

Summary

Parkinson's disease (PD) is the second most prevalent neurodegenerative disease. Degeneration of the midbrain dopaminergic (mesDA) neurons in the substantia nigra pars compacta (SNpc) region of the brain is the pathological hallmark of PD. Different types of transcriptional or other factors that mediate the generation, migration, and differentiation of mesDA neurons in SNpc, may undertake non-developmental roles in developed mesDA neurons, as several recent studies show that the mesDA neurons require such factors for survival and maintenance throughout life. The deficiency in these factors may also contribute to the vulnerability of SNpc neurons to degeneration, and may be causal to initiation and advancement of the disease. Several factors, including aging and exposure to environmental toxins, contribute to degeneration of this neuronal population and the identification of familial cases put genetics among such factors. This study takes advantage of the previous data to further understand the dynamics between the role of developmental factors, genetics and the classical etiology of the disease and to identify novel correlations between the genes with high expression levels in mesDA neurons and several processes within the SNpc. Utilizing the genes of known function in five categories of development, survival, genetics, pro-apoptosis and anti-apoptosis, and using two online software, ToppGene and Endeavour, I identified several genes which can be placed within each of these categories. The results of this study may be used in identification of novel molecular and biochemical processes, contributing to etiology of the disease, which may be used as new therapeutic targets.

Introduction

Development of Dopaminergic neurons

After developing three germ layers, endoderm, mesoderm, and ectoderm, by signaling and interaction between embryonic cells and during gastrulation, a part of ectoderm gives rise to neural progenitors. The signals, such as fibroblast growth factor (FGF) (Moreau and Leclerc, 2004), are secreted from dorsal mesoderm, underlay the dorsal ectoderm, in gastrula. BFGF induces the differentiation of dorsal ectodermic cells to neuronal tube cells, early in gastrula stage (Kengaku and Okamoto, 1993).

During later developmental stages, neuronal tube undergoes differentiation along anteroposterior axis, forming forebrain, midbrain, hindbrain and the spinal cord. These regions become further specified along dorsoventral axis (Gorman et al., 2005). The organizing center at the border between midbrain and hindbrain, isthmus, appears in its correct position by interactions between two homeodomain transcription factors that act as transcriptional repressors (Glavic et al., 2002), *Otx2* (Glavic et al., 2002; Gorman et al., 2005), that is expressed in anterior part of the ectoderm during early development and in forebrain and midbrain in later stages (Gorman et al., 2005; Millet et al., 1999), and *Gbx2* (Glavic et al., 2002), which is initially expressed in all three germ layers and later in the anterior part of hindbrain (Millet et al., 1999). The diffusible molecule, fibroblast growth factor 8 (*Fgf8*), is secreted within isthmus, (Prakash and Wurst, 2006). Another diffusible molecule, *Wnt1*, is secreted adjacent to isthmus in caudal midbrain (Glavic et al., 2002; Prakash and Wurst, 2006). *Fgf8* has positive and negative effect on expression of *Gbx2* and *Otx2*, respectively (Gorman et al., 2005). Other genes, expressed in this region include *En1/En2*, *Pax2*, and *Lmx1*, which are essential for initiation and maintenance of the *Fgf8* expression (Guo et al., 2007). *Fgf8* and *Wnt1* are both essential for developing midbrain (Guo et al., 2007; Sato and Joyner, 2009). *Fgf8* signaling from the isthmus, along with sonic hedgehog (*Shh*) from the floor plate are

crucial for both inducing the mesDA neuron progenitors and neurons from the progenitors (Prakash and Wurst, 2006).

Expression of Otx2 continues, even after establishing the isthmus, and it undertakes the role of regulating neurogenesis and differentiation in several neuronal populations like mesDA neurons in the midbrain (Omodei et al., 2008; Vernay et al., 2005). Differentiation and maintenance of mesDA neurons in ventral midbrain, in addition to Otx2 is controlled and mediated by other genes like; Tgf- α /Tgf- β , Pitx3, Lmx1a/ Lmx1b, Msx1, Mash1, Ngn2, and Nurr1. The expression of Otx2 (Puelles et al., 2004), Lmx1b, En1/En2 (Simon et al., 2001) starts in ventral midbrain DA progenitor and then Lmx1a and Msx1 are expressed. Moreover, expression of Ngn2 and Mash1 starts later for transformation the floor- plate cells into neuronal progenitor cells (Kele et al., 2006). Therefore, Shh, Fgf8, and Wnt1 induce the mesDA neuronal progenitors in the region and the mesDA neuronal fate is regulated by En1/2, Otx2, Lmx1a/ Lmx1b, Msx1, Mash1, and Ngn2 (Alavian et al., 2008; Ferri et al., 2007).

Nurr1 (NR4A2) is expressed as a transcription factor when the mesDA progenitor cells begin specifying and converting to immature mesDA neurons (Zetterstrom et al., 1997). In addition, Lmx1a (Ono et al., 2007)/ Lmx1b (Smidt et al., 2000), En1/En2 (Simon et al., 2001), and Ngn2 (Kele et al., 2006) are expressed in these newborn mesDA neurons, too. The expression of these genes continues even after the differentiation of immature mesDA neurons to mature mesDA neurons. However, mature mesDA neurons express tyrosine hydroxylase (TH), which is the rate-limiting enzyme in catecholamine synthesis and a marker of mesDA neurons, and Pitx3 (Ferri et al., 2007).

Lmx1b, which is also expressed in the isthmus during early development, is a transcriptional factor that, in addition to its effect on Fgf8 expression, is necessary for maintaining the expression of Wnt1, En1, En2, Pax2, and Gbx2 during mid/hindbrain development (Guo et al., 2007). Lmx1a/b are also needed for differentiating the mesDA neurons. Lmx1a is expressed in both mesDA progenitor cells, for regulating the gene expression in these cells, such as proneural factors, Mash1 and Ngn2 and mesDA neurons, and in mesDA neurons, for controlling the differentiation of mesDA neurons after mitosis (Andersson et al., 2006b; Ono et al., 2007). En1/En2, two homeobox

transcription factors, play essential role in maintaining mesDA neurons during early and late development, as well as after their differentiation throughout life (Alavian et al., 2009; Sgado et al., 2006; Simon et al., 2003).

It seems that both Lmx1a⁺ cells, in mesencephalon, and floor plate cells, in the ventral midline of neuronal tube, are mesDA progenitor cells because some pro-neural factors, such as Mash1 and Ngn2 are expressed adjacent to these cells in both regions and also homeodomain transcription factors, Lmx1a and Msx1, that are essential for differentiation of mesDA neurons are expressed in both of these regions (Ono et al., 2007). In addition to those gens that are mentioned above, investigating the null mutation in TGF- α /b and Ngn2 has indicated their crucial role in differentiation and especially in survival of mesDA neurons after generation (Jacobs et al., 2006).

In summary, the stages of development of the dopaminergic neurons in midbrain consist of the differentiation of DA progenitor cells in the neuroepithelium throughout the early stages of CNS development after appearing in the anteroposterior and dorsoventral axis and the partition of the neural tube to forebrain, mid and hindbrain. Then, DA neuronal progenitors differentiate to mesDA neurons and acquire the identity and the specific phenotype of this specific cell type. All of these stages are mediated by specific signals and transcription factors. Fgf8, Wnt1, Otx2, Nkx2-2, Shh, Lmx1a, Msx1 and Nkx6 control formation of mesDA neurons precursors, while homeobox genes Pitx3 and En1/2, and Nurr1 act in the terminal differentiation of mesDA neurons (Prakash and Wurst, 2006). Several of these factors such as En1/2, Nurr1 and Pitx3 are expressed in post-mitotic neurons and throughout life within mesDA neurons and seem to have a lifelong role in survival and maintenance of the neurons and functions such as regulating the neurotransmitter phenotype (Simon and Alavian, 2009).

Dopamine system in basal ganglia

Dopaminergic neurons connect mesencephalon to forebrain through three pathways; one group of dopaminergic neurons, which are located in substantia nigra pars compacta (SNpc), projects their axons to dorsal striatum. This pathway is essential for motor learning as well as initiation and coordination of movement. Another group of neurons are in ventral tegmental area (VTA) that project to limbic structures; ventral

striatum (VS) nuclei such as nucleus accumbens, olfactory tubercle, amygdala and hippocampus. Amygdala plays an important role in emotional learning and hippocampus (HPC) is responsible for long-term memory. Therefore, one of the functions of the second pathway is adjusting the motor behaviors (Girault and Greengard, 2004).

The last class of dopaminergic neurons project from VTA to the prefrontal cortex (PFC), anterior cingulate, orbitofrontal, entorhinal, also temporal and parietal cortices, and cerebellar areas. The target structures in this pathway, especially PFC, modulate cognitive functions such as short-term and long-term memory and attention. The relation between cerebral cortex and VTA and also limbic structures and VTA form two autonomous and closed loops, mesocortical and mesolimbic DA systems, respectively (Goto and Grace, 2007; Sidhu A et al., 2003).

Generally, some projections from cortex (excitatory inputs) pass through striatum to the internal part of the internal globus pallidum (GPi) and the substantia nigra pars reticulata (SNr) and then to thalamus. Then the projections of thalamus, which supply excitatory inputs, return to cortex. There are two pathways for these loops; direct and indirect pathways that provide excitatory inputs through D1 receptors and inhibitory inputs that are mediated by D2 receptor, respectively (Mailman et al., 2001). In direct pathway striatum outputs reach GPi and SNr, directly, but in the indirect pathway, striatum outputs pass through the external part of the external globus pallidus (GPe) and the subthalamic nuclei (STN) and the inputs of these structures get to GPi and SNr. Dopamine (DA) secretion controls inputs and outputs in these loops (Guillin et al., 2007).

DA receptors are located both in presynaptic and postsynaptic terminals and even though the tonic DA release is not able to stimulate postsynaptic DA receptors, it induces presynaptic DA receptors, D1 receptors are expressed just on the presynaptic surface of PFC neurons while only D2 receptors are expressed on the presynaptic surface of the striatum. Inducing presynaptic D2 receptors leads to reducing glutamate secretion and so reducing the excitatory postsynaptic potentials (EPSPs) in the striatum. Postsynaptic DA receptors are induced by higher level of DA release from stimulated mesDA neurons through excitatory inputs (Goto and Grace, 2007).

Striatum consist of two nuclei, putamen and caudate, putamen nucleus is affected through PD more than other part of striatum. Loss of DA input from SNpc to the striatum leads to increased activity in the indirect pathway because reduction of DA inputs in striatum activates the striatal GABAergic neurons that project to GPe and inhibits its GABAergic neurons. Therefore, the suppressive effect of GPe on subthalamic nucleus results in enhanced activation of basal ganglia output nuclei, GPi and SNpr. However the reduction of DA input from SNpc, which happens during the course of Parkinson's disease, leads to decreased activity in the direct pathway; the absence of DA input inhibits the GABAergic striatal neurons that innervate GPi and the disinhibition of the suppressive effect of the GABAergic projections results in the activation of GPi (Sidhu A et al., 2003) (Figure-1).

The difference in responses of the direct and indirect pathways to losing the dopaminergic input is due to the differential action of dopamine on the two pathways by means of D1 and D2 receptors, which stimulate the direct pathway and inhibit the indirect pathway, respectively. Both of these changes lead to increased activity in the GPi, which results in increased inhibition of thalamocortical and midbrain tegmental neurons and thus the hypokinetic features of the disease(Sidhu A et al., 2003).

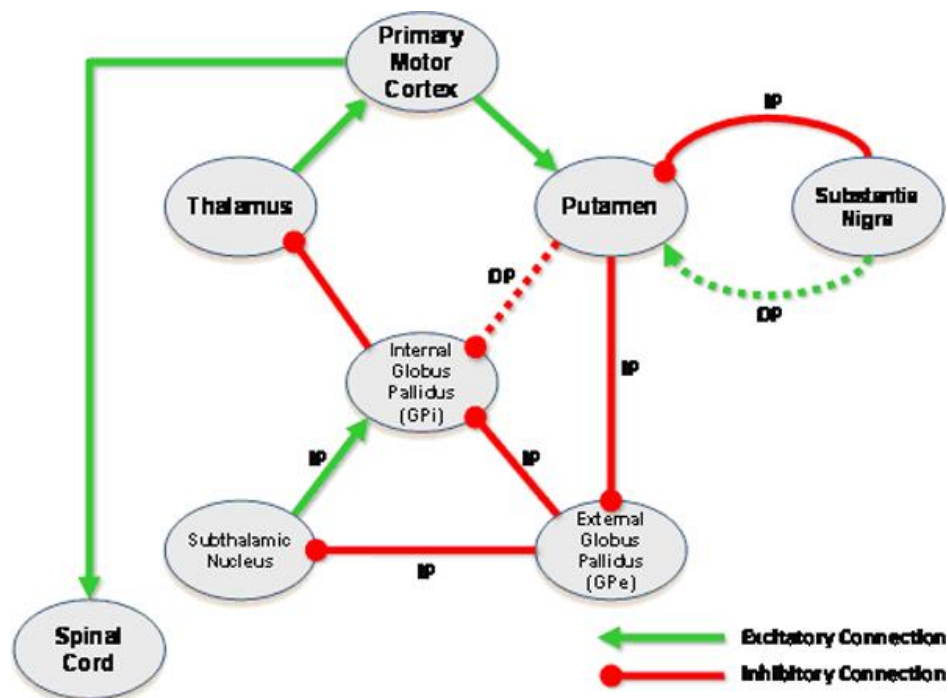


Figure-1: The relations between different nuclei of basal ganglia to each other and to motor cortex and spinal cord under normal conditions (continuous lines) and in Parkinson's disease (dashed lines). Green line: excitatory connection, Red line: inhibitory connection. Adapted from: Rubin *et al. BMC Bioinformatics* 2009 **10** (Suppl 2):S3 doi: 10.1186/1471-2105-10-S2-S3.

