratory chain complex IV	1.92E-02	19	transmembrane receptor	2.65E-02	6
regulation of homeostatic process	1.92E-02	19	protein kinase activity	2.65E-02	6
			nuclear ubiquitin ligase complex	2.65E-02	6
			cytoplasmic ubiquitin ligase complex	2.65E-02	6

positive regulation of cytokine production	1.92E-02	19	extracellular membrane-bounded organelle	2.65E-02	6
cell projection membrane regulation of protein complex assembly	1.92E-02	19	peptidase activator activity	2.65E-02	6
cell redox homeostasis	1.92E-02	19	glutathione binding	2.65E-02	6
regulation of cell projection organization	1.92E-02	19	cortical actin cytoskeleton	2.65E-02	6
protein polyubiquitination	1.92E-02	19	scavenger receptor activity	2.65E-02	6
pattern specification process	2.53E-02	18	carbohydrate kinase activity	2.65E-02	6
positive regulation of MAP kinase activity	2.53E-02	18	Ras guanyl-nucleotide exchange factor activity	2.65E-02	6
positive regulation of immune effector process	2.53E-02	18	peptide hormone binding	2.65E-02	6
response to carbohydrate stimulus	2.53E-02	18	translation initiation factor binding	2.65E-02	6
			glutathione peroxidase activity	2.65E-02	6
regulation of cellular response to stress	2.53E-02	18	mitochondrial proton-transporting ATP synthase complex, coupling factor F(o)	2.65E-02	6
ubiquitin protein ligase binding	2.53E-02	18	oxidoreductase activity, acting on the CH-NH group of donors, NAD or NADP as acceptor	2.65E-02	6
response to interferon-gamma	2.53E-02	18			
regulation of synaptic transmission	2.53E-02	18			
positive regulation of behavior	2.53E-02	18			
circadian rhythm	2.53E-02	18			
nicotinamide nucleotide metabolic process	2.53E-02	18			
regulation of Wnt receptor signaling pathway	2.53E-02	18			
mitochondrial large ribosomal subunit	2.53E-02	18			
negative regulation of cell growth	2.53E-02	18			
regulation of cellular component size	2.53E-02	18			
DNA-dependent transcription, termination	2.53E-02	18			
melanosome	2.53E-02	18			
monocarboxylic acid transport	2.53E-02	18			
response to amine stimulus	2.53E-02	18			
leukocyte chemotaxis	2.53E-02	18			
amine transport	2.53E-02	18			
platelet alpha granule	2.53E-02	18			
leucine metabolic process	2.53E-02	18			
microtubule-based movement	2.53E-02	18			
morphogenesis of a branching structure	2.53E-02	18			
positive regulation of I-kappaB kinase/NF-kappaB cascade	2.53E-02	18			

protein-DNA complex	2.53E-02	18
epidermal growth factor		
receptor signaling pathway	2.53E-02	18
cell killing	2.53E-02	18
regulation of DNA		
metabolic process	3.31E-02	17
hydrolase activity, acting		
on glycosyl bonds	3.31E-02	17
negative regulation of		
neuron apoptotic process	3.31E-02	17
amino acid transmembrane		
transporter activity	3.31E-02	17
regulation of viral		
reproduction	3.31E-02	17
microtubule binding	3.31E-02	17
positive regulation of		
lymphocyte activation	3.31E-02	17
negative regulation of lipid		
metabolic process	3.31E-02	17
locomotory behavior	3.31E-02	17
regulation of blood vessel		
size	3.31E-02	17
calmodulin binding	3.31E-02	17
vesicle coat	3.31E-02	17
pyridoxal phosphate		
binding	3.31E-02	17
rRNA binding	3.31E-02	17
iron-sulfur cluster binding	3.31E-02	17
peptidyl-tyrosine		
phosphorylation	3.31E-02	17
negative regulation of		
organelle organization	3.31E-02	17
nuclear chromosome part	3.31E-02	17
Golgi-associated vesicle	3.31E-02	17
maintenance of location in		
cell	3.31E-02	17
sequence-specific DNA		
binding RNA polymerase		
II transcription factor		
activity	3.31E-02	17
immunoglobulin mediated		
immune response	3.31E-02	17
DNA recombination	3.31E-02	17
positive regulation of		
innate immune response	3.31E-02	17
epidermis development	3.31E-02	17
RNA export from nucleus	3.31E-02	17
intracellular steroid		
hormone receptor		
signaling pathway	3.31E-02	17
small nuclear		
ribonucleoprotein complex	3.31E-02	17
response to starvation	3.31E-02	17
proton-transporting ATP		
synthase complex	3.31E-02	17
tyrosine metabolic process	3.31E-02	17
ATPase activity, coupled		
to transmembrane	3.31E-02	17

