

**Meta-analysis of microarray-derived data from PACAP-deficient adrenal gland in vivo and PACAP-treated chromaffin cells identifies distinct classes of PACAP-regulated genes**

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**Abstract**

Initial PACAP-regulated transcriptomes of PACAP-treated cultured chromaffin cells, and the adrenal gland of wild-type versus PACAP-deficient mice, have been assembled using microarray analysis. These were compared to previously acquired PACAP-regulated transcriptome sets from PC12 cells and mouse central nervous system, using the same microarray platform. The Ingenuity Pathways Knowledge Base was then employed to group regulated transcripts into common first and second messenger regulatory clusters. The purpose of our meta-analysis was to identify sets of genes regulated distinctly or in common by the neurotransmitter/neurotrophin PACAP in specific physiological contexts. Results suggest that PACAP participates in both the basal differentiated expression, and the induction upon physiological stimulation, of distinct sets of transcripts in neuronal and endocrine cells. PACAP in both developmental and acute regulatory paradigms acts on target genes regulated by either TNF $\alpha$  or TGF $\beta$ , two first messengers acting on transcription mainly through NF $\kappa$ B and Smads, respectively.

Keywords: adrenal gland, bovine chromaffin cells, Btg2, C/EBP, Ier3, meta-analysis, microarray, middle cerebral artery occlusion, PACAP, PC12, Scmh1, secretogranin, TGF $\beta$ , TNF $\alpha$ , YWAHZ

## 1. Introduction

Pituitary adenylate cyclase activating polypeptide (PACAP) is involved in neuroprotection, neurotransmission, glucohomeostasis, circadian rhythmicity, neuronal development, and cell proliferation and transformation [3, 4, 9, 16, 39, 48, 58]. To perform these roles, PACAP must influence the expression of multiple cohorts of genes. The concept of PACAP-dependent gene expression underlies previous work demonstrating a link between PACAP and glutamate-induced brain-derived neurotrophic factor (BDNF) expression [24, 52, 61], a role for PACAP in effects of lithium on cortical neurons [10], PACAP-dependent gene expression in response to cerebral ischemia [15], and impaired basal expression of specific genes in PACAP-deficient mice [14]. Some of these transcripts may be regulated not only by PACAP but by other agents and transmitters that elevate intracellular cAMP, a major downstream pathway for PACAP [13, 33, 38, 49]. PACAP is also a strong activator of ERK [7, 26, 34, 57], and some PACAP-dependent genes such as BDNF may be activated by other stimulators of this MAPK pathway, including therapeutic agents such as lithium [25]. Calcium elevation is a third known major mode of signaling to the nucleus through which PACAP, via the PAC1 receptor, might activate gene expression [6, 8, 29, 37, 40, 42, 53, 60, 62]. PACAP-specific regulation of particular target genes, including those encoding neuropeptides, may be due to the unique combinatorial elevation of cAMP, calcium and MAPK by PACAP [30].

PACAP-dependent genes may be either down-regulated or up-regulated directly in response to increased neuronal PACAP release during physiological or pathophysiological events. PACAP-dependent genes may also be regulated in less obvious ways, for example via the action of PACAP as a neurotrophin in development, or through basal rather than stimulated secretion of PACAP in vivo. Thus, strategies for

identifying PACAP-dependent transcripts, or ‘PACAP target genes’ have involved microarray analysis in PACAP knock-out mice, in wild-type mice treated with PACAP [15], and in cultured neuroendocrine cells exposed to PACAP [28, 45, 57]. Meta-analysis of transcriptome profiles in these different conditions may help to identify ‘intrinsically’ PACAP-responsive genes. This type of analysis entails certain caveats, however. One is that exogenous PACAP may interact with receptors (VPAC1, VPAC2) for which vasoactive intestinal polypeptide (VIP) rather than PACAP is the endogenous ligand. For this reason, pharmacological treatment with PACAP will not always represent the mirror image of PACAP deficiency, with respect to transcriptome analysis. Data acquisition using different transcriptomic platforms, differences in the times of exposure and treatment, and differences in cell types within a tissue may also mask PACAP-dependent transcriptional regulation. Comparison of differentially complex systems, for example the adrenomedullary synapse at which PACAP is the only known neuropeptide slow transmitter, and the brain which contains many overlapping and redundant ones, is an additional factor. Despite these concerns, analysis of multiple transcriptome data sets relevant to PACAP’s role in gene regulation (meta-analysis) has the potential to reveal genes uniquely regulated by PACAP, and thus PACAP’s underlying physiological function. Conversely, meta-analysis can potentially reveal genes commonly regulated by PACAP in neuronal cells and by other signaling molecules in other cellular contexts, providing insight into potential common signal transduction pathways employed by PACAP and cytokines, growth factors, and other neurotransmitters.

Here, we created a data manifold to reveal patterns of PACAP-dependent gene transcription. Data were collated from the literature to create an ‘anchor set’ of PACAP-responsive genes. This was augmented from specific data sets obtained for this purpose from wild-type versus PACAP-deficient mouse endocrine tissue, and PACAP-treated versus untreated bovine chromaffin cells, reported herein. Filtering of these additional data sets through the anchor set revealed a set of PACAP-dependent genes as a basis for drug discovery, regulatory network hierarchical arrangement, and identification of new regulatory functions for known genes.

## 2. Materials and Methods

### 2.1. Sources of data for meta-analysis

Six data sets were compared in this analysis. The first two are reported here for the first time. The first set consists in a comparison of the adrenal gland transcriptome differentially expressed in wild-type compared to PACAP knock-out mice. Briefly, RNA was extracted from both adrenal glands of individual mice, and cDNA synthesized and used for hybridization to the NIMH 36K microarray all as previously described [15]. The second set consists in a comparison of the bovine chromaffin cell (BCC) transcriptome differentially expressed in untreated cultured chromaffin cells and those treated for six hours with 100 nM PACAP-27. Briefly, BCCs were cultured in T150 flasks (~50 million cells/flask) following differential plating in T150 flasks for 24 hours following isolation, as described [30]. PACAP or vehicle was introduced into each flask from a 100x concentrated stock solution in complete medium the day following re-plating. Cells were harvested 6 hours later by scraping into medium, collected by centrifugation at 1000 rpm in Eppendorf 5810 centrifuge for five minutes, washed with PBS by re-suspension and re-centrifugation, and RNA was extracted. cDNA was synthesized and labeled, and hybridization to the NIMH 36K microarray was carried out, all as previously described [15]. The third through fifth data sets were extracted from the literature for the PACAP transcriptome of PC12 cells. These data sets represented i) the differential transcriptome derived from PACAP treatment of PC12 cells for six hours in the presence of cycloheximide to detect transcripts up-regulated by PACAP from 0-6 h and whose expression returns to baseline by 6 h [45]; ii) the differential transcriptome derived from PACAP treatment of PC12 cells for six hours (the minimal time of exposure to PACAP leading to full differentiation 48 hours later [57]); and iii) transcripts up-regulated by PACAP after PC12 cell treatment for the full 48 hours leading to a full PACAP-induced neuritogenic response [28]. The sixth and final data set is a composite of transcripts regulated by middle cerebral artery occlusion (MCAO) in the mouse at 1 and 24 hours post-MCAO, in both wild-type and PACAP knock-out mice as originally described by Chen et al. [15]. The NIA15K mouse embryo-derived clone set ([54], and see

<http://lgsun.grc.nia.nih.gov/cDNA/15k.html>) was used for PC12 cell microarray experiments [45, 57]. The NIMH 36K cDNA microarray containing NIA15K, and BMAP1 and BMAP2 brain-specific clone sets [59] was used for the mouse adrenal gland (MAG) and bovine chromaffin cell (BCC) microarray hybridization experiments reported here, as well as the MCAO data of Chen et al., [15], analyzed here. See also <http://lgsun.grc.nia.nih.gov/cDNA/15k.html>, <http://clones.invitrogen.com/cloneinfo.php?clone=est>, and <http://genome.uiowa.edu/projects/BMAP/> for additional information on the clone sets comprising the NIMH 36K cDNA microarray.

Raw data from the BCC and MAG microarray experiments have been submitted to the GEO (gene expression omnibus) database and can be accessed using the GS series designations GSE7405 and GSE7406.

## *2.2. Extraction of data from published literature*

In order to extract the data from the published literature for further analysis, tables containing the data in a given publication were saved in a PDF format using cutePDF (<http://www.cutepdf.com/Products/CutePDF/writer.asp>) and subsequently converted to an Excel table using *PDF to Excel Converter* (<http://www.bluelabelsoft.de/index.htm>). The GenBank accession numbers in each table were converted to Entrez GeneID (formerly known as LocusLink ID and gene symbols) using the SOURCE (<http://genome-www5.stanford.edu/cgi-bin/source/sourceSearch>) website. A few remaining unannotated expressed sequence tags (EST) were eliminated from further consideration in this report. The dataset extracted from each publication was then exported to Microsoft ACCESS for cross comparison using gene symbol as the common element. For comparison, the genes listed in multiple tables within each publication were combined to create a unique gene set for that condition (PC12 0-6 h, PC12 6 h, PC12 48 h, etc). The IMAGE and SSH (suppression subtractive hybridization) clones reported by Grumolato et al. [28] were also annotated in a similar manner. Data from Chen et al

(2006) [15] were extracted using the same tools but without need for ID conversion, as GeneIDs and gene symbols were provided in the publication.