Parkinson's disease

Parkinson's disease is the second most prevalent neurodegenerative disorder, after Alzheimer's disease, which appears in about 1.5 to 2 percent of the population over 55 (Fearnley and Lees, 1991). The primary symptoms of the disease are unilateral resting tremor, muscular rigidity, hypokinesia, akinesia and bradykinesia (Parkinson, 2002).

Parkinson's disease is the result of degeneration of the mesDA neurons in the SNpc, which project to dorsal striatum and secrete DA. Although serotonergic and noradrenergic pathways of the brain also play a role in progression of the symptoms of the disease, especially depression, dopaminergic cell loss in the SNpc is the fundamental factor for the initiation of PD. The primary symptoms appear after degeneration of about 50% of the mesDA neurons in SNpc (Fearnley and Lees, 1991). As the degeneration of these neurons continues and the disease gradually progresses, the secondary or advanced symptoms, which include dementia, depression, sleep disorders, sensory complaints, dysarthria, dysphagia, constipation, urinary and olfactory dysfunction, sialorrhea, seborrhea and orthostatic hypotension emerge (Guze and Barrio, 1991; Hamani and Lozano, 2003).

In the early stages of PD, degeneration is limited to the mesDA neurons of the SNpc (or the A9 area) and is only in the very advanced stages that the neurons in the VTA (A10 area) are affected (Damier *et al.*, 1999). Therefore, the reason for the vulnerability of the mesDA neurons in the SNpc can be the key to understanding the etiology of PD. Several studies have addressed the role of the specific physiological and the gene expression profile differences between the two DA neuronal populations, A9 and A10 in death of the neurons in the animals models of PD (Chung *et al.*, 2005; Liss *et al.*, 2005).

Based on DNA linkage studies, 13 distinct human chromosomal locations, PARK loci, have been linked to the disease: PARK1 (Polymeropoulos *et al.*, 1997), PARK2 (Matsumine *et al.*, 1997), PARK3 (Gasser *et al.*, 1998), PARK4 (Waters and Miller,

1994), PARK5 (Leroy et al., 1998), PARK6 (Valente et al., 2001), PARK7 (van Duijn et al., 2001), PARK8 (Funayama et al., 2002), PARK9 (Hampshire et al., 2001), PARK10 (Hicks et al., 2002), PARK11 (Pankratz et al., 2002), PARK12(Pankratz et al., 2002), PARK13 (Wakabayashi and Takahashi, 2007). These loci expand variably, from 7 to 40Mb, on different chromosomes each of which contains several hundreds of genes. There are 4 orphan PD loci with no associated genes so far and mutation/s in 8 genes, located in 9 out of 13 PARK loci have been linked to PD. Mutations in *α -synuclein* located on PARK1 and PARK 4, Parkin, Ubiquitin carboxy-terminal-hydrolase-L1(UCHL1), PTEN-induced-putative kinase (PINK1), DJ1, Leucine-rich repeat kinase 2 (LRRK2), ATPase type 13A2 (ATP13A2), HTRA2 genes in PARK2, 5, 6, 7, 8, 9 and 13 have been shown, respectively, to cause PD (Gasser, 2007). Additionally, two other susceptibility genes, Nurr1 (NR4A2) and tau, which show no linkage to previously described PARK Loci, have been linked to families with Parkinson's disease (Gherbassi et al., 2007). Each of the PARK loci contains a large number of genes and identification of disease genes requires proper criteria to narrow down the number of candidates. Since several of the mutations within the PD genes are loss of function mutations and five out of seven PD genes (*α -SYNUCLEIN*, PARKIN, UCHL1, PINK1 and LRRK2) plus the two latter genes (NURR1 and TAU) are expressed in midbrain dopaminergic neurons, it is quite possible that these genes play a critical role in the survival of the neurons under normal (non-pathological) conditions. This point is supported by many studies on transgenic and knockout animals, which show various degrees of functional deficiency in the nigrostriatal dopaminergic system (Abeliovich et al., 2000).

In addition to the loss of function of PD genes, deficiency in several developmental, survival, and anti-apoptotic factors has been implicated as the possible cause of degeneration and cell death within SNpc during the course of Parkinson's disease. Transcriptional and developmental factors, which play a vital role early in the embryonic stages of differentiation of mesDA neurons, have been shown to have neuroprotective functions during the postnatal stages and throughout life (Alavian et al., 2008).

The aim of this project was to identify genes with functional relevance to survival and death of mesDA neurons within five categories of development, survival, PD genes,

pro- and anti-apoptotic factors. To accomplish this goal, I utilized genes from each category that are known to play vital roles within the dopaminergic neurons of the SNpc or are implicated as part of the etiology of Parkinson's disease, in addition to the genes that are expressed within rodent mesDA neurons. Using two bioinformatics prioritization tools and specific statistical criteria, I identified genes that may belong to each of the aforementioned five categories.

Materials and Methods

In order to prioritize the expressed genes in mesDA neurons, we used two softwares, ToppGene and Endeavour. We used the set of genes with high levels of expression (detectable by in situ hybridization) in mesDA neurons, as candidate (in Endeavour software) or test gene set (in ToppGene software), and a functionally-relevant set of genes as training for comparison. We used the results of previous studies that defined the expression profile of mesDA neurons, including mesDA neurons in SNpc and VTA, in mice and rats (Barrett et al., 2001; Chung et al., 2005; Greene et al., 2005; Grimm et al., 2004; Stewart et al., 1997; Thuret et al., 2004). The list included 369 genes, which were identified through differential display and microarray studies (Alavian and Simon, 2009). The updated list of genes is presented in Table-A of appendix. The human homolog of the 369 (rodent) genes was collected by using the Gene function of the NCBI website (<http://www.ncbi.nlm.nih.gov/gene>).

We could identify the *Homo sapiens* official symbols for 362 out of 369 expressed genes in mesDA neurons, due to very low query coverage for the rest when compared with the mouse or rat genes through the BLAST function of the NCBI site <http://www.ncbi.nlm.nih.gov/BLAST/>. Table C of appendix shows the hits with no significant coverage for human genes.

As the training gene set, we classified the genes with known functions in development, survival, cell death and neuroprotection of mesDA neurons. An additional set was PD genes, comprising the genes causing the familial PD. Each training gene set was then entered into two online tools, Toppgene, <http://toppgene.cchmc.org/prioritization.jsp> and Endeavour <http://homes.esat.kuleuven.be/~bioiuser/endeavour/tool/endeavourweb.php> for comparison with the test gene set in table B of appendix, comprising the genes with high expression levels in mesDA neurons. The criteria for comparison are different in Toppgene and Endeavour programs (Table-2) but the method is similar in that both of these tools are used for identifying the functions of the test gene set by comparing them

to the training set. ToppGene ignored the genes in training or test sets, which either could not be identified or those repeated in both columns (Table-D of Appendix). For prioritization in ToppGene, all criteria (Table-2) were selected. The cutoff p-value was 0.001 and 8% of the genome (2000 genes) was used as the random sampling size.

Developmental & Survival	Survival	PD Genes	Pro-apoptotic	Anti-apoptotic
NR4A2	BDNF	SNCA	SLC25A5	
FOXA1	NTRK2	UCHL1		

Table-1: The repeated genes in training and test gene set which are automatically omitted by ToppGene.

For prioritizing the genes, using Endeavour, first the species (*Homo sapiens*) was selected. Then we inserted the training gene set, and selected all items in data sources used to build models. Finally, we added the candidate or the test gene sets to Endeavour for prioritization. Unlike ToppGene, Endeavour does not omit the repeated genes but omits genes that cannot be identified (Table-D of appendix). Similar to Toppgene, we only considered the prioritized gene with p-value < 0.001.

<u>Toppgene</u>	<u>Endeavour</u>
GO: Molecular Function	Annotation - <u>EnsemblEst</u>
GO: Biological Process	Annotation - <u>GeneOntology</u>
GO: Cellular Component	Annotation - <u>Interpro</u>
Human Phenotype	Annotation - <u>Kegg</u>
Mouse Phenotype	Annotation - <u>Swissprot</u>
Domain	Blast
Pathway	<u>CisRegModule</u>
<u>Pubmed</u>	Expression - <u>SonEtAl</u>
Interaction	Expression - <u>SuEtAl</u>
<u>Cytoband</u>	Interaction - Bind
TFBS	Interaction - <u>BioGrid</u>
Gene Family	Interaction - <u>Hprd</u>
<u>Coexpression</u>	Interaction - <u>InNetDb</u>
Computational	Interaction - Intact
<u>MicroRNA</u>	Interaction - Mint
Drug	Interaction - String
Disease	Motif
	<u>Precalculated</u> - <u>Ouzounis</u>
	<u>Precalculated</u> - <u>Prospectr</u>
	Text

Table-2: Feature (in Toppgene) and data source (in Endeavor) used for prioritization of the test gene set.

Results

After terminal differentiation of mesDA neurons the factors that play a crucial role in migration and differentiation of mesDA neurons assume other roles in the mature neurons. Some factors, such as brain derived neurotrophic factor (BDNF), are necessary for survival of mesDA neurons and maintenance of the neurons throughout life. It has been shown that the secretion of BDNF by immortalized engineered fibroblasts could protect the mesDA neurons of SNpc against degeneration, induced by infusion of the mesDA neuron-specific neurotoxin, 1-methyl-4-phenylpyridinium (MPP⁺) (Frim et al., 1994). NR4A2 (NURR1) is another crucial factor for development, survival and maintenance of mesDA neurons during both fetal and postnatal stages. Investigating the human peripheral blood lymphocytes (PBL) has indicated that the secretion of NR4A2 is significantly reduced in PD patients (Le et al., 2008).

Developmental & Survival	Survival	PD Gene	Pro-apoptotic	Anti-apoptotic
EN1	BDNF	SNCA	AIFM1	BCL2L1
EN2	GDNF	PARK2	APAF1	BCL2
NR4A2	NT3	PARK7	BAX	MCL1
PITX3	NTF4	PINK1	BAK1	BCL2A1
LMX1A	IGF1	UCHL1	BID	BCL2L10
LMX1B	GDF15	LRRK2	SLC25A5	
PAX2	TGFB1	ATP13A2	VDAC2	
FOXA1	MAPK1			
FOXA2	MAPK3			
NKX2-2	NTRK2			
NKX6-1	NTRK3			
FGF8	VEGFA			
SHH	GDF5			
NEUROG2				
WNT1				
WNT5A				

Table-3: The genes with known functions used as training sets for both ToppGene and Endeavour.

While mutations of PD genes such as PRKN (PARK2) and LRRK2 (Bras et al., 2008) can cause familial Parkinson's, pro-apoptotic genes, like BAX, are suggested to help the progression of the disease by expediting the degeneration of mesDA neurons (Vila et al., 2001). Other genes such as the anti-apoptotic members of the Bcl-2 family, Bcl2 and Bcl-xL, have an anti-apoptotic role and can prevent neuronal degeneration in the animal models of the disease (Natsume et al., 2001; Yamada et al., 1999).