movement of ions		
acetyltransferase activity	3.31E-02	17
negative regulation of cytokine production	3.31E-02	17
regulation of actin cytoskeleton organization	3.31E-02	17
intrinsic to endoplasmic reticulum membrane	3.31E-02	17
histone modification	3.31E-02	17
negative regulation of protein phosphorylation	3.31E-02	17
negative regulation of cellular catabolic process	3.31E-02	17
iron ion transport	3.31E-02	17
post-Golgi vesicle-mediated transport	3.31E-02	17
anchoring junction	4.32E-02	16
autophagy	4.32E-02	16
muscle contraction	4.32E-02	16
cell-substrate adhesion	4.32E-02	16
hydro-lyase activity	4.32E-02	16
lipid transporter activity	4.32E-02	16
aromatase activity	4.32E-02	16
positive regulation of protein transport	4.32E-02	16
immune response-activating signal transduction	4.32E-02	16
cell junction organization	4.32E-02	16
plasma lipoprotein particle clearance	4.32E-02	16
regulation of coagulation establishment of protein localization in mitochondrion	4.32E-02	16
gliogenesis	4.32E-02	16
hormone receptor binding	4.32E-02	16
regulation of blood pressure	4.32E-02	16
extracellular matrix organization	4.32E-02	16
immunoglobulin complex	4.32E-02	16
leukocyte proliferation	4.32E-02	16
energy reserve metabolic process	4.32E-02	16
organelle subcompartment establishment of vesicle localization	4.32E-02	16
trans-Golgi network	4.32E-02	16
multicellular organism growth	4.32E-02	16
cellular response to growth factor stimulus	4.32E-02	16
cellular response to steroid hormone stimulus	4.32E-02	16
glucose transport	4.32E-02	16
metalloendopeptidase	4.32E-02	16

metalloendopeptidase activity	4.32E-02	16
tRNA aminoacylation for protein translation	4.32E-02	16
regulation of glucose metabolic process	4.32E-02	16
induction of apoptosis by intracellular signals	4.32E-02	16
urogenital system development	4.32E-02	16
camera-type eye development	4.32E-02	16
heat shock protein binding	4.32E-02	16
sulfation	4.32E-02	16
helicase activity	4.32E-02	16
organ regeneration	4.32E-02	16
ATP synthesis coupled proton transport	4.32E-02	16
protein targeting to membrane	4.32E-02	16
N-acyltransferase activity	4.32E-02	16
glycolipid metabolic process	4.32E-02	16
protein secretion	4.32E-02	16
fat cell differentiation	4.32E-02	16
positive regulation of cysteine-type endopeptidase activity involved in apoptotic process	4.32E-02	16
contractile fiber	4.32E-02	16
fat-soluble vitamin metabolic process	4.32E-02	16
regulation of steroid metabolic process	4.32E-02	16
Rho protein signal transduction	4.32E-02	16
positive regulation of cellular catabolic process	4.32E-02	16
cytokine activity	4.32E-02	16
mitochondrion	4.32E-02	16

B

Brain to Liver			Brain to Gonads		
GO term	FDR	# Sequences	GO term	FDR	# Sequences
plasma membrane	2.41E-44	567	plasma membrane	4.30E-92	567
cell-cell signaling	3.86E-40	232	cell-cell signaling	2.79E-61	232
cell differentiation	1.11E-38	372	signal transduction	2.15E-39	525
cytoskeleton organization	1.48E-24	145	cytoskeleton	9.39E-34	369
multicellular organismal development	2.94E-24	555	anatomical structure	1.89E-30	291
signal transduction	1.62E-23	525	morphogenesis	5.07E-28	372
anatomical structure	1.77E-19	291	cell differentiation	5.07E-28	372
morphogenesis	1.77E-19	291	behavior	6.72E-28	133
actin binding	1.77E-19	93	cytoplasmic membrane-	1.33E-22	197