### *2.3. Acquisition of data from mAdb*

The microarray data sets (adrenal gland wild-type vs. PACAP knock-out and the bovine chromaffin cells treated with PACAP) were analyzed as follows:

#### 2.3.1. Creation of dataset

For the analysis of unpublished data (i.e. MAG and BCC), simple data extraction was done in the NIH Center for Information Technology's mAdb, and data sets were stored as permanent files in mAdb for further analysis.

#### 2.3.2. Group analysis for missing values

Genes with low quality values in more than 60% of the arrays per group were removed from analysis using the missing value filter tool in mAdb. The remaining genes were used for group statistical analysis as well as for SAM (Significance Analysis of Microarrays) [56].

#### 2.3.3. SAM analysis

SAM was carried out using the resident SAM [56] tool in mAdb, setting the number of permutations to 1000, and the false discovery rate (FDR) to 10% or less, depending on whether input hybridization cDNA was obtained from mouse tissue or bovine cells (see Table 1).

### *2.4. Cross comparison of different data sets*

SAM-significant transcripts along with their values and gene annotation were exported from mAdb into an Excel format and then to Microsoft ACCESS. Only the clone IDs of the genes along with the fold change expression value were exported to eliminate the discrepancy in the gene annotation between different datasets. The latest clone annotation for the entire array set was then obtained from its mAdb GIPO file as a comprehensive report used to annotate the clones represented in both MAG and BCC microarrays. SAM-

significant values were converted to linear scale and expressed in the form of fold change (see Section 2.7, below). Only the clone IDs of the genes along with the fold change expression value were exported to eliminate the discrepancy in the gene annotation between different datasets. The latest clone annotation for the entire array set was then obtained from its mAdb GIPO file as a comprehensive report used to annotate the clones represented in both MAG and BCC microarrays.

### *2.5. Resolution of data obtained from multiple clones for the same gene*

In a few cases there were multiple clones (microarray hybridization targets) with the same GeneID but with divergent (conflicting) values. To authenticate each target, the available GenBank sequences of the clones were compared to the gene RefSeq sequence (<http://www.ncbi.nlm.nih.gov/blast/bl2seq/wblast2.cgi>). If the clone sequences on both the 5' and 3' ends matched to the RefSeq sequence, the target was deemed authentic. If there was a match only with the sequence on one side of the clone but not on the other side, it was considered a mixed clone and was rejected. Likewise, clones having sequence for only one end available were rejected, in favor of clones with both ends sequenced

### *2.6. Definitions and ontological values of terms used to cross-reference gene sets*

The following terms and designations for cDNA clones on microarrays, and links to curated information about their gene loci, actual and hypothetical translation products, and relationship to other cDNA clones, are defined in detail at the following URL: <http://atlasgeneticsoncology.org/extdef.html>.

*2.6.1 Clone ID.* This designates a GIPO file accession number, and is the name given to a specific clone regardless of the gene content when it was cloned into a vector and then deposited in the GenBank database.

*2.6.2. UniGene cluster ID.* UniGene is an experimental system for automatically partitioning GenBank sequences into a non-redundant set of gene-oriented clusters. Each

UniGene cluster contains sequences that represent a unique gene, as well as related information such as the tissue types in which the gene is expressed and map location.

2.6.3. Gene name. The Human Gene Nomenclature Database (HUGO) provides currently approved human gene symbols or names as maintained by the HUGO gene nomenclature committee.

2.6.4. GenBank accession number. GenBank is the NIH database of all deposited nucleotide and protein sequences. Each deposit gets a unique ID.

2.6.5. LocusLink/GeneID. Entrez\_Gene is the primary identification for the genes in Entrez database and links to other databases such as RefSeq, maps, OMIM (Online Mendelian Inheritance in Man), UniGene and PubMed.

## *2.7. Network analysis of individual and composite data sets.*

Interaction networks for gene symbol lists of the up-regulated transcripts for BCC (188 transcripts), PC12 composite (168 transcripts), MCAO-1h (76 transcripts), MCAO-24 h (74 transcripts), and final composite (26 transcripts) were obtained employing the Ingenuity Pathways Knowledge Base (<http://www.ingenuity.com/>; see also [11]). A total of 29 networks were obtained [nine for BCC, ten for PC12 composite, four each for MCAO-1 and MCAO-24, and two for the final composite], using a threshold of at least eight focus genes (i.e. input genes, or genes up-regulated by PACAP or PACAP-dependent within the given set) per network assembled. Three networks were filtered out, based on a) reliance of entire network on a single reference (network 1, PC12 composite), b) containing a major component known not to be expressed in cells of interest (network 4, BCC, features CAMKIV not expressed in BCCs), and c) dominance by direct interactions (protein-protein interactions) dependent on post-translational modifications for which evidence was lacking in these studies (network 2, BCC, featuring multiple JAK-STAT protein-protein interactions not involving changes in mRNA levels for either encoded protein). All 23 remaining networks were considered in meta-analysis. For purposes of illustration, only the highest-ranked networks in each remaining set are shown as figures.



### 3. Results and Discussion

#### 3.1. PACAP-responsive transcripts of mouse adrenal gland and bovine chromaffin cells

PACAP regulation of transcripts at six hours following treatment of primary post-mitotic bovine chromaffin cells in culture with 100 nM PACAP-27, and of mouse adrenal gland in wild-type compared to PACAP-deficient mice without additional treatment, was determined as summarized in Table 1. Different false discovery rates were applied to obtain the significant genes from SAM analysis (Table 1). For MAG, the FDR was set low while for BCC, it was set high to take into account the potential loss of signal due to cross-species hybridization. As a two-fold cut off was used to obtain the data in the published literature, a similar cut off was used for both of these data sets after SAM analysis.

First, transcripts were determined to be up-regulated by PACAP (down-regulated transcripts were not considered in this analysis) if their abundance was i) significantly higher by SAM in wild-type compared to PACAP-deficient adrenal gland or in PACAP-treated compared to non-treated bovine chromaffin cells, and ii) the difference between the two conditions was at least two-fold, based on the SAM-derived mean values of the ratio between the two respective sets of conditions. The number of transcripts regulated by this criterion was 228 in the MAG microarray data set, and these transcripts are listed in Supplementary Table S1. Some of the transcripts reported to be regulated in the rodent adrenal gland upon splanchnicoadrenomedullary synaptic activation were down-regulated by lack of PACAP expression (i.e. in PACAP-deficient mice) under quiescent conditions. Prominent among these was the neuropeptide precursor secretogranin II, which generates the neuroactive peptide secretoneurin, and is not regulated by splanchnic nerve activity at the protein level [21]. Transcripts for other characteristic products of the adrenal medulla including chromogranin A, chromogranin B, and tyrosine hydroxylase (TH) were not significantly decreased by the absence of PACAP, consistent with the apparent lack of effect of PACAP deficiency on adrenomedullary chromogranin A, TH, and phenylethanolamine N-methyltransferase (PNMT) at the protein level as previously reported [31]. Secretogranin III mRNA levels were also significantly decreased in the

PACAP-deficient adrenal gland, while mRNA encoding neuropeptides known to be regulated by stimuli that release PACAP and ACh at the splanchnicoadrenomedullary synapse, including neuropeptide Y (NPY), neurotensin and substance P, were not altered in the basal state. This suggests either that the fast and slow co-transmitters ACh and PACAP may separately regulate the abundance of different classes of secretory products in the adrenal gland. Alternatively, regulation by PACAP for some neuropeptide-encoding genes may occur only under conditions in which stimulus-secretion-synthesis coupling is engaged by prolonged PACAP release, for example following splanchnic nerve stimulation by insulin, reserpine, or physiological stress. Among transcripts likely to be developmentally important, and likely to be expressed in the adrenal medulla as well as or in addition to adrenal cortex, *Scmh1*, *Btg2*, *Jarid1c* and *BMPR2* were at least two-fold less abundant in PACAP-deficient compared to normal mouse adrenal.

In contrast, transcripts regulated in fully differentiated, mature chromaffin cells in culture by treatment with PACAP included substance P, enkephalin, and secretogranin II as reported previously in either PACAP-treated BCC [5, 29] or rodent adrenal in vivo after stimulation with insulin [2, 20, 22, 23]. In total, 187 transcripts were found to be PACAP-regulated in bovine chromaffin cells (Table S2). Ingenuity analysis was used to determine if the core set of genes regulated by PACAP are regulated by other signal transduction components, thus providing some clues to novel signaling pathways used by PACAP. Transcripts encoding YWHAZ (14-3-3-zeta) and several proteins interacting with it, are up-regulated by PACAP, suggesting that a 14-3-3 network may be fundamentally modulated by PACAP as part of its slow transmitter function at the adrenomedullary synapse (Figure 1a). Increased expression of YWHAZ activation may provide a molecular mechanism, in addition to direct phosphorylation of TH by adenylate cyclase, for the long-term PACAP-dependent activation of adrenomedullary TH in vivo subserving glucohomeostasis during metabolic stress [31]. Strikingly, as shown in Figures 1b and 1c, several PACAP target genes are also targets of TGF $\beta$  and TNF $\alpha$  in other cellular contexts, implicating Smads [19], and NF $\kappa$ B [27], respectively, in PACAP signaling in neuroendocrine cells.