Developmental	Survival	PD Genes	Pro-apoptotic	Anti-apoptotic
NKX2-1	NGFR	SLC6A3	MYC	SNCA
SATB1	MAPK9	MAPT	MAPK9	MYC
BDNF	MAPK11	NR4A2	MAPT	PRKCA
SLC18A2	TH	TH		BAG1
PBX1	FGF1	SLC18A2		PBX1
PBX3	MYC	DRD2		PRKCE
	RHOA	SNCG		MAPT
	GPNMB	CHRNA4		
	PRKCA	MAOA		
	DRD2	SLC25A5		
	SYT1	BDNF		
	ERBB4	SDHB		
	PPP3R1	NDUFS2		
	CCK	GRIK3		
	CHRNA4	CCK		
		GCH1		
		MAPK9		
		MYO5A		
		NDUFS8		
		NKX2-1		
		GRIN2C		

Table-4: Results of comparing dopamiergic gene profile with the known genes (functional table including developmental, survival, and so one) by using Topppgen software (7th February 2010)

We used the functions of these known genes as the criteria and basis for finding the genes that have similar functions among the known mesDA neurons gene expression profile (Table-B of appendix), because some mutations in these genes would make mesDA neurons susceptible to degeneration, initiation the process that can lead to PD disease appears.

First we compared each column of genes in Table-3 with the genes in Table-B (appendix) by using Topppgene to find the genes that are expressed in DA neurons and

have the same function, like survival, pro and anti-apoptotic genes and so on. The genes with overall p-value of less than 0.001 ($p < 0.001$) were identified (Table-4).

We then used Endeavour and compared the results with those of the Topgene program. Like the previous procedure, we compared genes in each column of Table-2 to the entire mesDA neuron gene expression profile (Table-B of appendix). Only the genes with $p < 0.001$ were considered as positive hits (Table-5).

Developmental	Survival	PD Genes	Pro-apoptotic	Anti-apoptotic
NR4A2	BDNF	SNCA	SLC25A5	BAG1
FOXA1	NTRK2	UCHL1	BAG1	MYC
PBX1	PRKCA	MAPT	ATP5A1	SNCA
	ERBB4		ATP2A2	
	MAPK9			
	PRKCE			
	MAPK11			
	NRCAM			

Table-5: Results of comparing dopamiergic gene profile with the know genes (functional table including developmental, survival, and so one) by means of <http://homes.esat.kuleuven.be/~bioiuser/endeavour/index.php>, software. (28th February 2010)

Despite the differences in the criteria being used by each software some genes are common between the two prioritized sets (Table-6). This may be an indicative of the validity of the method and/or the functional importance of these genes.

Developmental	Survival	PD genes	Pro-apoptotic	Anti-apoptotic
PBX1	MAPK9	MAPT		SNCA
	MAPK11			MYC
	PRKCA			BAG1
	ERBB4			

Table-6: Common genes to both ToppGene and Endeavour software.

Discussion

Although the gold standard for finding the function of a gene is investigating its function in vitro or in vivo, using prioritization software can be a first step in narrowing down a relatively large gene set to the genes with relevant functions that can be used for in vitro and in vivo studies. In order to prioritize the set of genes which are expressed in mesDA neurons on the basis of their functional significance for generation, specification, and survival of mesDA neurons under normal and pathological conditions, we compared the mesDA neurons gene expression profile with the genes with known developmental, survival, pro/anti-apoptotic functions in these neurons by using ToopGene and Endeavour software.

Emerging of mesDA neurons from ventral midbrain includes several phases. Each phase is regulated and identified by several distinct factors. First phase is specification the regions and progenitor cells that is regulated by expression homeodomain Otx2 (Vernay et al., 2005), Lmx1a/ Lmx1b, Msx1, Mash1, and Ngn2 (Ferri et al., 2007; Omodei et al., 2008). Then these progenitor cells differentiate to immature mesDA neurons. This phase is mediated by expression of Lmx1a/b, En1/En2, Ngn2, Pitx3, and Nurr1 (NR4A2). Subsequently mature mesDA neurons engender from immature mesDA neurons. In mature form of mesDA neurons TH, in addition to the genes in immature state, is expressed (Andersson et al., 2006a; Ferri et al., 2007; Kele et al., 2006; Martinat et al., 2006; Omodei et al., 2008; Simon et al., 2001; Smidt et al., 2000; Zetterstrom et al., 1997). After terminal differentiation, mesDA neurons like other cells require different factors and signaling pathways for their survival and functional integrity. Degeneration of mesDA neurons, in SNpc region, which causes PD, can be considered a failure of these pathways.

MesDA neurons undergo two developmental cell death events on postnatal day 2 and 14 in mice (Burke, 2003). These events are shown to be regulated by neurotrophic factors like glia-derived neurotrophic factor (GDNF) and BDNF. GDNF that is expressed in stratum during both prenatal and postnatal stages supports mesDA neurons by suppressing apoptosis (Oo et al., 2003). Although there is still controversy about expression of BDNF in mesDA neurons or the neighboring neuronal populations such

as locus ceruleus or by SNpc neurons in autocrine form, it has been proposed that BDNF has a regulatory role at first phase of developmental cell death in postnatal mesDA neurons in addition to its survival and differentiation role in mesDA neurons that express BDNF receptors, TrkB/ NTRK2 receptors (von Bohlen und Halbach et al., 2005). These findings confirm our result, since we found BDNF as the member of both developmental ($p < 0.0002$) and survival ($p < 0.0005$) categories among ToppGene results and TrkB as the survival factor in Endeavour results ($p < 0.0001$). FOXA1 and FOXA2 are other essential developmental factors for all stages of mesDA neurons maturity; they control the generation of mesDA neurons from their progenitors by regulating NEUROG2 (Ngn2) expression. Also, they induce the expression of EN1 and NR4A2 (NURR1) in immature and tyrosine hydroxylase (TH) and 1-amino acid decarboxylase (DDC) in mature or adult mesDA neurons (Ferri et al., 2007). On the basis of Endeavour results FOXA1 was classified in developmental group ($p < 0.0001$). Additionally TH was set in both survival and PD gene subgroups of ToppGene outcomes ($p < 0.000002$ and $p < 0.00000002$, respectively). NEUROG2 and EN1, which have fundamental role in both early and further stages of mesDA neurons, are listed as developmental factors in the training sets (Table-3).

Homeodomain transcription factor1, PBX1, is a further factor for brain development due to its interaction with other homeodomain proteins, encoded by Hox genes, and forming heterodimers, which binds with high affinity to a specific DNA region and regulates the expression of downstream genes which control growth and specification of neurons (McWhirter et al., 1997) or neurogenesis in progenitor cells in particular regions of brain through development (Redmond et al., 1996). In our results, PBX1 appeared in developmental subgroup in both ToppGene ($p < 0.0007$) and Endeavour results ($p < 0.0001$) and also in the anti-apoptotic subset of ToppGene results ($p < 0.0002$). This result has already been confirmed by our unpublished data showing that Pbx1 is required for axonal guidance and survival of the neurons in postmitotic developmental stages and throughout life of mesDA neurons in mice.

Another homeodomain transcription factor, NKX2.1, is required for ventral forebrain development. Since SHH regulates the expression of this protein, absence of SHH leads to disruption in dorsoventral development of forebrain (Marcucio et al.,

2005). In addition, NKX2.1 has a role in migration of the medial ganglionic eminence (the target tissue for mesDA neurons during axonal outgrowth) interneurons. Expression of NKX2.1 in postmitotic GABAergic interneurons determines the destination of these cells; the interneurons which express this factor migrate toward stratum because NKX2.1 suppress the semaphorin III receptors and so such cells are not induced by semaphoring signaling, but those do not express NKX2.1 are influenced by semaphoring signaling and migrate to cortex (Nobrega-Pereira et al., 2008). Our result supports the developmental role of NKX2.1 ($p < 0.00002$) in addition to suggesting that it may have a role in predisposing mesDA neurons for degeneration, since NKX2.1 appeared as a hit in the set compared to the PD gene ($p < 0.0009$). Both results were obtained by using ToppGene.

Another group of factors that are expressed in mesDA neurons and in addition to its possible role during development is critical for survival of these neurons postnatally includes NR4A2 (Nurr1) and FGFs. In addition to specifying the immature mesDA neurons from their progenitors, NR4A2 (Nurr1) is critical for differentiation and maintenance of mesDA neurons and their phenotype after creation. It has been proposed that some part of this effect is the result of the role of NR4A2 in regulating the expression of tyrosine hydroxylase, dopamine transporter, and the receptor tyrosine kinase signaling subunit Ret, the genes that are involved in defining the neurotransmitter phenotype of the neurons (Filippi et al., 2007; Chu et al., 2006). NR4A2 was among the genes identified by Endeavour ($p\text{-value} < 0.0001$). Both acidic fibroblast growth factors (aFGFs) and basic fibroblast growth factors (bFGFs) are shown to enhance the number of mesDA neurons, their regeneration, specification and survival in vitro in cultures where serum was withdrawn (Engele and Bohn, 1991), deprived of FGFs (Hisajima et al., 1991), or treated with mesDA-specific neurotoxins such as MPP⁺ (Leonard et al., 1993). In agreement with these findings, we showed, through ToppGene results included FGF1 as a potential survival factor for mesDA neurons ($p < 0.00001$). Moreover, throughout the development, Neuregulins (NRGs), a group of differentiation and developmental factors, mediate the growth, differentiation, migration, and survival of variety of cells and neurons through binding to epithelial growth factor-like, ERBB receptors. It has been indicated that disturbance in

NRG/ERBB4 signaling increase the vulnerability of mesencephalic mesDA neurons and losing these neurons in age-dependent pattern (Dickerson et al., 2009). Although NRGs were not part of our result, presence of ERBB4 among ToppGene and Endeavour survival sets ($p < 0.001$) indicates the possible role of this pathway in survival of mesDA neurons. Another factor in this group is Ciliary neurotrophic factor (CNTF). Although CNTF was not among the genes within the expression profile, the dopamine D2 receptor (DRD2), a member of G-protein-coupled receptors which enhances the CNTF neurogenesis activity through inhibition of cAMP (Yang et al., 2008) was among the ToppGene survival and PD groups with ($p < 0.001$ and $p < 0.000001$, respectively).

Another set of genes with anti- and pro-apoptotic functions in the brain and mesDA neurons are members of the Bcl-2 family. BCL2-associated athanogene 1 (BAG1) protects neurons by means of suppressing the apoptosis pathway, anti-apoptotic factor. BAG1 is found in both cytosol and nucleus in different stages of development. It is found in nucleus during neuronal development, mediating the specification of post-mitotic neurons and it translocates to the cytosol after neuronal differentiation and has exerts its neuroprotective effect through interaction with BCL2 (Gotz et al., 2005; Liman et al., 2008) or by binding to and activation of C-Raf which results in phosphorylation of Bad, and other kinases like Akt (Gotz et al., 2005). BAG1 was found among the ToppGene anti-apoptosis results ($p < 0.0001$) and in both anti-apoptotic ($p < 0.001$) and pro-apoptotic ($p < 0.001$) groups of Endeavour results. The appearance of Bag-1 in the pro-apoptotic column may be due to the shared structural features among the anti- and pro-apoptotic members of the Bcl-2 family.

The third group of genes that we considered was PD genes, including α -synuclein (SNCA), and Ubiquitin C-terminal hydrolase L1 (UCH-L1). Alpha-synuclein is expressed in presynaptic terminals in neurons and is the main component of Lewy bodies, the inclusions in dying dopaminergic cells that is one of the pathological hallmarks of PD. Over-expression and lack of function of α -synuclein can be equally harmful to dopaminergic neurons, as triplication or loss of function point mutations both lead to PD (Lou et al., 2010) (Lotharius et al., 2002). α -synuclein was among the anti-apoptotic factors in both ToppGene and Endeavour results ($p < 0.00001$ and $p < 0.0001$,

respectively), and also as among the PD gene matched set within the Endeavour results ($p < 0.001$).

The vesicular monoamine transporter-2 (SLC18A2 or VMAT2) is a gene involved in the neurotransmitter pathway. Studies on the heterozygous and homozygous SLC18A2 knockout mice has shown that elimination of VMAT2 causes inhibition of the activity of dopamine transport in mesDA neurons but does not lead to cell death (Yamamoto et al., 2007). A53T (loss of function) mutation of α -synuclein results in disrupted VMAT2 function and causes enhanced amphetamine-dependent DA release and therefore increased cytoplasmatic dopamine concentration and increased levels of superoxide anions inside the neurons through the oxidization of dopamine to reactive oxygen species (Lotharius et al., 2002). VMAT2 was found among the ToppGene PD gene-corresponding set ($p < 0.0000001$) and the developmental set ($p < 0.001$). Another PD associated gene is microtubule-associated protein tau (MAPT). Under normal conditions, MAPT has a role in construction of cytoskeleton (Wang et al.). α -synuclein regulates axonal tau phosphorylation through activating protein kinase A, which results in mediating the stability of axonal microtubule (Jensen et al., 1999). This gene could be found among both the pro- and anti-apoptotic results of ToppGene (p -value < 0.001 and $p < 0.001$ respectively), suggesting a connection between these pathways and their known components, used in our training sets, and the etiology of PD.