behavior	2.81E-15	133	bounded vesicle		
ion channel activity	6.50E-14	62	ion transport	3.13E-17	209
cytoplasmic membrane-			ion channel activity	5.21E-17	62
bounded vesicle	1.72E-11	197	cellular homeostasis	9.82E-16	134
motor activity	2.08E-11	48	actin binding	3.54E-15	93
protein kinase activity	5.16E-09	77	response to external stimulus	9.26E-15	201
protein complex	6.06E-09	569	receptor activity	1.97E-14	110
cellular homeostasis	1.52E-08	134	receptor binding	2.79E-14	151
calcium ion binding	3.14E-07	109	calcium ion binding	7.69E-13	109
cilium	8.46E-07	27	cytoskeleton organization	9.13E-13	145
ion transport	4.08E-06	209	enzyme regulator activity	1.28E-11	149
structural molecule			Golgi apparatus	1.51E-10	168
activity	1.93E-05	141	cytosol	1.79E-08	411
transcription regulator			response to abiotic stimulus	4.97E-08	88
activity	2.73E-05	59	lipid binding	5.13E-07	89
cell cycle	6.17E-05	166	response to stress	1.13E-06	308
cytosol	9.77E-05	411	protein complex	1.27E-06	569
chromosome	1.20E-03	91	cell death	1.78E-06	247
microtubule organizing			motor activity	8.38E-06	48
center	2.08E-03	52	endosome	8.46E-06	70
nucleus	2.09E-03	514	response to endogenous		
cell death	3.06E-03	247	stimulus	1.04E-05	122
response to abiotic			embryo development	5.12E-05	92
stimulus	3.12E-03	88	proteinaceous extracellular		
chromatin binding	2.90E-02	29	matrix	1.90E-04	34
Golgi apparatus	3.96E-02	168	nucleotide binding	1.92E-04	331
			protein transport	3.24E-04	152
			signal transducer activity	8.24E-04	48
			protein kinase activity	1.61E-03	77
			cell envelope	1.88E-03	6
			carbohydrate binding	8.60E-03	43
			external encapsulating		
			structure	1.38E-02	6
			structural molecule activity	2.03E-02	141
			neurotransmitter transporter		
			activity	2.73E-02	6
			extracellular space	3.68E-02	68
			generation of precursor		
			metabolites and energy	4.94E-02	134

C

Gonads to Liver			Gonads to Brain		
GO term	FDR	# Sequences	GO term	FDR	# Sequences
cilium	1.26E-14	104	translation	3.96E-05	449
cell cycle	8.88E-12	571	reproduction	3.96E-05	680
transcription regulator activity	3.57E-08	183	ribosome	1.43E-03	383
nucleolus	2.16E-07	498	viral reproduction	4.24E-03	339
reproduction	1.92E-06	680	nuclear chromosome	4.34E-03	119
nuclear chromosome	9.86E-06	119	peptidase activity	4.51E-03	230
cytoskeleton organization	1.75E-04	218	RNA binding	8.05E-03	637
nucleoplasm	1.77E-04	687	mitochondrion	1.03E-02	836
regulation of gene expression, epigenetic	1.91E-04	41	electron carrier activity	1.31E-02	109
microtubule organizing center	6.18E-04	150			
protein kinase activity	6.52E-04	161			
RNA binding	6.70E-04	637			
structural molecule activity	1.13E-02	369			
motor activity	1.71E-02	64			
viral reproduction	1.75E-02	339			
cell differentiation	3.89E-02	613			
chromatin binding	4.61E-02	78			