### *3.2. Meta-analysis of transcripts regulated by PACAP in PC12 cells*

Transcriptome changes in PC12 cells treated with PACAP presumably represent both regulation at the level of differentiation from a dividing cell to a growth-arrested one and stimulus-secretion-synthesis coupling during physiological activation of the adrenomedullary synapse under conditions of metabolic, psychogenic, or thermoregulatory stress. Consequently, we derived a composite set of regulated transcripts representing the ‘transitional transcriptomes’ for both development and mature functioning of the adrenal gland, by combining immediate-early response, differentiation response, and differentiated response periods of PACAP exposure (0-6, 6 and >24 hours of exposure) for comparison to the MAG and BCC data sets. Using our previous comprehensive analysis at these time points (for 0-6 h, a ‘CHX superinduction’ paradigm was used) yielded the data shown in Table S3. Ingenuity analysis suggests that TNF $\alpha$ - (Figure 2a) and TGF $\beta$ -like (Figure 2b) patterns of gene induction were also noted for the PACAP transcriptome of PC12 cells, linking the transcript set regulated by PACAP in fully differentiated chromaffin cells to a set of genes regulated by PACAP in PC12 cells (Figure 2).

### *3.3. Meta-analysis of transcripts regulated by PACAP following middle cerebral artery occlusion*

PACAP is neuroprotective in stroke [46, 47], and the pathogenic and neurological sequelae of stroke are exacerbated in PACAP-deficient mice [14, 15, 41]. PACAP-dependent CNS genes defined in the context of response to ischemic injury (MCAO) were reported previously [15], and were re-analyzed here (Table S4) using Ingenuity (Figure 3). In CNS, PACAP-responsive transcripts appear to link PACAP signaling to both the immediate-early transcription factor Jun, and to the GSK-regulated signal transduction factor for transcription, beta-catenin.

### *3.4. Composite transcriptome changes in MAG, BCC, PC12, and MCAO paradigms of PACAP gene regulation*

A final analysis of common PACAP-responsive genes in MAG, BCC, PC12 cells, and the MCAO model yielded 26 transcripts regulated in the PC12 anchor set and at least one other (MAG, BCC, MCAO) (Table 2). Ingenuity analysis of this set (Figure 4) reveals a high density of PACAP-regulated genes that are also targets of TNF $\alpha$  and TGF $\beta$ , supporting the suggestion that PACAP may use NF $\kappa$ B and Smad pathways, in addition to its established signaling through cAMP, calcium and phospholipase C, in a wide variety of physiological responses and during development.

Meta-analysis, whose final results are shown in Table 2 and Figure 4, has revealed several key points about PACAP-responsive genes mobilized for adrenomedullary function in peripheral nervous system (PNS) and for neuroprotection in central nervous system (CNS). First, there appears to be three distinct types of gene regulation of PACAP-responsive transcripts in PC12 cells that correspond most closely to developmental (wild-type versus PACAP-deficient MAG), physiological (PACAP-stimulated chromaffin cells) and pathophysiological (mouse MCAO) roles for PACAP. Of immediate interest is the finding that of the 26 PACAP-regulated transcripts that span these arenas of PACAP action, at least four encode translational regulators, and these fall into two categories. *Cpeb4* expression in quiescent MAG appears to require PACAP, i.e. is related to 'basal' or developmental actions of PACAP. *Eif2c2*, *Eif4e* and *Eprs* expression are enhanced by PACAP in mature BCCs, and might therefore be regulatory loci for slow transmitter function related to cell plasticity. Transcripts up-regulated by PACAP in PC12 cells are largely those that require endogenous PACAP for full expression in adrenal gland *in vivo* or are induced by PACAP in bovine chromaffin cells. The lack of overlap between PC12 composite transcripts which are also decreased in PACAP-deficient MAG, and up-regulated by PACAP in BCCs suggests that the neurotrophic and neurotransmitter roles of PACAP are largely distinct. Genes regulated pathophysiologically, e.g. in MCAO, appear to be a third category of PACAP-responsive genes also up-regulated by PACAP in PC12 cells. The abundance of the previously reported PACAP-responsive transcript *Ier3* (a.k.a. PACAP-regulated gene-1, or PRG-1) [51] is increased in both PC12 cells upon PACAP exposure [57], and in a PACAP-dependent manner after MCAO [15], but is not dependent on PACAP in the unstimulated MAG, or in BCCs treated with PACAP (Table 2). It will be of interest to

determine if other adrenomedullary stimuli, such as metabolic or psychogenic stress, elicit a PACAP-dependent activation of *Ier3* or related immediate-early genes as occurs in pathophysiological conditions, such as ischemia, in the brain. *Anxa2* was the single transcript found up-regulated by PACAP in all paradigms examined here. *Anxa2* is required for generation of plasmin during NGF-initiated neuritogenesis in PC12 cells [32]. The role of the plasminogen activator system in both catecholamine secretion [50] and ischemia [35] may link PACAP function to this transcriptional target in these diverse physiological contexts.

Second, overlap of transcriptional targets of  $\text{TNF}\alpha$  and  $\text{TGF}\beta$ , and PACAP, suggests alternative modes of transcriptional signaling for PACAP in addition to cAMP, i.e.  $\text{NF}\kappa\text{B}$  and Smad.  $\text{TGF}\beta$ -like signaling initiated by PACAP, i.e. proceeding through Smad transactivation, has not been explored. However, the *VIP* gene, a major target of PACAP signaling in vivo and in BCCs and neuroblastoma cells, contains responsive elements for Smads and is stimulated by  $\text{TGF}\beta$  in NBFL neuroblastoma cells [44]. With respect to  $\text{TNF}\alpha$ -like signaling by PACAP, it is clear that  $\text{TNF}\alpha$  itself can activate several genes in common with PACAP in chromaffin cells via activation of the  $\text{TNF}\alpha$  type 2 receptor, including secretogranin II and galanin [1]. It will be worthwhile to explore whether this signaling also proceeds through  $\text{NF}\kappa\text{B}$  following elevation in intracellular calcium, as suggested for cerebellar neurons [36].

Third, we have noticed that at least four of the 26 PACAP-dependent transcripts listed in Table 2 are also known to be targets for the transcription factor *C/EBP* in various cell types including PC12 cells. These include *Btg2*, involved in PC12 cell differentiation by NGF; *Ier3*, a regulator of apoptosis whose human homolog is called *Dif-2*; *Rgs2*, which is highly up-regulated by PACAP in PC12 cells; and *APC*, like *Btg2* important in PC12 cell differentiation by NGF [12, 17, 18, 43, 55]. Thus *C/EBP*, in addition to *CREB*, may be a trans-activator for PACAP signaling in neuroendocrine cells.

In summary, meta-analysis suggests that PACAP might share signaling pathways with  $\text{TNF}\alpha$  and  $\text{TGF}\beta$ . In addition, it may utilize a converging trans-activator, *C/EBP* in addition to its known activation of MAP kinases, PKA, calcineurin, PKA, and *CREB*, to exert its pleiotropic effects on neuronal differentiation and slow transmission.

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## Figure Legends:

**Figure 1. Regulatory networks for PACAP-dependent transcripts in BCC (bovine chromaffin cells).** Transcripts with an abundance of two-fold or greater in PACAP-treated (6 h) compared to vehicle-treated bovine chromaffin cells by two-color microarray analysis (187 transcripts; see Supplementary Table S2) were used as the input for analysis of potential networks using the signal transduction knowledge environment of Ingenuity (<http://www.ingenuity.com>). **a.** Network solely involving 35 PACAP-regulated transcripts. **b.** Network involving 16 PACAP-regulated transcripts and 12 additional components with Ingenuity-confirmed direct or indirect links to them. **c.** Network involving 12 PACAP-regulated transcripts and 8 additional components with Ingenuity-confirmed direct or indirect links to them. PACAP-regulated transcripts are depicted in gray and linked components in white. Circular lines above symbols indicate auto-regulation; connecting lines without arrows indicate direct protein interaction deduced from either yeast two-hybrid, enzymatic, or immunoprecipitation assays; dashed and solid arrows indicate indirect (e.g. regulation of mRNA levels) and direct (e.g. enzymatic) activation, and lines ending in orthogonal dash indicate inhibition. Symbols and notations used by the Ingenuity Pathway Assistant in assembling of the networks shown in this and subsequent figures are as follows. The node shapes denote enzymes ( $\diamond$ ), phosphatases ( $\triangle$ ), kinases ( $\nabla$ ), peptidases ( $\langle \diamond \rangle$ ), G-protein coupled receptor ( $\square$ ), transmembrane receptor ( $\circ$ ), cytokines ( $\square$ ), growth factor ( $\square$ ), ion channel ( $\square$ ), transporter ( $\triangle$ ), translation factor ( $\diamond$ ), nuclear receptor ( $\square$ ), transcription factor ( $\circ$ ), and other ( $\circ$ ). The edge labels (when included) are represented as follows: A, activation, deactivation; B, binding; E, expression; I, inhibition; L, proteolysis; M, biochemical modification; O, other; P, phosphorylation, dephosphorylation; T, transcription. Edge types include solid lines, direct interactions; dotted lines, indirect interactions; lines without arrows, binding only; arrows, factor acting upon factor nearest to arrowhead; lines terminating in short orthogonal line, inhibition of factor closest to orthogonal line; lines terminating in a combination of the last two edge types, both action upon and inhibition of factor closest to arrowhead. All gene products are defined in the glossary in Supplementary Table S5, which includes active links to Entrez Gene for each component.