NDUFS8 of complex1, succinate dehydrogenase subunit B (SDHB) is another gene which was identified in the PD genes group. NDUFS2, NDUFS8, NDUFB4, and NDUFA6 are the subunits of complex-I, (NADH) ubiquinone oxidoreductase, which localizes to the inner membrane of mitochondria and is one of the complexes in the mitochondrial respiratory chain (Benit et al., 2001). Complex-I, II and V can be suppressed by reactive oxygen or nitrogen species such as peroxynitrite, as byproducts of oxidative phosphorylation in mitochondria (Benit et al., 2001). Also, the inhibition of complex-I can cause enhanced generation of reactive oxygen species and also reduced cellular energy levels. This can cause cell death especially in (the more sensitive) mesDA neurons (Marella et al., 2009). In addition, amphetamine-regulated transcript (CART) is expressed in different brain regions and has a protective effect on neurons.

This neuroprotective activity is due to binding to succinate dehydrogenase

subunit B (SDHB). SDHB is one enzyme in Kereps cycle and the internal part of mitochondrial complex II in electron transport chain, and so participates in oxidative metabolism and ATP synthesis. Therefore, stimulation of SDHB by CART leads to increase ATP production through increasing the complex II activity. Thus, it seems, the increase of energy supply for neurons can play as protective function for neurons against degeneration or death (Mao et al., 2007). Both NDUFS8 and SDHB were among the PD gene-associated ToppGene results ($p < 0.001$ for both), confirming previous studies on the connection between mitochondria and the etiology of PD and suggesting a specific role for NDUFS8 and SDHB in this process.

Although we specified the categories of genes very distinctly, some of the genes such as BDNF, α -synuclein, MAPT, DRD2, had multiple functions and were found by using different training set categories. This suggests the interconnected nature of the five categories, as shown especially by the transgenic and knockdown studies on the animals carrying mutations of PD genes or the genes involved in the development of mesDA neurons, where alteration of the expression level of these genes interferes with various functions required for survival of the neurons.

Furthermore, the presence of genes such as FOXA1 or BDNF, with crucial roles in differentiation, development, survival and maintenance of mesDA neurons, among the results of different categories suggests that the rest of genes in Tables -4 and -5, which do not have as of yet a known function within mesDA neurons may play significant roles in mesDA neurons under normal of pathological conditions. Experimental data from in vitro and in vivo assays will be needed to confirm the precise relevance of those genes to functional pathways within mesDA neurons.

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Appendix

Table A- Mouse and rat's DA neurons gene expression profile

	Gene Name	Gene Symbol	Accession Number
1	myosin X	MYO10	NM_012334.2
2	actin, beta	ACTB	NM_001101.3
3	neuronal cell adhesion molecule	NRCAM	NM_001037132.1
4	complexin 1	CPLX1	NM_006651.3
5	contactin associated protein-like 4	CNTNAP4	NM_033401.3
6	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila)	MLL	NM_005933.2
7	Mof4 family associated protein 1	MRFAP1	NM_033296.1
8	pyridoxal (pyridoxine, vitamin B6) phosphatase	PDXP	NM_020315.4
9	polo-like kinase 1 (Drosophila)	PLK1	NM_005030.3
10	RUN domain containing 3A	RUNDC3A	NM_001144825.1
11	Ran GTPase activating protein 1	RANGAP1	NM_002883.2
12	roundabout, axon guidance receptor, homolog 1 (Drosophila)	ROBO1	NM_001145844.1
13	signal-induced proliferation-associated 1 like 1	SIPA1L1	NM_015556.1
14	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2	SMARCA2	NM_003070.3
15	synaptotagmin I	SYT1	NM_001135805.1
16	thymidine kinase 2, mitochondrial	TK2	NM_004614.3
17	HLA-B associated transcript 2-like 1	BAT2L	NM_013318.3
18	insulin-like growth factor binding protein-like 1	IGFBPL1	NM_001007563.1
19	5-azacytidine induced 2	AZI2	NM_001134432.1
20	hydroxysteroid (17-beta) dehydrogenase 12	HSD17B12	NM_016142.2
21	BCL2-associated athanogene	BAG1	NM_004323.4
22	ubiquitin protein ligase E3 component n-recogin 3 (putative)	UBR3	NM_172070.3
23	transmembrane protein 66	TMEM66	NM_016127.4
24	OTU domain containing 6B	OTUD6B	NM_016023.3
25	acyl-CoA synthetase long-chain family member 3	ACSL3	NM_004457.3
26	ARP2 actin-related protein 2 homolog	ACTR2	NM_001005386.2

	(yeast)		
27	ADP-ribosylation factor guanine nucleotide-exchange factor 2 (brefeldin A-inhibited)	ARFGEF2	NM_006420.2
28	ATPase, H ⁺ transporting, lysosomal 16kDa, V0 subunit c	ATP6V0C	NM_001694.2
29	ATPase, H ⁺ transporting, lysosomal 31kDa, V1 subunit E1	ATP6V1E1	NM_001039366.1
30	ATPase, H ⁺ transporting, lysosomal 70kDa, V1 subunit A	ATP6V1A	NM_001690.2
31	pleckstrin and Sec7 domain containing 3	PSD3	NM_015310.3
32	calmodulin 2 (phosphorylase kinase, delta)	CALM2	NM_001743.4
33	calmodulin 3 (phosphorylase kinase, delta)	CALM3	NM_005184.2
34	integrin alpha FG-GAP repeat containing 1	ITFG1	NM_030790.3
35	cholinergic receptor, nicotinic, beta 3	CHRNA3	NM_000749.3
36	coatamer protein complex, subunit gamma 2	COPG2	NM_012133.4
37	SPY-like 4	TSPYL4	NM_021648.4
38	DEAD (Asp-Glu-Ala-Asp) box polypeptide 5	DDX5	NM_004396.3
39	dispatched homolog 2 (Drosophila)	DISP2	NM_033510.1
40	v-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)	ERBB4	NM_001042599.1
41	transmembrane protein 196	TMEM196	NM_152774.3
42	guanine nucleotide binding protein (G protein), beta polypeptide 1	GNB1	NM_002074.2
43	Impact homolog (mouse)	IMPACT	NM_018439.3
44	kinesin family member 1A	KIF1A	NM_004321.4
45	kelch-like 9 (Drosophila)	KLHL9	NM_018847.2
46	LATS, large tumor suppressor, homolog 2 (Drosophila)	LATS2	NM_014572.2
47	LON peptidase N-terminal domain and ring finger 2	LONRF2	NM_198461.3
48	microtubule-associated protein, RP/EB family, member 1	MAPRE1	NM_012325.2
49	microtubule-associated protein 1A	MAP1A	NM_002373.5
50	microtubule-associated protein 4	Mtap4	NM_008633
51	p21 protein (Cdc42/Rac)-activated kinase 1	PAK1	NM_001128620.1
52	protocadherin 10	PCDH10	NM_020815.1
53	protein kinase (cAMP-dependent,	PKIA	NM_006823.2

	catalytic) inhibitor alpha		
54	protein kinase, cAMP-dependent, catalytic, beta	PRKACB	NM_002731.2
55	reticulocalbin 2, EF-hand calcium binding domain	RCN2	NM_002902.2
56	ras homolog gene family, member A	RHOA	NM_001664.2
57	roundabout, axon guidance receptor, homolog 2 (Drosophila)	ROBO2	NM_001128929.1
58	SAC1 suppressor of actin mutations 1-like (yeast)	SACM1L	NM_014016.3
59	stearoyl-CoA desaturase 5	SCD5	NM_001037582.2
60	Sec23 homolog A (S. cerevisiae)	SEC23A	NM_006364.2
61	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6D	SEMA6D	NM_020858.1
62	solute carrier family 18 (vesicular monoamine), member 2	SLC18A2	NM_003054.3
63	solute carrier family 30 (zinc transporter), member 4	SLC30A4	NM_013309.4
64	solute carrier family 4, sodium bicarbonate transporter, member 10	SLC4A10	NM_022058.3
65	synuclein, alpha (non A4 component of amyloid precursor)	SNCA	NM_000345.3
66	synaptosomal-associated protein, 91kDa homolog (mouse)	SNAP91	NM_014841.2
67	synaptic vesicle glycoprotein 2B	SV2B	NM_001167580.1
68	synaptogyrin 3	SYNGR3	NM_004209.4
69	synaptotagmin IV	SYT4	NM_020783.3
70	Tax1 (human T-cell leukemia virus type I) binding protein 1	TAX1BP1	NM_001079864.1
71	thymosin beta 4, X-linked	TMSB4X	NM_021109.3
72	thymosin beta 10	TMSB10	NM_021103.3
73	UDP-glucose pyrophosphorylase 2	UGP2	NM_001001521.1
74	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, gamma polypeptide	YWHAG	NM_012479.3
75	CAAX box 1 homolog A (human)	Cxx1a	NM_024170.2
76	aldo-keto reductase family 1, member B3 (aldose reductase)	Akr1b3	NM_009658.3
77	cholinergic receptor, nicotinic, alpha 4	CHRNA4	NM_000744.5
78	GDNF family receptor alpha 1	GFRA1	NM_001145453.1
79	tyrosine hydroxylase	TH	NM_000360.3
80	peripherin	PRPH	NM_006262.3
81	dopa decarboxylase (aromatic L-amino	DDC	NM_000790.3

	acid decarboxylase)		
82	pterin-4 alpha-carbinolamine dehydratase/dimerization cofactor of hepatocyte nuclear factor 1 alpha	PCBD1	NM_000281.2
83	cell growth regulator with EF-hand domain 1	CGREF1	NM_001166239.1
84	calcyon neuron-specific vesicular protein	CALY	NM_015722.3
85	protein arginine methyltransferase 2	PRMT2	NM_001535.2
86	TSPY-like 2	TSPYL2	NM_022117.3
87	aldehyde dehydrogenase 1 family, member A1	ALDH1A1	NM_000689.3
88	regulator of calcineurin 2	RCAN2	NM_005822.2
89	RNA binding motif, single stranded interacting protein	RBMS3	NM_001003792.1
90	protein kinase C, alpha	PRKCA	NM_002737.2
91	RIKEN cDNA 2010011I20 gene	2010011I20Rik	NM_025912.4
92	LY6/PLAUR domain containing 1	LYPD1	NM_001077427.2
93	solute carrier family 39 (zinc transporter), member 4	SLC39A4	NM_017767.2
94	serine (or cysteine) peptidase inhibitor, clade B, member 6a	Serpinb6a	NM_009254
95	NEL-like 2 (chicken)	NELL2	NM_001145107.1
96	potassium voltage-gated channel, Shal-related subfamily, member 3	KCND3	NM_004980.3
97	protein kinase C, epsilon	PRKCE	NM_005400.2
98	leucine rich repeat containing 3B	LRRC3B	NM_052953.2
99	serine threonine kinase 39 (STE20/SPS1 homolog, yeast)	STK39	NM_013233.2
100		A030009H04Rik	
101	ELKS/RAB6-interacting/CAST family member 2	ERC2	NM_015576.1
102	glucan (1,4-alpha-), branching enzyme 1	GBE1	NM_000158.3
103	dehydrogenase/reductase (SDR family) member 3	DHRS3	NM_004753.4
104	kelch-like 13 (Drosophila)	KLHL13	NM_001168299.1
105	aurora kinase A	AURKA	NM_003600.2
106	LIM domain only 4	LMO4	NM_006769.3
107	phospholipase C, beta 1 (phosphoinositide-specific)	PLCB1	NM_015192.2
108	cytochrome b-561	CYB561	NM_001017916.1
109	CUG triplet repeat, RNA binding protein 2	CUGBP2	NM_001025076.2
110	latrophilin 2	LPHN2	NM_012302.2
111	protein tyrosine phosphatase, receptor type, U	PTPRU	NM_005704.3