Table S3

Pairwise Urban:Rural Comparisons	Sequence name	p_N/p_S	Gene name	Gene function
	HP_contig02521	0.51	Apoptogenic protein mitochondrial	Regulation of mitochondrial induced apoptosis
	HP_contig01711	0.51	Fibrinogen alpha chain	Glycoprotein circulating in the blood; functions in blood coagulation and part of the most abundant component of blood clots
	HP_contig02065	0.52	Complement factor h	Glycoprotein circulating in plasma; regulation of complement activation
	HP_contig00430	0.53	Murinoglobulin-1 precursor	Protease activity; acute phase response
	HP_contig01727	0.54	Ornithine mitochondrial	Transfer of ornithine across inner mitochondrial membrane
	HP_contig00783	0.54	Carboxymethylenebutenolide homolog	Cysteine hydrolase, protein binding
	HP_contig00807*	0.54	Isoform cra_a	Uncharacterized cellular membrane protein
	HP_contig01783	0.58	Cytochrome p450 2a15	Metabolic process; testosterone 7a-hydroxylase activity
	HP_contig00737	0.58	Catechol o-methyltransferase	Catalyzes methylation for degradation of neurotransmitters and catecholic xenobiotics
	HP_contig05051	0.60	Hypothetical protein I79_019498	Uncharacterized
	HP_contig02710	0.63	L-xylulose reductase	Metabolic processes; catalyzes NADPH-dependent reduction
	HP_contig01169	0.64	Alpha-1-acid glycoprotein precursor	Transport protein in the blood stream; binds and distributes synthetic drugs throughout body; modulates innate immune response
	HP_contig02231	0.66	Isoform cra_b	Transmembrane transport protein
	HP_contig02824	0.67	Nadh dehydrogenase	Mitochondrial respiratory chain complex; electron transport
	HP_contig03468	0.73	Coatomer subunit beta	Protein transportation between Golgi body and ER; required for budding from Golgi body
	HP_contig01714	0.74	Complement factor i	Serine protease; regulation of complement activation by cleavage of complement system components
	HP_contig01785	0.77	Kininogen-1 isoform 2 precursor	Inflammatory response; involved in blood coagulation - negative regulation
	HP_contig03812	0.79	Biorientation of chromosomes in cell division protein 1	Required for proper orientation of chromosomes during cell division
	HP_contig01991	0.80	Calcium binding and coiled-coil domain 2	Innate immune response; receptor protein for bacteria; mediate macroautophagy
	HP_contig01688	0.83	Polymeric immunoglobulin receptor	Transports immunoglobulins across cell to apical surface for secretion; adaptive immune system
	HP_contig02433	0.99	40s ribosomal protein s3a	RNA binding; translational initiation
	HP_contig03921	1.00	Bile salt sulfotransferase-like	Transferase activity
Pairwise Urban:Urban Comparisons	RR_contig00497	0.50	Arginase-1 like	Arginine metabolism
	RR_contig00554	0.51	Ornithine mitochondrial	Metabolic processes; mitochondrial membrane
	NYBG_contig00478*	0.54	Fibrinogen alpha chain	Glycoprotein circulating in the blood; functions in blood coagulation and part of the most abundant component of blood clots
	NYBG_contig00650	0.54	Leucine-rich repeat and wd	Involved with DNA replication initiation and silencing;

NYBG_contig00650	0.54	Leucine-rich repeat and wd repeat-containing protein 1	Involved with DNA replication initiation and silencing; Binds to methylated histones and restricts transcription
CP_contig00326	0.55	---NA---	Uncharacterized
CP_contig00764	0.55	Murinoglobulin-2 precursor	Protease activity; acute phase response
RR_contig00859	0.59	Liver carboxylesterase b-1-like	Xenobiotic metabolism, detoxification through hydrolysis of ester and amide bonds
NYBG_contig00447	0.59	Complement c3 precursor	Innate immune response; major role in activation of complement pathway
RR_contig00239	0.59	Cytochrome p450 family 2 subfamily b	Xenobiotic metabolism
RR_contig00587	0.63	Estradiol 17-beta-dehydrogenase 2	Steroid biosynthetic process; oxidation-reduction
CP_contig00527	0.65	Cytochrome p450 2d27-like	Xenobiotic metabolism; oxidation-reduction
NYBG_contig00664*	0.73	Protein maelstrom homolog isoform 1	Reproductive process; active in spermatogenesis; repress transposable elements to retain germline integrity
NYBG_contig00513	0.74	Cytochrome family subfamily polypeptide 13	Xenobiotic metabolism; oxidation-reduction
NYBG_contig00284	0.81	Catechol o-methyltransferase	Methylation activity; introduces methyl groups to inactivate neurotransmitters
CP_contig00544	0.91	Gametogenetin-binding protein 1	Reproductive processes; mitochondrial morphogenesis during spermatogenesis
RR_contig01212	0.91	Isoform cra_a	Uncharacterized cellular membrane protein
NYBG_contig00790*	0.98	Orosomucoid 1	Transport protein in the blood stream; binds and distributes synthetic drugs throughout body; modulates innate immune response
CP_contig00444*	0.99	Vitamin d-binding protein	Albumin gene family; transports vitamin D throughout body
		Kininogen-1 isoform 2	Inflammatory response; involved in blood coagulation

* = Gene contained p_N/p_S between 0.5 and 1 in two independent population pairwise

comparisons