**Figure 2. Regulatory networks for PACAP-dependent transcripts in PC12 cells.** Transcripts with an abundance two-fold or greater in PACAP-treated PC12 cells at 0 to 6 h (deduced from cycloheximide superinduction at 6 h), 6 h, or 48 h (168 transcripts; see Supplementary Table S3 and references [28, 45, 57] respectively) were used as the input for analysis of regulatory networks using Ingenuity as described in Figure 1. **a.** Network involving 15 PACAP-regulated transcripts and 5 additional components with Ingenuity-confirmed direct or indirect links. **b.** Network involving 14 PACAP-regulated transcripts and 11 additional components with Ingenuity-confirmed direct or indirect links. Symbols and abbreviations are as described in Figure 1 and Supplementary Table S5.

**Figure 3. Regulatory networks for PACAP-dependent transcripts in middle cerebral artery occlusion (MCAO).** Up-regulated transcripts in wild-type compared to PACAP-deficient mice **a.** 1 h and **b.** 24 h after MCAO. 64 and 74 transcripts respectively (see

Supplementary Table S4 and reference [15]) were used as the input for analysis of regulatory networks using Ingenuity as described in Figure 1. **a.** Network involving 15 PACAP-regulated transcripts and 17 additional components with Ingenuity-confirmed direct or indirect links. **b.** Network involving 15 PACAP-regulated transcripts and 20 additional components with Ingenuity-confirmed direct or indirect links. Symbols and abbreviations are as described in Figure 1 and Supplementary Table S5.

**Figure 4. Regulatory networks for PACAP-dependent transcripts in PC12 cells and MAG, BCC or MCAO.** PACAP-regulated transcripts common to PC12 cells and either MAG, BCC or cerebral cortex in MCAO as listed in Table 2 were used as input for analysis of regulatory networks using Ingenuity as described in Figure 1. **a.** Network involving 13 PACAP-regulated transcripts and 5 additional components with Ingenuity-confirmed direct or indirect links. **b.** Network involving 8 PACAP-regulated transcripts and 17 additional components with Ingenuity-confirmed direct or indirect links. Symbols and abbreviations are as described in Figure 1 and Supplementary Table S5.

#### **Supplementary Table Legends:**

##### **Supplementary Table S1. MAG Transcripts.**

Entrez GeneID, Gene Symbol, Gene Description and Fold Change. The Fold Change is the linear SAM mean value for the red:green ratio (wild-type:PACAP-deficient) for the 228 transcripts up-regulated in wild-type versus PACAP-deficient mouse adrenal gland.

##### **Supplementary Table S2. BCC Transcripts.**

Entrez GeneID, Gene Symbol, Gene Description and Fold Change. The Fold Change is the linear SAM mean value for the red:green ratio (PACAP-treated BCC:vehicle-treated BCC) for the 187 transcripts up-regulated in PACAP-treated versus vehicle-treated BCCs.

##### **Supplementary Table S3. PC12 Transcripts.**

Entrez GeneID, Gene Description, Gene Symbol for the 168 transcripts previously reported to be up-regulated in either 6-h cycloheximide plus PACAP-treated PC12 cells but not by PACAP alone during this time period (PC12—0 to 6 h: see [45]), or in PC12 cells treated with PACAP at 6 h versus untreated cells (PC12—6 h: see [57]), or in PC12 cells treated with PACAP for 48 hours (PC12—48 h: see [28]) Filled cells: up-regulation of this transcript under the given condition; unfilled cells-no up-regulation of this transcript under the given condition.

##### **Supplementary Table S4. MCAO Transcripts.**

Entrez Gene ID, Gene Symbol, Gene Description of transcripts up-regulated in wild-type but not in PACAP-deficient mouse cortex 1 h or 24 h following MCAO (see [15]).

##### **Supplementary Table S5. Gene Glossary**

Gene Symbol, Synonyms, Gene Description, Encoded Protein Location, Protein Family, and Human, Mouse and Rat GeneIDs for the 212 components of Figures 1-4.

**Table 1. Mouse Adrenal Gland and Bovine Chromaffin Cell Microarray Analysis.**

Source of Transcriptome	Number of Arrays	Clones per Array	FDR	Named Upregulated Genes	Named Upregulated Genes > 2-fold
MAG	6	29686	0.014	1353	228
BCC	4	21795	0.100	340	187

cDNA from mouse adrenal gland (MAG) of wild-type versus PACAP-deficient animals was hybridized and represented as wild-type:PACAP-deficient ratio for each gene (i.e. up-regulation refers to greater transcript abundance in wild-type than in PACAP-deficient MAG). cDNA from bovine chromaffin cells (BCC) of 6-h PACAP-treated (100 nM PACAP-27) versus untreated cells hybridized and represented as PACAP-treated:untreated ratio for each gene (i.e. up-regulation refers to greater transcript abundance in PACAP-treated than in untreated cells). Each array consisted in a separate paired experiment. The number of clones per array shown above represents the gene targets passing the filter for signal quality in each set (see Materials and Methods). Significantly up-regulated transcripts were those determined using SAM (statistical analysis of microarrays) at the false discovery rates (FDR) shown, after filtration for named genes (Named Upregulated) and after further filtration to remove values less than two-fold upregulated (Named Upregulated Genes > 2-fold).

**Table 2. PACAP-dependent Transcripts in PC12 Cells and MAG, BCC or MCAO.**

<b>GeneID</b>	<b>Gene Name</b>	<b>Gene Symbol</b>	<b>PC12</b>	<b>MAG</b>	<b>BCC</b>	<b>MCAO</b>
12306	Annexin A2	Anxa2				
71994	Calponin 3, acidic	Cnn3				
13205	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 3, X-linked	Ddx3x				
11789	Adenomatosis polyposis coli	Apc				
12227	B-cell translocation gene 2, anti-proliferative	Btg2				
67579	Cytoplasmic polyadenylation element binding protein 4	Cpeb4				
20321	Ferric-chelate reductase 1	Frrs1				
52118	Poliovirus receptor	Pvr				
83486	RNA binding motif protein 5	Rbm5				
19735	Regulator of G-protein signaling 2	Rgs2				
29871	Sex comb on midleg homolog 1	Scmh1				
11843	ADP-ribosylation factor 4	Arf4				
54375	Antizyme inhibitor 1	Azin1				
12653	Chromogranin B	Chgb				
239528	Eukaryotic translation initiation factor 2C, 2	Eif2c2				
13684	Eukaryotic translation initiation factor 4E	Eif4e				
107508	Glutamyl-prolyl-tRNA synthetase	Eprs				
319448	Fibronectin type III domain containing 3a	Fndc3a				
18148	Nucleophosmin 1	Npm1				
20848	Signal transducer and activator of transcription 3	Stat3				
326618	Tropomyosin 4	Tpm4				
50770	ATPase, class VI, type 11A	Atp11a				
12512	Cd63 antigen	Cd63				
14284	Fos-like antigen 2	Fosl2				
15937	Immediate early response 3	Ier3				
75909	Transmembrane protein 49	Tmem49				

PACAP-responsive transcripts identified in the six data sets described in Table 1 and Tables S1-S4 and regulated in both the anchor set (PC12 cells; Table S4) and at least one other (mouse adrenal gland, MAG; bovine chromaffin cells, BCC; mouse middle cerebral artery occlusion model, MCAO) are depicted. Filled square, transcript elevated at least 2-fold; empty square, transcript not significantly elevated.

Abbreviations used:

ACh	acetylcholine
BCC	bovine chromaffin cells
BDNF	brain-derived neurotrophic factor
BMAP1/2	Brain Molecular Anatomy Project clone sets 1 and 2
BMPR2	bone morphogenic protein receptor, type II (serine/threonine kinase)
Btg2	B-cell translocation gene 2, anti-proliferative
cAMP	3'-5'-cyclic adenosine monophosphate
cDNA	complementary DNA (deoxyribonucleic acid)
CHX	cycloheximide
CNS	central nervous system
DNA	deoxyribonucleic acid
ERK	Extracellular signal-regulated protein kinase
EST	expressed sequence tag
FDR	false discovery rate
GIPO	gene in position order
GSK	glycogen synthase kinase
HUGO	Human Genome Organisation
Jarid1c	jumonji, AT rich interactive domain 1C
mAdb	<u>microArray database</u>
MAG	mouse adrenal gland
MAPK	Mitogen-activated protein kinase
MCAO	middle cerebral artery occlusion
mRNA	messenger ribonucleic acid
NFκB	nuclear factor of kappa light chain gene enhancer in B-cells 1, p105
NHGRI	National Human Genome Research Institute
NIA	National Institute on Aging
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NINDS	National Institute of Neurological Disorders and Stroke
NPY	neuropeptide tyrosine
OMIM	Online Mendelian Inheritance in Man
PACAP	pituitary adenylate cyclase-activating polypeptide
PBS	phosphate-buffered saline
PC12	rat pheochromocytoma cells
pdf	portable document format
PNMT	phenylethanolamine N-methyltransferase
PNS	peripheral nervous system
RNA	ribonucleic acid
SAM	Significance Analysis of Microarrays
SCMH1	sex comb on midleg homolog 1
Smad	MAD homolog 1
SSH	suppression subtractive hybridization
STAT	signal transducer and activator of transcription
TFGβ	transforming growth factor, beta 1
TH	tyrosine hydroxylase



TNF $\alpha$	tumor necrosis factor, alpha
VIP	vasoactive intestinal polypeptide
YWHAZ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide

Note: Abbreviations for molecules in the Abbreviation Table above obtained from <http://www.ihop-net.org/UniPub/iHOP/>. Supplementary Table S5 is a glossary for all additional abbreviations found in Figures 1-4.