112	family with sequence similarity 167, member A	FAM167A	NM_053279.2
113	solute carrier organic anion transporter family, member 4A1	SLCO4A1	NM_016354.3
114	cadherin 13, H-cadherin (heart)	CDH13	NM_001257.3
115	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2	SERPINE2	NM_001136528.1
116	pleckstrin homology domain containing, family A member 7	PLEKHA7	NM_175058.4
117	angiomin like 1	AMOTL1	NM_130847.2
118	pre-B-cell leukemia homeobox 1	PBX1	NM_002585.2
119	ets variant 5	ETV5	NM_004454.2
120	family with sequence similarity 84, member B	FAM84B	NM_174911.3
121	Purkinje cell protein 4 like 1	PCP4L1	NM_001102566.1
122	lysophosphatidic acid receptor 1	LPAR1	NM_001401.3
123	teashirt zinc finger homeobox 1	TSHZ1	NM_005786.4
124	glutamate receptor interacting protein 2	GRIP2	NM_001080423.1
125	par-3 partitioning defective 3 homolog (C. elegans)	PARD3	NM_019619.2
126	Ras association (RalGDS/AF-6) domain family member 6	RASSF6	NM_177532.3
127	eyes absent homolog 2 (Drosophila)	EYA2	NM_005244.4
128	shisa homolog 9 (Xenopus laevis)	SHISA9	NM_001145204.1
129	zinc finger homeobox 3	ZFXH3	NM_001164766.1
130	solute carrier family 31 (copper transporters), member 1	SLC31A1	NM_001859.3
131		Rho	
132	glycoprotein (transmembrane) nmb	GPNMB	NM_001005340.1
133	Ca ⁺⁺ -dependent secretion activator 2	CADPS2	NM_001009571.3
134	fatty acid desaturase 3	FADS3	NM_021727.3
135	calcium-sensing receptor	CASR	NM_000388.3
136	transmembrane inner ear	TMIE	NM_147196.2
137	glutathione peroxidase 3 (plasma)	GPX3	NM_002084.3
138	chromosome 4 open reading frame 31	C4orf31	NM_024574.3
139	fibronectin type III domain containing 3B	FNDC3B	NM_001135095.1
140	protein phosphatase 1, regulatory (inhibitor) subunit 14B	PPP1R14B	NM_138689.2
141	myosin VB	MYO5B	NM_001080467.2
142	phosphofructokinase, liver	PFKL	NM_002626.4
143	NK2 homeobox 1	NKX2-1	NM_001079668.2
144	claudin 1	CLDN1	NM_021101.3

145	guanine nucleotide binding protein (G protein), gamma 11	GNG11	NM_004126.3
146	stimulator of chondrogenesis 1	SCRG1	NM_007281.2
147	X-box binding protein 1	XBP1	NM_001079539.1
148	G protein-coupled receptor, family C, group 5, member A	GPRC5A	NM_003979.3
149	phosphoglucomutase 2-like 1	PGM2L1	NM_173582.3
150	regulator of G-protein signaling 2, 24kDa	RGS2	NM_002923.3
151	cytochrome P450, family 51, subfamily A, polypeptide 1	CYP51A1	NM_000786.3
152	ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)	UCHL1	NM_004181.4
153	brain-derived neurotrophic factor	BDNF	NM_001143805.1
154	pyruvate dehydrogenase (lipoamide) alpha 1	PDHA1	NM_000284.2
155	phospholipase C, beta 4	PLCB4	NM_000933.2
156	lysophospholipase I	LYPLA1	NM_006330.2
157	solute carrier family 24 (sodium/potassium/calcium exchanger), member 2	SLC24A2	NM_020344.1
158	ATPase, Ca ⁺⁺ transporting, cardiac muscle, slow twitch 2	ATP2A2	NM_001135765.1
159	calpain, small subunit 1	CAPNS1	NM_001003962.1
160	inositol 1,4,5-triphosphate receptor, type 1	ITPR1	NM_001099952.2
161	cysteine-rich protein 2	CRIP2	NM_001312.2
162	dynein, cytoplasmic 1, intermediate chain 1	DYNC1I1	NM_001135556.1
163	ubiquinol-cytochrome c reductase, Rieske iron-sulfur polypeptide 1	UQCRCF1	NM_006003.2
164	ATP synthase, H ⁺ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle	ATP5A1	NM_001001937.1
165	glutamic-oxaloacetic transaminase 2, mitochondrial (aspartate aminotransferase 2)	GOT2	NM_002080.2
166	pyruvate kinase, muscle	PKM2	NM_002654.3
167	creatine kinase, brain	CKB	NM_001823.3
168	adenylate kinase 1	AK1	NM_000476.2
169	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide O	GNAO1	NM_020988.2
170	enolase 3 (beta, muscle)	ENO3	NM_001976.3
171	dopamine receptor D2	DRD2	NM_000795.3
172	calcium channel, voltage-dependent, T	CACNA1G	NM_018896.3

	type, alpha 1G subunit		
173	protein kinase C, beta	PRKCB	NM_002738.6
174	protein kinase, cAMP-dependent, regulatory, type II, beta	PRKAR2B	NM_002736.2
175	proprotein convertase subtilisin/kexin type 2	PCSK2	NM_002594.2
176	neuritin 1	NRN1	NM_016588.2
177	monoamine oxidase A	MAOA	NM_000240.2
178	GTP cyclohydrolase 1	GCH1	NM_000161.2
179	solute carrier family 7 (cationic amino acid transporter, y+ system), member 3	SLC7A3	NM_001048164.1
180	cathepsin D	CTSD	NM_001909.3
181	vesicle-associated membrane protein 2 (synaptobrevin 2)	VAMP2	NM_014232.2
182	transducin-like enhancer of split 1 (E(sp1) homolog, Drosophila)	TLE1	NM_005077.3
183	growth factor receptor-bound protein 10	GRB10	NM_001001549.2
184	target of myb1-like 2 (chicken)	TOM1L2	NM_001033551.2
185	prune homolog 2 (Drosophila)	PRUNE2	NM_015225.2
186	calbindin 1, 28kDa	CALB1	NM_004929.2
187	GDP dissociation inhibitor 2	GDI2	NM_001115156.1
188	LAG1 homolog, ceramide synthase 4	LASS4	NM_024552.2
189	microtubule-associated protein 1 light chain 3 alpha	MAP1LC3A	NM_032514.2
190	nuclear receptor interacting protein 3	NRIP3	NM_020645.2
191	CD24 molecule	CD24	NM_013230.2
192	RAB3C, member RAS oncogene family	RAB3C	NM_138453.2
193	acyl-CoA synthetase long-chain family member 6	ACSL6	NM_001009185.1
194	myosin VA (heavy chain 12, myosin)	MYO5A	NM_000259.3
195	RAR-related orphan receptor A	RORA	NM_002943.3
196	syndecan 2	SDC2	NM_002998.3
197	fibroblast growth factor 1 (acidic)	FGF1	NM_000800.3
198	poliovirus receptor-related 3	PVRL3	NM_015480.1
199	glutamate receptor, ionotropic, N-methyl D-aspartate 2C	GRIN2C	NM_000835.3
200	zinc finger, DHHC-type containing 2	ZDHHC2	NM_016353.4
201	cytochrome P450, family 4, subfamily v, polypeptide 3	Cyp4v3	NM_133969
202	SATB homeobox 1	SATB1	NM_001131010.1
203	acyl-Coenzyme A dehydrogenase, long chain	ACADL	NM_001608.3
204	solute carrier family 25 (mitochondrial	SLC25A5	NM_001152.4

	carrier; adenine nucleotide translocator), member 5		
205	vav 3 guanine nucleotide exchange factor	VAV3	NM_001079874.1
206	calcium channel, voltage-dependent, alpha 2/delta subunit 3	CACNA2D3	NM_018398.2
207	synuclein, gamma (breast cancer-specific protein 1)	SNCG	NM_003087.2
208	oxysterol binding protein-like 11	OSBPL11	NM_022776.4
209	Lix1 homolog (chicken)	LIX1	NM_153234.4
210	annexin A1	ANXA1	NM_000700.1
211	Ca ⁺⁺ -dependent secretion activator	CADPS	NM_003716.3
212	RAS-like, family 11, member B	RASL11B	NM_023940.2
213	polymerase (DNA directed), beta	POLB	NM_002690.1
214	cyclin I	CCNI	NM_006835.2
215	RNA terminal phosphate cyclase domain 1	RTCD1	NM_001130841.1
216	lysosomal protein transmembrane 4 beta	LAPTM4B	NM_018407.4
217	cadherin 8, type 2	CDH8	NM_001796.2
218	ganglioside-induced differentiation-associated protein 1	GDAP1	NM_001040875.1
219	adenosine kinase	ADK	NM_001123.2
220	dynein, light chain, Tctex-type 3	DYNLT3	NM_006520.2
221	aspartyl aminopeptidase	DNPEP	NM_012100.2
222	regulator of G-protein signaling 8	RGS8	NM_001102450.1
223	pre-B-cell leukemia homeobox 3	PBX3	NM_001134778.1
224	trophoblast glycoprotein	TPBG	NM_001166392.1
225	CDP-diacylglycerol synthase (phosphatidate cytidyltransferase) 2	CDS2	NM_003818.2
226	myocyte enhancer factor 2A	MEF2A	NM_001130926.1
227	mitogen-activated protein kinase 9	MAPK9	NM_001135044.1
228	F-box protein 2	FBXO2	NM_012168.4
229	macrophage migration inhibitory factor (glycosylation-inhibiting factor)	MIF	NM_002415.1
230	NADH dehydrogenase (ubiquinone) Fe-S protein 8, 23kDa (NADH-coenzyme Q reductase)	NDUFS8	NM_002496.2
231	ELOVL family member 6, elongation of long chain fatty acids (FEN1/Elo2, SUR4/Elo3-like, yeast)	ELOVL6	NM_001130721.1
232	CD47 molecule	CD47	NM_001025079.1
233	citrate synthase	CS	NM_004077.2
234	phosphatidylinositol transfer protein, alpha	PITPNA	NM_006224.3

235	homer homolog 2 (Drosophila)	HOMER2	NM_004839.2
236	RASD family, member 2	RASD2	NM_014310.3
237	thioredoxin-related transmembrane protein 2	TMX2	NM_001144012.1
238	3-oxoacid CoA transferase 1	OXCT1	NM_000436.3
239	translocase of outer mitochondrial membrane 20 homolog (yeast)	TOMM20	NM_014765.2
240	N-ethylmaleimide-sensitive factor attachment protein, beta	NAPB	NM_022080.2
241	amyloid beta (A4) precursor protein-binding, family A, member 2	APBA2	NM_001130414.1
242	NIMA (never in mitosis gene a)-related kinase 7	NEK7	NM_133494.2
243	vacuolar protein sorting 35 homolog (S. cerevisiae)	VPS35	NM_018206.4
244	RAB6A, member RAS oncogene family	RAB6A	NM_002869.4
245	very low density lipoprotein receptor	VLDLR	NM_001018056.1
246	Rho GTPase activating protein 24	ARHGAP24	NM_001025616.2
247	visinin-like 1	VSNL1	NM_003385.4
248	protein tyrosine phosphatase, non-receptor type 5 (striatum-enriched)	PTPN5	NM_001039970.1
249	prohibitin 2	PHB2	NM_001144831.1
250	NADH dehydrogenase (ubiquinone) Fe-S protein 2, 49kDa (NADH-coenzyme Q reductase)	NDUFS2	NM_001166159.1
251	transducin-like enhancer of split 3 (E(sp1) homolog, Drosophila)	TLE3	NM_001105192.1
252	tachykinin receptor 3	TACR3	NM_001059.1
253	serine peptidase inhibitor, Kunitz type, 2	SPINT2	NM_001166103.1
254	colony stimulating factor 2 receptor, beta, 2 pseudogene	CSF2RB2	
255	reticulocalbin 1, EF-hand calcium binding domain	RCN1	NM_002901.2
256	collagen, type XI, alpha 1	COL11A1	NM_001168249.1
257	FXYD domain containing ion transport regulator 6	FXYD6	NM_001164831.1
258	calbindin 2	CALB2	NM_001740.3
259	MARCKS-like 1	MARCKSL1	NM_023009.5
260	cholecystokinin	CCK	NM_000729.3
261	mesoderm development candidate 2	MESDC2	NM_015154.1
262	prostate androgen-regulated mucin-like protein 1	PARM1	NM_015393.2
263	family with sequence similarity 114, member A1	FAM114A1	NM_138389.1