Figure 1a BCC

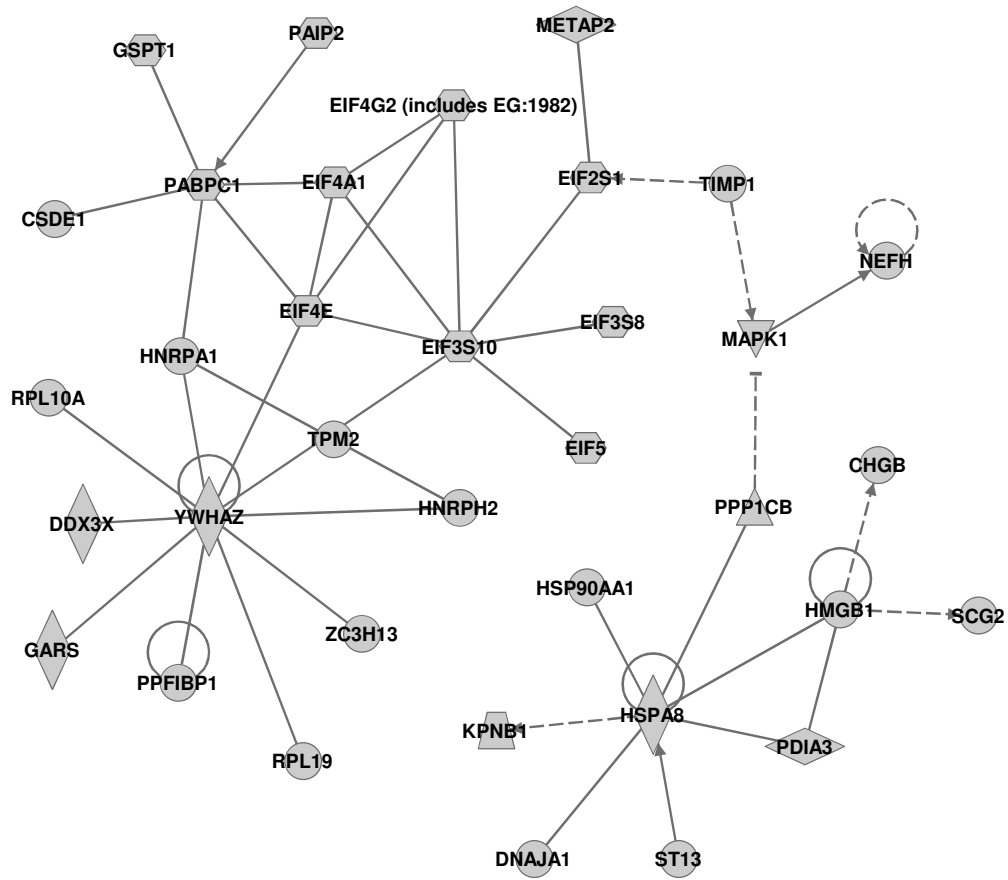


Figure 1b BCC

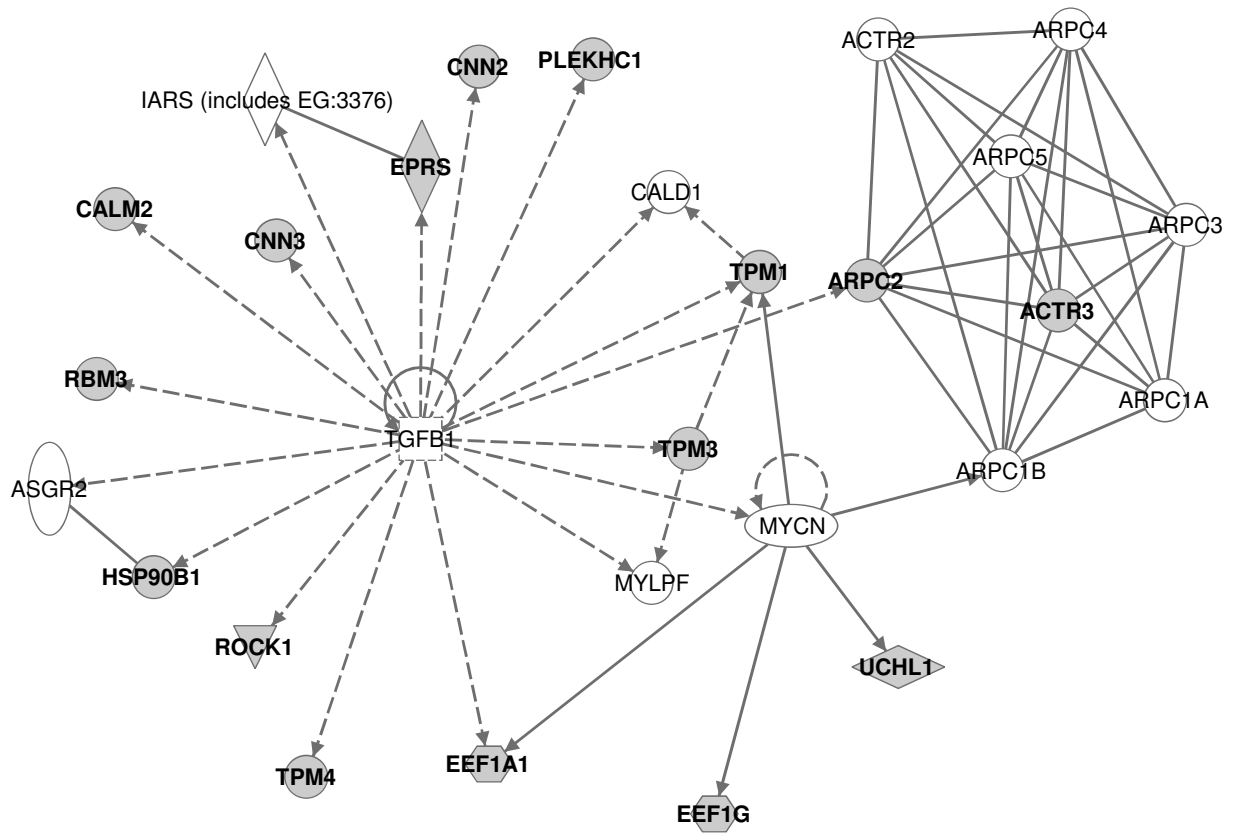


Figure 1c BCC

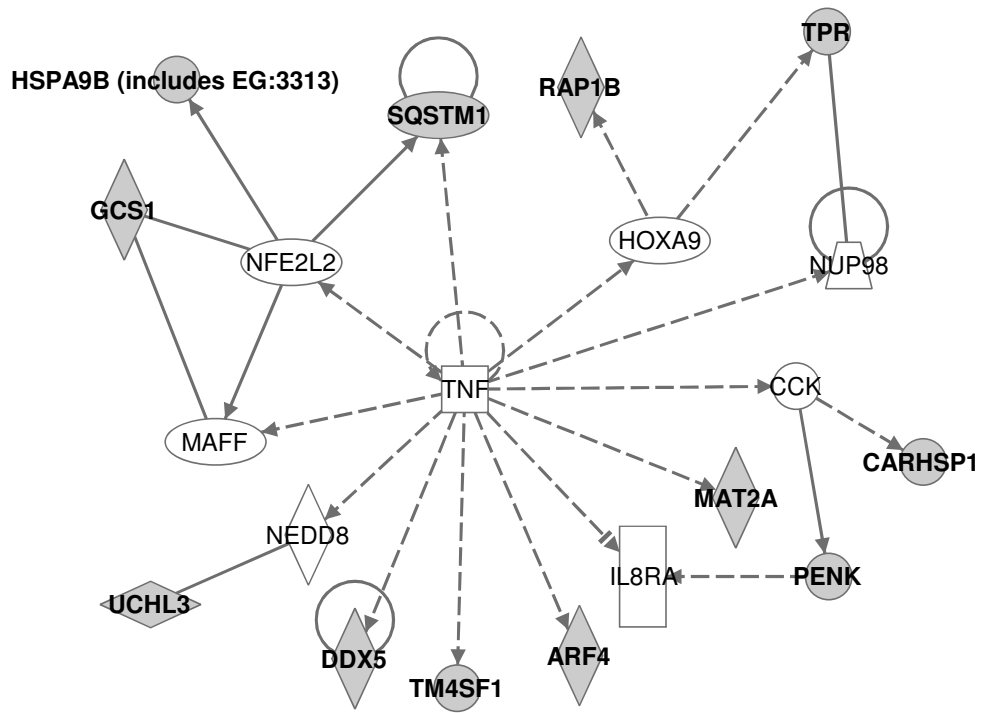


Figure 2a PC12

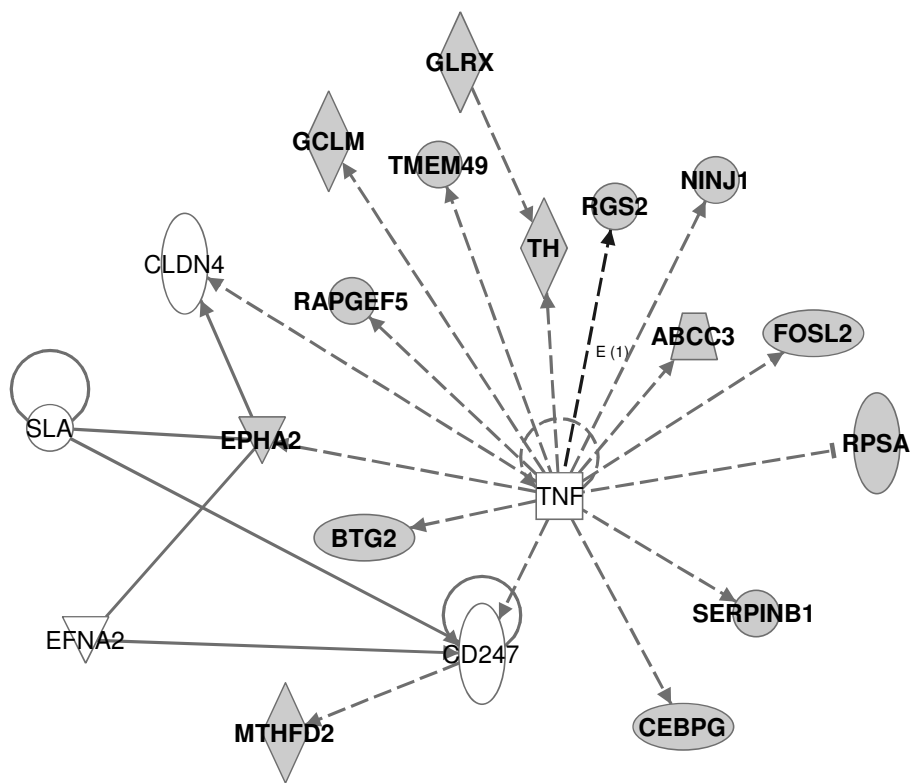


Figure 2b PC12

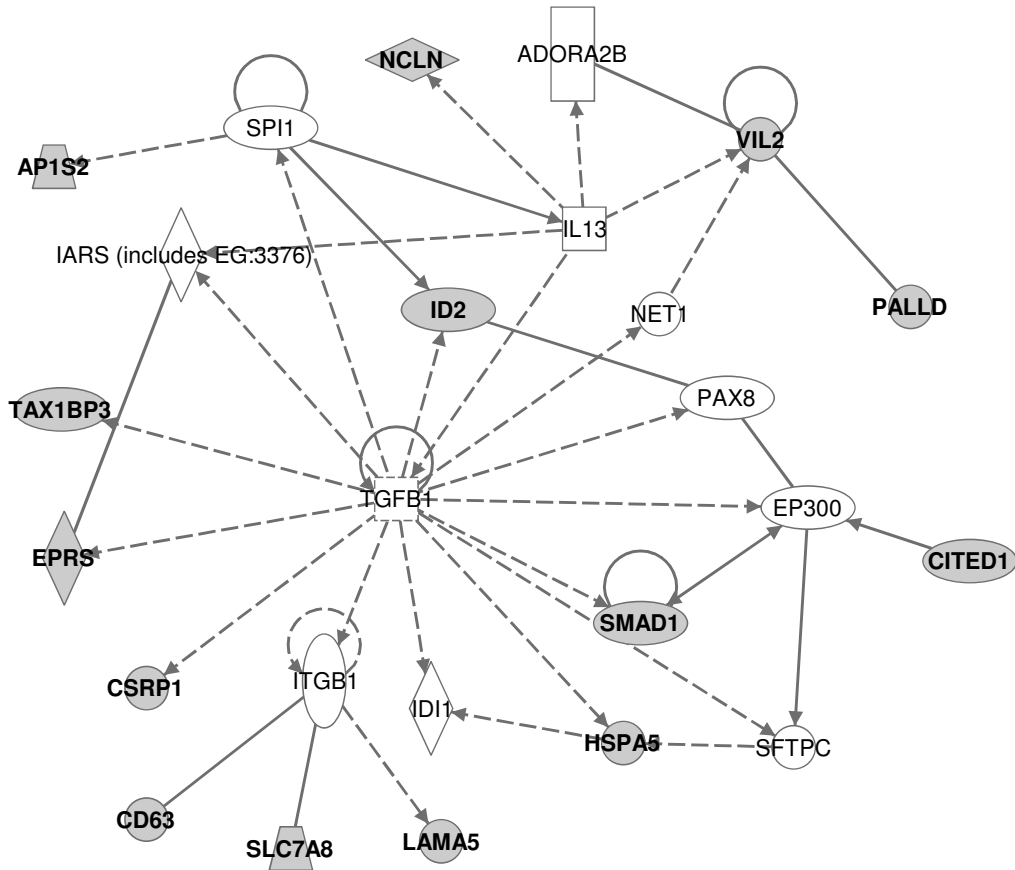


Figure 3a MCAO 1 hr

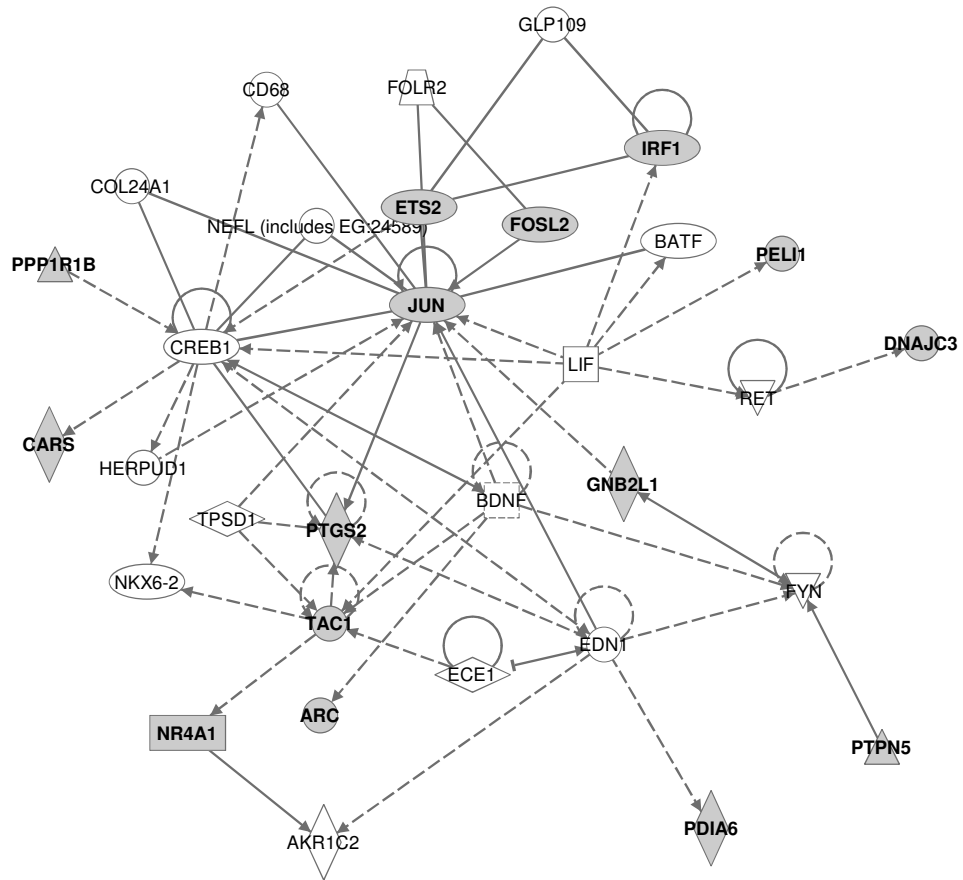


Figure 3b MCAO 24hr

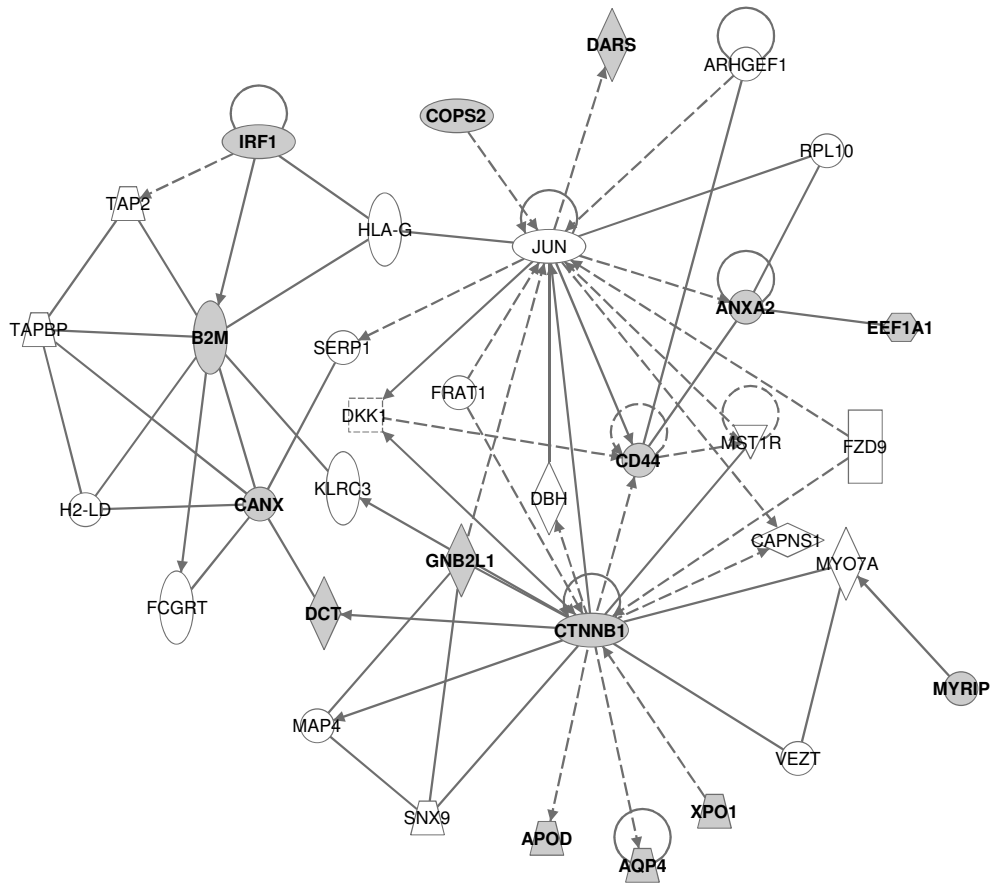




Figure 4a Composite

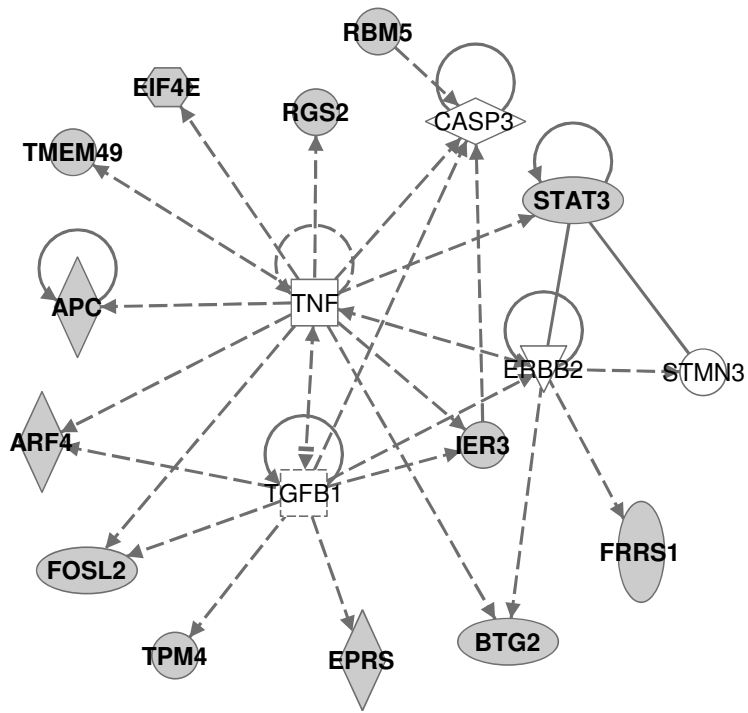
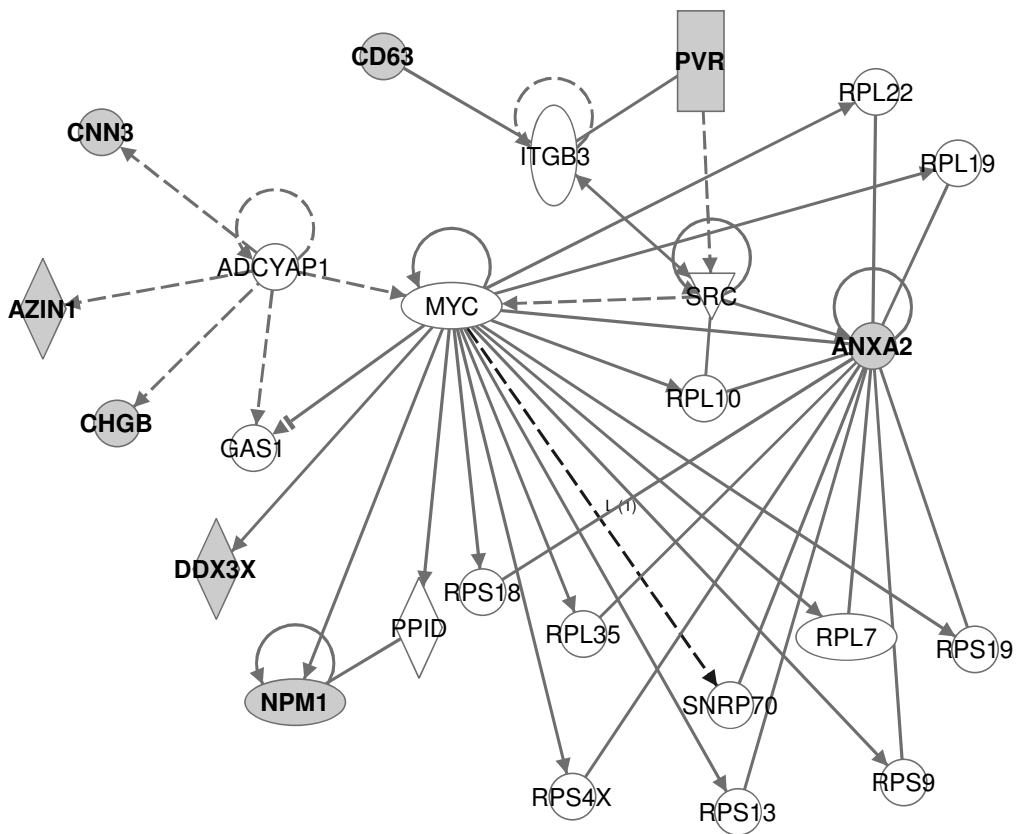


Figure 4b Composite



**Supplementary Table S1-MAG Transcripts**

Entrez GeneID	Gene Symbol	Gene Description	fold change
21923	Tnc	Tenascin C	4.26
16593	Kns2	Kinesin 2	3.71
13542	Dvl1	Dishevelled, dsh homolog 1 (Drosophila)	3.49
29871	Scmh1	Sex comb on midleg homolog 1	3.39
11602	Angpt4	Angiopoietin 4	3.34
52808	Tspyl2	TSPY-like 2	3.27
22190	Ubc	Ubiquitin C	3.22
26374	Rfwd2	Ring finger and WD repeat domain 2	3.20
52118	Pvr	Poliovirus receptor	3.19
320472	Ppm1e	Protein phosphatase 1E (PP2C domain containing)	3.05
13627	Eef1a1	Eukaryotic translation elongation factor 1 alpha 1	3.01
76025	Cant1	Calcium activated nucleotidase 1	2.94
19335	Rab23	RAB23, member RAS oncogene family	2.90
67785	Zmym4	Zinc finger, MYM-type 4	2.87
12313	Calm1	Calmodulin 1	2.80
553127	Cxx1b	CAAX box 1 homolog B (human)	2.79
20527	Slc2a3	Solute carrier family 2 (facilitated glucose transporter), member 3	2.73
51810	Hnrpu	Heterogeneous nuclear ribonucleoprotein U	2.73
19735	Rgs2	Regulator of G-protein signaling 2	2.73
54151	Cyhr1	Cysteine and histidine rich 1	2.72
26926	Pcd8	Programmed cell death 8	2.70
51791	Rgs14	Regulator of G-protein signaling 14	2.69
63872	Zfp296	Zinc finger protein 296	2.68
58810	Akr1a4	Aldo-keto reductase family 1, member A4 (aldehyde reductase)	2.67
55988	Snx12	Sorting nexin 12	2.67
66898	Baiap2l1	BAI1-associated protein 2-like 1	2.66
319455	Pld5	Phospholipase D family, member 5	2.63
15502	Dnaj1	DnaJ (Hsp40) homolog, subfamily A, member 1	2.63
65970	Lima1	LIM domain and actin binding 1	2.60
12747	Clk1	CDC-like kinase 1	2.58
14694	Gnb2l1	Guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1	2.58
15494	Hsd3b3	Hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-5-isomerase	2.57
22070	Tpt1	Tumor protein, translationally-controlled 1	2.56
71720	Osbpl3	Oxysterol binding protein-like 3	2.55
74901	Kbtbd11	Kelch repeat and BTB (POZ) domain containing 11	2.53
544963	Iqgap2	IQ motif containing GTPase activating protein 2	2.52
17775	Laptn4a	Lysosomal-associated protein transmembrane 4A	2.50