264	huntingtin-associated protein 1	HAP1	NM_001079870.1
265	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 1	SMARCA1	NM_003069.3
266	dedicator of cytokinesis 6	DOCK6	NM_020812.2
267	CaM kinase-like vesicle-associated	CAMKV	NM_024046.3
268	isocitrate dehydrogenase 1 (NADP+), soluble	IDH1	NM_005896.2
269	nucleobindin 2	NUCB2	NM_005013.2
270	ribosomal protein L36a	RPL36A	NM_021029.4
271	lipoprotein lipase	LPL	NM_000237.2
272	adenylate cyclase activating polypeptide 1 (pituitary)	ADCYAP1	NM_001099733.1
273	chromosome 7 open reading frame 16	C7orf16	NM_001145123.1
274	cDNA sequence BC005537	BC005537	NM_024473
275	coiled-coil domain containing 91	CCDC91	NM_018318.3
276	cadherin 11, type 2, OB-cadherin (osteoblast)	CDH11	NM_001797.2
277	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 11	MLLT11	NM_006818.3
278	acidic ribosomal phosphoprotein P0	Arbp	NM_007475
279	chimerin (chimaerin) 1	CHN1	NM_001025201.2
280	IQ motif containing J	IQCJ	NM_001042705.1
281	transmembrane protein 30A	TMEM30A	NM_001143958.1
282	drebrin 1	DBN1	NM_004395.3
283	deleted in colorectal carcinoma	DCC	NM_005215.3
284	delta/notch-like EGF repeat containing	DNER	NM_139072.3
285	solute carrier family 10 (sodium/bile acid cotransporter family), member 4	SLC10A4	NM_152679.3
286	eukaryotic translation elongation factor 1 alpha 1	EEF1A1	NM_001402.5
287	fatty acid binding protein 5 (psoriasis-associated)	FABP5	NM_001444.1
288	coagulation factor II (thrombin) receptor	F2R	NM_001992.3
289	farnesyl-diphosphate farnesyltransferase 1	FDFT1	NM_004462.3
290	farnesyl diphosphate synthase (farnesyl pyrophosphate synthetase, dimethylallyltransferase, geranyltransferase)	FDPS	NM_001135821.1
291	forkhead box A1	FOXA1	NM_004496.2
292	four and a half LIM domains 1	FHL1	NM_001159699.1
293	growth associated protein 43	GAP43	NM_001130064.1

294	heat shock factor binding protein 1	HSBP1	NM_001537.2
295	iduronate 2-sulfatase	IDS	NM_000202.5
296	limbic system-associated membrane protein	LSAMP	NM_002338.3
297	mitogen-activated protein kinase 11	MAPK11	NM_002751.5
298	microtubule-associated protein tau	MAPT	NM_001123066.2
299	matrin 3	MATR3	NM_018834.4
300	mortality factor 4 like 2	MORF4L2	NM_001142418.1
301	mortality factor 4 like 1	MORF4L1	NM_006791.2
302	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 10, 42kDa	NDUFA10	NM_004544.3
303	NDRG family member 3	NDRG3	NM_022477.2
304	neural precursor cell expressed, developmentally down-regulated 4	NEDD4	NM_006154.2
305	nicolin 1	NICN1	NM_032316.3
306	nuclear receptor subfamily 4, group A, member 2	NR4A2	NM_006186.3
307	neurotrophic tyrosine kinase, receptor, type 2	NTRK2	NM_001007097.1
308	neurexin 3	NRXN3	NM_001105250.1
309	progesterone receptor membrane component 1	PGRMC1	NM_006667.3
310	phosphoglycerate kinase 1	PGK1	NM_000291.3
311	PQ loop repeat containing 1	PQLC1	NM_001146343.1
312	protein phosphatase 3 (formerly 2B), regulatory subunit B, alpha isoform	PPP3R1	NM_000945.3
313	RNA binding motif protein 4	RBM4	NM_002896.2
314	RNA binding motif protein 18	RBM18	NM_033117.3
315	ring finger protein 7	RNF7	NM_014245.3
316	ataxin 10	ATXN10	NM_001167621.1
317	secretogranin II (chromogranin C)	SCG2	NM_003469.3
318	succinate dehydrogenase complex, subunit B, iron sulfur (lp)	SDHB	NM_003000.2
319	single-stranded DNA binding protein 2	SSBP2	NM_012446.2
320	translocase of inner mitochondrial membrane 10 homolog (yeast)	TIMM10	NM_012456.2
321	serine incorporator 1	SERINC1	NM_020755.2
322	ubiquitin-conjugating enzyme E2B (RAD6 homolog)	UBE2B	NM_003337.2
323	valosin-containing protein	VCP	NM_007126.3
324	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide	YWHAE	NM_006761.4

325	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide	YWHAB	NM_003404.3
326	SH3 domain binding glutamic acid-rich protein like	SH3BGRL	NM_003022.2
327	chaperonin containing TCP1, subunit 5 (epsilon)	CCT5	NM_012073.3
328	RIKEN cDNA 5730410E15 gene	5730410E15Rik	NM_001032727.1
329	asparagine-linked glycosylation 2, alpha-1,3-mannosyltransferase homolog (S. cerevisiae)	ALG2	NM_033087.3
330	calcium channel, voltage-dependent, beta 2 subunit	CACNB2	NM_000724.3
331	carbonic anhydrase IV	CA4	NM_000717.3
332	dickkopf homolog 3 (Xenopus laevis)	DKK3	NM_001018057.1
333	dystrophia myotonica, WD repeat containing	DMWD	NM_004943.1
334	EPH receptor A6	EPHA6	NM_001080448.2
335	non-metastatic cells 1, protein (NM23A) expressed in	NME1	NM_000269.2
336	glutamate receptor, ionotropic, kainate 3	GRIK3	NM_000831.3
337	heme oxygenase (decycling) 2	HMOX2	NM_001127204.1
338	histone cluster 3, H2a	HIST3H2A	NM_033445.2
339	HIV-1 Tat interactive protein 2, 30kDa	HTATIP2	NM_001098520.1
340	mannosyl (alpha-1,6-)-glycoprotein beta-1,6-N-acetyl-glucosaminyltransferase, isozyme B	MGAT5B	NM_144677.2
341	RIKEN cDNA 9630033F20 gene	9630033F20Rik	
342	ribosomal protein L11	RPL11	NM_000975.2
343	ubiquitin-conjugating enzyme E2K (UBC1 homolog, yeast)	UBE2K	NM_001111112.1
344	zinc finger, MYND domain containing 11	ZMYND11	NM_001161482.1
345	potassium inwardly-rectifying channel, subfamily J, member 6	KCNJ6	NM_002240.2
346	4-aminobutyrate aminotransferase	ABAT	NM_000663.4
347	solute carrier family 6 (neurotransmitter transporter, dopamine), member 3	SLC6A3	NM_001044.4
348	translocase of inner mitochondrial membrane 8 homolog A (yeast)	TIMM8A	NM_001145951.1
349	SH3-binding domain kinase 1	SBK1	NM_001024401.2
350	v-myc myelocytomatosis viral oncogene homolog (avian)	MYC	NM_002467.4
351	nerve growth factor receptor (TNFR	NGFR	NM_002507.2

	superfamily, member 16)		
352	nucleoporin 93kDa	NUP93	NM_014669.3
353	protocadherin alpha 10	PCDHA10	NM_018901.2
354	protein phosphatase 2, regulatory subunit B', delta isoform	PPP2R5D	NM_006245.2
355	receptor accessory protein 1	REEP1	NM_001164730.1
356	ribophorin I	RPN1	NM_002950.3
357	septin 5	5-Sep	NM_002688.4
358	solute carrier family 35, member C2	SLC35C2	NM_015945.10
359	SET domain containing (lysine methyltransferase) 7	SETD7	NM_030648.2
360	SNF related kinase	SNRK	NM_001100594.1
361	single stranded DNA binding protein 4	SSBP4	NM_001009998.2
362	suppressor of Ty 5 homolog (S. cerevisiae)	SUPT5H	NM_001111020.2
363	serine/threonine kinase 32C	STK32C	NM_173575.2
364	transmembrane BAX inhibitor motif containing 6	TMBIM6	NM_001098576.1
365	transmembrane protein 50B	TMEM50B	NM_006134.5
366	tousled-like kinase 1	TLK1	NM_001136554.1
367	tumor protein p53 binding protein 1	TP53BP1	NM_001141979.1
368	tetraspanin 6	TSPAN6	NM_003270.2
369	hypothetical LOC385068	LOC385068	

Table B- The genes in table 1 that are adjusted for human (*Homo sapiens*) by blasting

	Gene Name	Gene Symbol	Accession Number
1	myosin X	MYO10	NM_012334.2
2	actin, beta	ACTB	NM_001101.3
3	neuronal cell adhesion molecule	NRCAM	NM_001037132.1
4	complexin 1	CPLX1	NM_006651.3
5	contactin associated protein-like 4	CNTNAP4	NM_033401.3
6	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila)	MLL	NM_005933.2
7	Mof4 family associated protein 1	MRFAP1	NM_033296.1
8	pyridoxal (pyridoxine, vitamin B6)	PDXP	NM_020315.4

	phosphatase		
9	polo-like kinase 1 (Drosophila)	PLK1	NM_005030.3
10	RUN domain containing 3A	RUNDC3A	NM_001144825.1
11	Ran GTPase activating protein 1	RANGAP1	NM_002883.2
12	roundabout, axon guidance receptor, homolog 1 (Drosophila)	ROBO1	NM_001145844.1
13	signal-induced proliferation-associated 1 like 1	SIPA1L1	NM_015556.1
14	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2	SMARCA2	NM_003070.3
15	synaptotagmin I	SYT1	NM_001135805.1
16	thymidine kinase 2, mitochondrial	TK2	NM_004614.3
17	HLA-B associated transcript 2-like 1	BAT2L	NM_013318.3
18	insulin-like growth factor binding protein-like 1	IGFBPL1	NM_001007563.1
19	5-azacytidine induced 2	AZI2	NM_001134432.1
20	hydroxysteroid (17-beta) dehydrogenase 12	HSD17B12	NM_016142.2
21	BCL2-associated athanogene	BAG1	NM_004323.4
22	ubiquitin protein ligase E3 component n-recognin 3 (putative)	UBR3	NM_172070.3
23	transmembrane protein 66	TMEM66	NM_016127.4
24	OTU domain containing 6B	OTUD6B	NM_016023.3
25	acyl-CoA synthetase long-chain family member 3	ACSL3	NM_004457.3
26	ARP2 actin-related protein 2 homolog (yeast)	ACTR2	NM_001005386.2
27	ADP-ribosylation factor guanine nucleotide-exchange factor 2 (brefeldin A-inhibited)	ARFGEF2	NM_006420.2
28	ATPase, H ⁺ transporting, lysosomal 16kDa, V0 subunit c	ATP6V0C	NM_001694.2
29	ATPase, H ⁺ transporting, lysosomal 31kDa, V1 subunit E1	ATP6V1E1	NM_001039366.1
30	ATPase, H ⁺ transporting, lysosomal 70kDa, V1 subunit A	ATP6V1A	NM_001690.2
31	pleckstrin and Sec7 domain containing 3	PSD3	NM_015310.3
32	calmodulin 2 (phosphorylase kinase, delta)	CALM2	NM_001743.4
33	calmodulin 3 (phosphorylase kinase, delta)	CALM3	NM_005184.2
34	integrin alpha FG-GAP repeat containing 1	ITFG1	NM_030790.3
35	cholinergic receptor, nicotinic, beta 3	CHRNB3	NM_000749.3
36	coatamer protein complex, subunit gamma 2	COPG2	NM_012133.4
37	SPY-like 4	TSPYL4	NM_021648.4
38	DEAD (Asp-Glu-Ala-Asp) box polypeptide 5	DDX5	NM_004396.3
39	dispatched homolog 2 (Drosophila)	DISP2	NM_033510.1

40	v-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)	ERBB4	NM_001042599.1
41	transmembrane protein 196	TMEM196	NM_152774.3
42	guanine nucleotide binding protein (G protein), beta polypeptide 1	GNB1	NM_002074.2
43	Impact homolog (mouse)	IMPACT	NM_018439.3
44	kinesin family member 1A	KIF1A	NM_004321.4
45	kelch-like 9 (Drosophila)	KLHL9	NM_018847.2
46	LATS, large tumor suppressor, homolog 2 (Drosophila)	LATS2	NM_014572.2
47	LON peptidase N-terminal domain and ring finger 2	LONRF2	NM_198461.3
48	microtubule-associated protein, RP/EB family, member 1	MAPRE1	NM_012325.2
49	microtubule-associated protein 1A	MAP1A	NM_002373.5
50	microtubule-associated protein 4	MAP4	NM_001134364.1
51	p21 protein (Cdc42/Rac)-activated kinase 1	PAK1	NM_001128620.1
52	protocadherin 10	PCDH10	NM_020815.1
53	protein kinase (cAMP-dependent, catalytic) inhibitor alpha	PKIA	NM_006823.2
54	protein kinase, cAMP-dependent, catalytic, beta	PRKACB	NM_002731.2
55	reticulocalbin 2, EF-hand calcium binding domain	RCN2	NM_002902.2
56	ras homolog gene family, member A	RHOA	NM_001664.2
57	roundabout, axon guidance receptor, homolog 2 (Drosophila)	ROBO2	NM_001128929.1
58	SAC1 suppressor of actin mutations 1-like (yeast)	SACM1L	NM_014016.3
59	stearoyl-CoA desaturase 5	SCD5	NM_001037582.2
60	Sec23 homolog A (S. cerevisiae)	SEC23A	NM_006364.2
61	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6D	SEMA6D	NM_020858.1
62	solute carrier family 18 (vesicular monoamine), member 2	SLC18A2	NM_003054.3
63	solute carrier family 30 (zinc transporter), member 4	SLC30A4	NM_013309.4
64	solute carrier family 4, sodium bicarbonate transporter, member 10	SLC4A10	NM_022058.3
65	synuclein, alpha (non A4 component of amyloid precursor)	SNCA	NM_000345.3
66	synaptosomal-associated protein, 91kDa homolog (mouse)	SNAP91	NM_014841.2
67	synaptic vesicle glycoprotein 2B	SV2B	NM_001167580.1

68	synaptogyrin 3	SYNGR3	NM_004209.4
69	synaptotagmin IV	SYT4	NM_020783.3
70	Tax1 (human T-cell leukemia virus type I) binding protein 1	TAX1BP1	NM_001079864.1
71	thymosin beta 4, X-linked	TMSB4X	NM_021109.3
72	thymosin beta 10	TMSB10	NM_021103.3
73	UDP-glucose pyrophosphorylase 2	UGP2	NM_001001521.1
74	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, gamma polypeptide	YWHAG	NM_012479.3
75	aldo-keto reductase family 1, member B1 (aldose reductase)	AKR1B1	NM_001628.2
76	cholinergic receptor, nicotinic, alpha 4	CHRNA4	NM_000744.5
77	GDNF family receptor alpha 1	GFRA1	NM_001145453.1
78	tyrosine hydroxylase	TH	NM_000360.3
79	peripherin	PRPH	NM_006262.3
80	dopa decarboxylase (aromatic L-amino acid decarboxylase)	DDC	NM_000790.3
81	pterin-4 alpha-carbinolamine dehydratase/dimerization cofactor of hepatocyte nuclear factor 1 alpha	PCBD1	NM_000281.2
82	cell growth regulator with EF-hand domain 1	CGREF1	NM_001166239.1
83	calcyon neuron-specific vesicular protein	CALY	NM_015722.3
84	protein arginine methyltransferase 2	PRMT2	NM_001535.2
85	TSPY-like 2	TSPYL2	NM_022117.3
86	aldehyde dehydrogenase 1 family, member A1	ALDH1A1	NM_000689.3
87	regulator of calcineurin 2	RCAN2	NM_005822.2
88	RNA binding motif, single stranded interacting protein	RBMS3	NM_001003792.1
89	protein kinase C, alpha	PRKCA	NM_002737.2
90	LY6/PLAUR domain containing 1	LYPD1	NM_001077427.2
91	solute carrier family 39 (zinc transporter), member 4	SLC39A4	NM_017767.2
92	serpin peptidase inhibitor, clade B (ovalbumin), member 6	SERPINB6	NM_004568.4
93	NEL-like 2 (chicken)	NELL2	NM_001145107.1
94	potassium voltage-gated channel, Shal-related subfamily, member 3	KCND3	NM_004980.3
95	protein kinase C, epsilon	PRKCE	NM_005400.2
96	leucine rich repeat containing 3B	LRRC3B	NM_052953.2
97	serine threonine kinase 39 (STE20/SPS1 homolog, yeast)	STK39	NM_013233.2
98	ELKS/RAB6-interacting/CAST family	ERC2	NM_015576.1

	member 2		
99	glucan (1,4-alpha-), branching enzyme 1	GBE1	NM_000158.3
100	dehydrogenase/reductase (SDR family) member 3	DHRS3	NM_004753.4
101	kelch-like 13 (Drosophila)	KLHL13	NM_001168299.1
102	aurora kinase A	AURKA	NM_003600.2
103	LIM domain only 4	LMO4	NM_006769.3
104	phospholipase C, beta 1 (phosphoinositide-specific)	PLCB1	NM_015192.2
105	cytochrome b-561	CYB561	NM_001017916.1
106	CUG triplet repeat, RNA binding protein 2	CUGBP2	NM_001025076.2
107	latrophilin 2	LPHN2	NM_012302.2
108	protein tyrosine phosphatase, receptor type, U	PTPRU	NM_005704.3
109	family with sequence similarity 167, member A	FAM167A	NM_053279.2
110	solute carrier organic anion transporter family, member 4A1	SLCO4A1	NM_016354.3
111	cadherin 13, H-cadherin (heart)	CDH13	NM_001257.3
112	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2	SERPINE2	NM_001136528.1
113	pleckstrin homology domain containing, family A member 7	PLEKHA7	NM_175058.4
114	angiotensin like 1	AMOTL1	NM_130847.2
115	pre-B-cell leukemia homeobox 1	PBX1	NM_002585.2
116	ets variant 5	ETV5	NM_004454.2
117	family with sequence similarity 84, member B	FAM84B	NM_174911.3
118	Purkinje cell protein 4 like 1	PCP4L1	NM_001102566.1
119	lysophosphatidic acid receptor 1	LPAR1	NM_001401.3
120	teashirt zinc finger homeobox 1	TSHZ1	NM_005786.4
121	glutamate receptor interacting protein 2	GRIP2	NM_001080423.1
122	par-3 partitioning defective 3 homolog (C. elegans)	PARD3	NM_019619.2
123	Ras association (RalGDS/AF-6) domain family member 6	RASSF6	NM_177532.3
124	eyes absent homolog 2 (Drosophila)	EYA2	NM_005244.4
125	shisa homolog 9 (Xenopus laevis)	SHISA9	NM_001145204.1
126	zinc finger homeobox 3	ZFH3	NM_001164766.1
127	solute carrier family 31 (copper transporters), member 1	SLC31A1	NM_001859.3
128	glycoprotein (transmembrane) nmb	GNMB	NM_001005340.1
129	Ca++-dependent secretion activator 2	CADPS2	NM_001009571.3

130	fatty acid desaturase 3	FADS3	NM_021727.3
131	calcium-sensing receptor	CASR	NM_000388.3
132	transmembrane inner ear	TMIE	NM_147196.2
133	glutathione peroxidase 3 (plasma)	GPX3	NM_002084.3
134	chromosome 4 open reading frame 31	C4orf31	NM_024574.3
135	fibronectin type III domain containing 3B	FNDC3B	NM_001135095.1
136	protein phosphatase 1, regulatory (inhibitor) subunit 14B	PPP1R14B	NM_138689.2
137	myosin VB	MYO5B	NM_001080467.2
138	phosphofructokinase, liver	PFKL	NM_002626.4
139	NK2 homeobox 1	NKX2-1	NM_001079668.2
140	claudin 1	CLDN1	NM_021101.3
141	guanine nucleotide binding protein (G protein), gamma 11	GNG11	NM_004126.3
142	stimulator of chondrogenesis 1	SCRG1	NM_007281.2
143	X-box binding protein 1	XBP1	NM_001079539.1
144	G protein-coupled receptor, family C, group 5, member A	GPRC5A	NM_003979.3
145	phosphoglucomutase 2-like 1	PGM2L1	NM_173582.3
146	regulator of G-protein signaling 2, 24kDa	RGS2	NM_002923.3
147	cytochrome P450, family 51, subfamily A, polypeptide 1	CYP51A1	NM_000786.3
148	ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)	UCHL1	NM_004181.4
149	brain-derived neurotrophic factor	BDNF	NM_001143805.1
150	pyruvate dehydrogenase (lipoamide) alpha 1	PDHA1	NM_000284.2
151	phospholipase C, beta 4	PLCB4	NM_000933.2
152	lysophospholipase I	LYPLA1	NM_006330.2
153	solute carrier family 24 (sodium/potassium/calcium exchanger), member 2	SLC24A2	NM_020344.1
154	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	ATP2A2	NM_001135765.1
155	calpain, small subunit 1	CAPNS1	NM_001003962.1
156	inositol 1,4,5-triphosphate receptor, type 1	ITPR1	NM_001099952.2
157	cysteine-rich protein 2	CRIP2	NM_001312.2
158	dynein, cytoplasmic 1, intermediate chain 1	DYNC1I1	NM_001135556.1
159	ubiquinol-cytochrome c reductase, Rieske iron-sulfur polypeptide 1	UQCRCF1	NM_006003.2
160	ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle	ATP5A1	NM_001001937.1
161	glutamic-oxaloacetic transaminase 2,	GOT2	NM_002080.2

	mitochondrial (aspartate aminotransferase 2)		
162	pyruvate kinase, muscle	PKM2	NM_002654.3
163	creatine kinase, brain	CKB	NM_001823.3
164	adenylate kinase 1	AK1	NM_000476.2
165	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide O	GNAO1	NM_020988.2
166	enolase 3 (beta, muscle)	ENO3	NM_001976.3
167	dopamine receptor D2	DRD2	NM_000795.3
168	calcium channel, voltage-dependent, T type, alpha 1G subunit	CACNA1G	NM_018896.3
169	protein kinase C, beta	PRKCB	NM_002738.6
170	protein kinase, cAMP-dependent, regulatory, type II, beta	PRKAR2B	NM_002736.2
171	proprotein convertase subtilisin/kexin type 2	PCSK2	NM_002594.2
172	neuritin 1	NRN1	NM_016588.2
173	monoamine oxidase A	MAOA	NM_000240.2
174	GTP cyclohydrolase 1	GCH1	NM_000161.2
175	solute carrier family 7 (cationic amino acid transporter, y+ system), member 3	SLC7A3	NM_001048164.1
176	cathepsin D	CTSD	NM_001909.3
177	vesicle-associated membrane protein 2 (synaptobrevin 2)	VAMP2	NM_014232.2
178	transducin-like enhancer of split 1 (E(sp1) homolog, Drosophila)	TLE1	NM_005077.3
179	growth factor receptor-bound protein 10	GRB10	NM_001001549.2
180	target of myb1-like 2 (chicken)	TOM1L2	NM_001033551.2
181	prune homolog 2 (Drosophila)	PRUNE2	NM_015225.2
182	calbindin 1, 28kDa	CALB1	NM_004929.2
183	GDP dissociation inhibitor 2	GDI2	NM_001115156.1
184	LAG1 homolog, ceramide synthase 4	LASS4	NM_024552.2
185	microtubule-associated protein 1 light chain 3 alpha	MAP1LC3A	NM_032514.2
186	nuclear receptor interacting protein 3	NRIP3	NM_020645.2
187	CD24 molecule	CD24	NM_013230.2
188	RAB3C, member RAS oncogene family	RAB3C	NM_138453.2
189	acyl-CoA synthetase long-chain family member 6	ACSL6	NM_001009185.1
190	myosin VA (heavy chain 12, myoxin)	MYO5A	NM_000259.3
191	RAR-related orphan receptor A	RORA	NM_002943.3
192	syndecan 2	SDC2	NM_002998.3
193	fibroblast growth factor 1 (acidic)	FGF1	NM_000800.3
194	poliovirus receptor-related 3	PVRL3	NM_015480.1

195	glutamate receptor, ionotropic, N-methyl D-aspartate 2C	GRIN2C	NM_000835.3
196	zinc finger, DHHC-type containing 2	ZDHHC2	NM_016353.4
197	SATB homeobox 1	SATB1	NM_001131010.1
198	acyl-Coenzyme A dehydrogenase, long chain	ACADL	NM_001608.3
199	solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 5	SLC25A5	NM_001152.4
200	vav 3 guanine nucleotide exchange factor	VAV3	NM_001079874.1
201	calcium channel, voltage-dependent, alpha 2/delta subunit 3	CACNA2D3	NM_018398.2
202	synuclein, gamma (breast cancer-specific protein 1)	SNCG	NM_003087.2
203	oxysterol binding protein-like 11	OSBPL11	NM_022776.4
204	Lix1 homolog (chicken)	LIX1	NM_153234.4
205	annexin A1	ANXA1	NM_000700.1
206	Ca++-dependent secretion activator	CADPS	NM_003716.3
207	RAS-like, family 11, member B	RASL11B	NM_023940.2
208	polymerase (DNA directed), beta	POLB	NM_002690.1
209	cyclin I	CCNI	NM_006835.2
210	RNA terminal phosphate cyclase domain 1	RTCD1	NM_001130841.1
211	lysosomal protein transmembrane 4 beta	LAPTM4B	NM_018407.4
212	cadherin 8, type 2	CDH8	NM_001796.2
213	ganglioside-induced differentiation-associated protein 1	GDAP1	NM_001040875.1
214	adenosine kinase	ADK	NM_001123.2
215	dynein, light chain, Tctex-type 3	DYNLT3	NM_006520.2
216	aspartyl aminopeptidase	DNPEP	NM_012100.2
217	regulator of G-protein signaling 8	RGS8	NM_001102450.1
218	pre-B-cell leukemia homeobox 3	PBX3	NM_001134778.1
219	trophoblast glycoprotein	TPBG	NM_001166392.1
220	CDP-diacylglycerol synthase (phosphatidate cytidyltransferase) 2	CDS2	NM_003818.2
221	myocyte enhancer factor 2A	MEF2A	NM_001130926.1
222	mitogen-activated protein kinase 9	MAPK9	NM_001135044.1
223	F-box protein 2	FBXO2	NM_012168.4
224	macrophage migration inhibitory factor (glycosylation-inhibiting factor)	MIF	NM_002415.1
225	NADH dehydrogenase (ubiquinone) Fe-S protein 8, 23kDa (NADH-coenzyme Q reductase)	NDUFS8	NM_002496.2
226	ELOVL family member 6, elongation of long chain fatty acids (FEN1/Elo2, SUR4/Elo3-	ELOVL6	NM_001130721.1

	like, yeast)		
227	CD47 molecule	CD47	NM_001025079.1
228	citrate synthase	CS	NM_004077.2
229	phosphatidylinositol transfer protein, alpha	PITPNA	NM_006224.3
230	homer homolog 2 (Drosophila)	HOMER2	NM_004839.2
231	RASD family, member 2	RASD2	NM_014310.3
232	thioredoxin-related transmembrane protein 2	TMX2	NM_001144012.1
233	3-oxoacid CoA transferase 1	OXCT1	NM_000436.3
234	translocase of outer mitochondrial membrane 20 homolog (yeast)	TOMM20	NM_014765.2
235	N-ethylmaleimide-sensitive factor attachment protein, beta	NAPB	NM_022080.2
236	amyloid beta (A4) precursor protein-binding, family A, member 2	APBA2	NM_001130414.1
237	NIMA (never in mitosis gene a)-related kinase 7	NEK7	NM_133494.2
238	vacuolar protein sorting 35 homolog (S. cerevisiae)	VPS35	NM_018206.4
239	RAB6A, member RAS oncogene family	RAB6A	NM_002869.4
240	very low density lipoprotein receptor	VLDLR	NM_001018056.1
241	Rho GTPase activating protein 24	ARHGAP24	NM_001025616.2
242	visinin-like 1	VSNL1	NM_003385.4
243	protein tyrosine phosphatase, non-receptor type 5 (striatum-enriched)	PTPN5	NM_001039970.1
244	prohibitin 2	PHB2	NM_001144831.1
245	NADH dehydrogenase (ubiquinone) Fe-S protein 2, 49kDa (NADH-coenzyme Q reductase)	NDUFS2	NM_001166159.1
246	transducin-like enhancer of split 3 (E(sp1) homolog, Drosophila)	TLE3	NM_001105192.1
247	tachykinin receptor 3	TACR3	NM_001059.1
248	serine peptidase inhibitor, Kunitz type, 2	SPINT2	NM_001166103.1
249	colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	CSF2RB	NM_000395.2
250	reticulocalbin 1, EF-hand calcium binding domain	RCN1	NM_002901.2
251	collagen, type XI, alpha 1	COL11A1	NM_001168249.1
252	FXD domain containing ion transport regulator 6	FXD6	NM_001164831.1
253	calbindin 2	CALB2	NM_001740.3
254	MARCKS-like 1	MARCKSL1	NM_023009.5
255	cholecystokinin	CCK	NM_000729.3
256	mesoderm development candidate 2	MESDC2	NM_015154.1

257	prostate androgen-regulated mucin-like protein 1	PARM1	NM_015393.2
258	family with sequence similarity 114, member A1	FAM114A1	NM_138389.1
259	huntingtin-associated protein 1	HAP1	NM_001079870.1
260	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 1	SMARCA1	NM_003069.3
261	dedicator of cytokinesis 6	DOCK6	NM_020812.2
262	CaM kinase-like vesicle-associated	CAMKV	NM_024046.3
263	isocitrate dehydrogenase 1 (NADP+), soluble	IDH1	NM_005896.2
264	nucleobindin 2	NUCB2	NM_005013.2
265	ribosomal protein L36a	RPL36A	NM_021029.4
266	lipoprotein lipase	LPL	NM_000237.2
267	adenylate cyclase activating polypeptide 1 (pituitary)	ADCYAP1	NM_001099733.1
268	chromosome 7 open reading frame 16	C7orf16	NM_001145123.1
269	chromosome 6 open reading frame 62	C6orf62	NM_030939.4
270	coiled-coil domain containing 91	CCDC91	NM_018318.3
271	cadherin 11, type 2, OB-cadherin (osteoblast)	CDH11	NM_001797.2
272	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 11	MLLT11	NM_006818.3
273	ribosomal protein, large, P0	RPLP0	NM_001002.3
274	chimerin (chimaerin) 1	CHN1	NM_001025201.2
275	IQ motif containing J	IQCJ	NM_001042705.1
276	transmembrane protein 30A	TMEM30A	NM_001143958.1
277	drebrin 1	DBN1	NM_004395.3
278	deleted in colorectal carcinoma	DCC	NM_005215.3
279	delta/notch-like EGF repeat containing	DNER	NM_139072.3
280	solute carrier family 10 (sodium/bile acid cotransporter family), member 4	SLC10A4	NM_152679.3
281	eukaryotic translation elongation factor 1 alpha 1	EEF1A1	NM_001402.5
282	fatty acid binding protein 5 (psoriasis-associated)	FABP5	NM_001444.1
283	coagulation factor II (thrombin) receptor	F2R	NM_001992.3
284	farnesyl-diphosphate farnesyltransferase 1	FDFT1	NM_004462.3
285	farnesyl diphosphate synthase (farnesyl pyrophosphate synthetase, dimethylallyltranstransferase, geranyltranstransferase)	FDPS	NM_001135821.1
286	forkhead box A1	FOXA1	NM_004496.2

287	four and a half LIM domains 1	FHL1	NM_001159699.1
288	growth associated protein 43	GAP43	NM_001130064.1
289	heat shock factor binding protein 1	HSBP1	NM_001537.2
290	iduronate 2-sulfatase	IDS	NM_000202.5
291	limbic system-associated membrane protein	LSAMP	NM_002338.3
292	mitogen-activated protein kinase 11	MAPK11	NM_002751.5
293	microtubule-associated protein tau	MAPT	NM_001123066.2
294	matrin 3	MATR3	NM_018834.4
295	mortality factor 4 like 2	MORF4L2	NM_001142418.1
296	mortality factor 4 like 1	MORF4L1	NM_006791.2
297	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 10, 42kDa	NDUFA10	NM_004544.3
298	NDRG family member 3	NDRG3	NM_022477.2
299	neural precursor cell expressed, developmentally down-regulated 4	NEDD4	NM_006154.2
300	nicotin 1	NICN1	NM_032316.3
301	nuclear receptor subfamily 4, group A, member 2	NR4A2	NM_006186.3
302	neurotrophic tyrosine kinase, receptor, type 2	NTRK2	NM_001007097.1
303	neurexin 3	NRXN3	NM_001105250.1
304	progesterone receptor membrane component 1	PGRMC1	NM_006667.3
305	phosphoglycerate kinase 1	PGK1	NM_000291.3
306	PQ loop repeat containing 1	PQLC1	NM_001146343.1
307	protein phosphatase 3 (formerly 2B), regulatory subunit B, alpha isoform	PPP3R1	NM_000945.3
308	RNA binding motif protein 4	RBM4	NM_002896.2
309	RNA binding motif protein 18	RBM18	NM_033117.3
310	ring finger protein 7	RNF7	NM_014245.3
311	ataxin 10	ATXN10	NM_001167621.1
312	secretogranin II (chromogranin C)	SCG2	NM_003469.3
313	succinate dehydrogenase complex, subunit B, iron sulfur (lp)	SDHB	NM_003000.2
314	single-stranded DNA binding protein 2	SSBP2	NM_012446.2
315	translocase of inner mitochondrial membrane 10 homolog (yeast)	TIMM10	NM_012456.2
316	serine incorporator 1	SERINC1	NM_020755.2
317	ubiquitin-conjugating enzyme E2B (RAD6 homolog)	UBE2B	NM_003337.2
318	valosin-containing protein	VCP	NM_007126.3
319	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide	YWHAE	NM_006761.4

320	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide	YWHAB	NM_003404.3
321	SH3 domain binding glutamic acid-rich protein like	SH3BGRL	NM_003022.2
322	chaperonin containing TCP1, subunit 5 (epsilon)	CCT5	NM_012073.3
323	Golgi-localized protein	GOLSYN	NM_001099743.1
324	asparagine-linked glycosylation 2, alpha-1,3-mannosyltransferase homolog (S. cerevisiae)	ALG2	NM_033087.3
325	calcium channel, voltage-dependent, beta 2 subunit	CACNB2	NM_000724.3
326	carbonic anhydrase IV	CA4	NM_000717.3
327	dickkopf homolog 3 (Xenopus laevis)	DKK3	NM_001018057.1
328	dystrophia myotonica, WD repeat containing	DMWD	NM_004943.1
329	EPH receptor A6	EPHA6	NM_001080448.2
330	non-metastatic cells 1, protein (NM23A) expressed in	NME1	NM_000269.2
331	glutamate receptor, ionotropic, kainate 3	GRIK3	NM_000831.3
332	heme oxygenase (decycling) 2	HMOX2	NM_001127204.1
333	histone cluster 3, H2a	HIST3H2A	NM_033445.2
334	HIV-1 Tat interactive protein 2, 30kDa	HTATIP2	NM_001098520.1
335	mannosyl (alpha-1,6-)-glycoprotein beta-1,6-N-acetyl-glucosaminyltransferase, isozyme B	MGAT5B	NM_144677.2
336	ribosomal protein L11	RPL11	NM_000975.2
337	ubiquitin-conjugating enzyme E2K (UBC1 homolog, yeast)	UBE2K	NM_001111112.1
338	zinc finger, MYND domain containing 11	ZMYND11	NM_001161482.1
339	potassium inwardly-rectifying channel, subfamily J, member 6	KCNJ6	NM_002240.2
340	4-aminobutyrate aminotransferase	ABAT	NM_000663.4
341	solute carrier family 6 (neurotransmitter transporter, dopamine), member 3	SLC6A3	NM_001044.4
342	translocase of inner mitochondrial membrane 8 homolog A (yeast)	TIMM8A	NM_001145951.1
343	SH3-binding domain kinase 1	SBK1	NM_001024401.2
344	v-myc myelocytomatosis viral oncogene homolog (avian)	MYC	NM_002467.4
345	nerve growth factor receptor (TNFR superfamily, member 16)	NGFR	NM_002507.2
346	nucleoporin 93kDa	NUP93	NM_014669.3
347	protocadherin alpha 10	PCDHA10	NM_018901.2
348	protein phosphatase 2, regulatory subunit B', delta isoform	PPP2R5D	NM_006245.2

349	receptor accessory protein 1	REEP1	NM_001164730.1
350	ribophorin I	RPN1	NM_002950.3
351	septin 5	SETP5	NM_002688.4
352	solute carrier family 35, member C2	SLC35C2	NM_015945.10
353	SET domain containing (lysine methyltransferase) 7	SETD7	NM_030648.2
354	SNF related kinase	SNRK	NM_001100594.1
355	single stranded DNA binding protein 4	SSBP4	NM_001009998.2
356	suppressor of Ty 5 homolog (S. cerevisiae)	SUPT5H	NM_001111020.2
357	serine/threonine kinase 32C	STK32C	NM_173575.2
358	transmembrane BAX inhibitor motif containing 6	TMBIM6	NM_001098576.1
359	transmembrane protein 50B	TMEM50B	NM_006134.5
360	tousled-like kinase 1	TLK1	NM_001136554.1
361	tumor protein p53 binding protein 1	TP53BP1	NM_001141979.1
362	tetraspanin 6	TSPAN6	NM_003270.2

Table C- Differences between table A and B

	Gene Name	Gene Symbol	Accession Number
1	CAAX box 1 homolog A (human)	Cxx1a	NM_024170.2
2	RIKEN cDNA 2010011I20 gene	2010011I20Rik	NM_025912.4
3		A030009H04Rik	
4		Rho	
5	cytochrome P450, family 4, subfamily v, polypeptide 3	Cyp4v3	NM_133969
6	RIKEN cDNA 9630033F20 gene DNA 9630033F20 gene	9630033F20Rik	
7	hypothetical LOC385068	LOC385068	

Table D- The genes that are not found by ToppGene (Left column) and Endeavour (Right column) softwares

The genes that ToppGene does not find	The genes that Endeavour does not find
BAT2L	CPLX1
CUGBP2	RUNDC3A
GOLSYN	BAT2L
SETP5	UBR3
	COPG2
	TMEM196
	RCAN2
	CALY
	FAM167A
	SHISA9
	LPAR1
	PCP4L1
	ZFHX3
	NKX2-1
	SCRG1
	PRKCB
	TMX2
	PHB2
	PARM1
	IQCJ
	UBE2K
	GOLSYN
	SETP5
	TMBIM6