228961	Npepl1	Aminopeptidase-like 1	2.49
18671	Abcb1a	ATP-binding cassette, sub-family B (MDR/TAP), member 1A	2.48
67963	Npc2	Niemann Pick type C2	2.48
236266	Alms1	Alstrom syndrome 1 homolog (human)	2.46
14799	Gria1	Glutamate receptor, ionotropic, AMPA1 (alpha 1)	2.46
65019	Rpl23	Ribosomal protein L23	2.45
228543	Rhov	Ras homolog gene family, member V	2.45
78294	Rps27a	Ribosomal protein S27a	2.45
140858	Wdr5	WD repeat domain 5	2.45
71770	Ap2b1	Adaptor-related protein complex 2, beta 1 subunit	2.44
399510	Map4k5	Mitogen-activated protein kinase kinase kinase 5	2.44
14897	Trip12	Thyroid hormone receptor interactor 12	2.44
14325	Ftl1	Ferritin light chain 1	2.43
225027	Sfrs7	Splicing factor, arginine/serine-rich 7	2.43
385354	Frmd7	FERM domain containing 7	2.42
26943	Serinc3	Serine incorporator 3	2.42
11757	Prdx3	Peroxiredoxin 3	2.41
17252	Rdh11	Retinol dehydrogenase 11	2.41
244329	Mcp1	Microcephaly, primary autosomal recessive 1	2.41
102693	Phldb1	Pleckstrin homology-like domain, family B, member 1	2.41
107829	Thoc5	THO complex 5	2.40
17436	Mod1	Malic enzyme, supernatant	2.40
19012	Ppap2a	Phosphatidic acid phosphatase 2a	2.40
12321	Calu	Calumenin	2.39
19672	Rcn1	Reticulocalbin 1	2.39
22021	Tpst1	Protein-tyrosine sulfotransferase 1	2.38
28295	D10Jhu81e	DNA segment, Chr 10, Johns Hopkins University 81 expresse	2.38
67579	Cpeb4	Cytoplasmic polyadenylation element binding protein 4	2.38
13829	Epb4.9	Erythrocyte protein band 4.9	2.38
12842	Col1a1	Procollagen, type I, alpha 1	2.37
17761	Mtap7	Microtubule-associated protein 7	2.37
18477	Prdx1	Peroxiredoxin 1	2.36
68041	Mid1ip1	Mid1 interacting protein 1 (gastrulation specific G12-like (zebrafish))	2.36
22187	Ubb	Ubiquitin B	2.36
12825	Col3a1	Procollagen, type III, alpha 1	2.36
13205	Ddx3x	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 3, X-linked	2.35
22027	Hsp90b1	Heat shock protein 90kDa beta (Grp94), member 1	2.35
15492	Hsd3b1	Hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid d	2.35
18578	Pde4b	Phosphodiesterase 4B, cAMP specific	2.34

13144	Dapk3	Death-associated kinase 3	2.34
67916	Ppap2b	Phosphatidic acid phosphatase type 2B	2.34
68095	Ociad1	OCIA domain containing 1	2.34
78926	Gas2l1	Growth arrest-specific 2 like 1	2.33
74155	Errf1	ERBB receptor feedback inhibitor 1	2.33
20684	Sp100	Nuclear antigen Sp100	2.33
140577	Ankrd6	Ankyrin repeat domain 6	2.33
21672	Prdx2	Peroxiredoxin 2	2.31
72898	Asphd2	Aspartate beta-hydroxylase domain containing 2	2.30
12305	Ddr1	Discoidin domain receptor family, member 1	2.30
98732	Rab3gap2	RAB3 GTPase activating protein subunit 2	2.29
23856	Dido1	Death inducer-obliterator 1	2.29
75739	Mpp7	Membrane protein, palmitoylated 7 (MAGUK p55 subfamily m	2.28
16528	Kcnk4	Potassium channel, subfamily K, member 4	2.28
27981	D4Wsu53e	DNA segment, Chr 4, Wayne State University 53, expressed	2.28
14664	Slc6a9	Solute carrier family 6 (neurotransmitter transporter, glycine),	2.28
52206	Anapc4	Anaphase promoting complex subunit 4	2.28
11837	Arbp	Acidic ribosomal phosphoprotein P0	2.27
27367	Rpl3	Ribosomal protein L3	2.27
78943	Ern1	Endoplasmic reticulum (ER) to nucleus signalling 1	2.26
20638	Snrpb	Small nuclear ribonucleoprotein B	2.26
22284	Usp9x	Ubiquitin specific peptidase 9, X chromosome	2.26
67030	Fancl	Fanconi anemia, complementation group L	2.26
54208	Arl6ip1	ADP-ribosylation factor-like 6 interacting protein 1	2.25
229279	Hnrpa3	Heterogeneous nuclear ribonucleoprotein A3	2.24
22381	Wbp5	WW domain binding protein 5	2.24
83486	Rbm5	RNA binding motif protein 5	2.24
13135	Dad1	Defender against cell death 1	2.23
93961	B3galt5	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypep	2.23
227154	Als2cr2	Amyotrophic lateral sclerosis 2 (juvenile) chromosome region,	2.23
227331	Tnrc15	Trinucleotide repeat containing 15	2.23
19290	Pura	Purine rich element binding protein A	2.22
210146	Irgq	Immunity-related GTPase family, Q	2.22
252870	Usp7	Ubiquitin specific peptidase 7	2.22
19983	Rpl5	Ribosomal protein L5	2.22
71994	Cnn3	Calponin 3, acidic	2.22
20652	Soat1	Sterol O-acyltransferase 1	2.22
20220	Sap18	Sin3-associated polypeptide 18	2.22
20130	Rras	Harvey rat sarcoma oncogene, subgroup R	2.21

17391	Mmp24	Matrix metalloproteinase 24	2.21
19125	Prodh	Proline dehydrogenase	2.21
52231	D1Ert161e	DNA segment, Chr 1, ERATO Doi 161, expressed	2.20
212518	Sprn	Shadow of prion protein	2.20
108100	Baiap2	Brain-specific angiogenesis inhibitor 1-associated protein 2	2.20
12894	Cpt1a	Carnitine palmitoyltransferase 1a, liver	2.20
226849	Ppp2r5a	Protein phosphatase 2, regulatory subunit B (B56), alpha isoform	2.20
13202	Ddt	D-dopachrome tautomerase	2.19
53333	Tomm40	Translocase of outer mitochondrial membrane 40 homolog (yeast)	2.19
208628	Kntc1	Kinetochore associated 1	2.19
12227	Btg2	B-cell translocation gene 2, anti-proliferative	2.19
11819	Nr2f2	Nuclear receptor subfamily 2, group F, member 2	2.18
77044	Arid2	AT rich interactive domain 2 (Arid-rfx like)	2.18
66480	Rpl15	Ribosomal protein L15	2.18
12759	Clu	Clusterin	2.17
228876	Zfp334	Zinc finger protein 334	2.17
15926	Idh1	Isocitrate dehydrogenase 1 (NADP+), soluble	2.16
94109	Csmd1	CUB and Sushi multiple domains 1	2.16
330171	Kctd10	Potassium channel tetramerisation domain containing 10	2.16
320799	Zhx3	Zinc fingers and homeoboxes 3	2.16
12570	Cdk5r2	Cyclin-dependent kinase 5, regulatory subunit 2 (p39)	2.16
105445	Dock9	Dedicator of cytokinesis 9	2.16
230163	Aldob	Aldolase 2, B isoform	2.15
74493	Tnks2	Tankyrase, TRF1-interacting ankyrin-related ADP-ribose polymerase 2	2.15
56442	Serinc1	Serine incorporator 1	2.15
65963	Tmem176b	Transmembrane protein 176B	2.14
12306	Anxa2	Annexin A2	2.14
27632	Rdbp	RD RNA-binding protein	2.14
11773	Ap2m1	Adaptor protein complex AP-2, mu1	2.14
14793	Cdca3	Cell division cycle associated 3	2.14
14683	Gnas	GNAS (guanine nucleotide binding protein, alpha stimulating)	2.14
20255	Scg3	Secretogranin III	2.14
11842	Arf3	ADP-ribosylation factor 3	2.13
12876	Cpe	Carboxypeptidase E	2.13
110196	Fdps	Farnesyl diphosphate synthetase	2.12
67247	Mosc2	MOCO sulphurase C-terminal domain containing 2	2.12
23999	Ptk9l	Protein tyrosine kinase 9-like (A6-related protein)	2.12
21858	Timp2	Tissue inhibitor of metalloproteinase 2	2.12
71389	Chd6	Chromodomain helicase DNA binding protein 6	2.12

56706	Ccn1	Cyclin L1	2.12
330593	5430421B17	Hypothetical protein 5430421B17	2.12
246710	Rhobtb2	Rho-related BTB domain containing 2	2.11
66335	Atp6v1c1	VATPase, H+ transporting, lysosomal V1 subunit C1	2.11
22619	Siae	Sialic acid acetyltransferase	2.11
319710	Frmd6	FERM domain containing 6	2.11
192662	Arhgdia	Rho GDP dissociation inhibitor (GDI) alpha	2.10
11947	Atp5b	ATP synthase, H+ transporting mitochondrial F1 complex, beta	2.10
72141	Adpgk	ADP-dependent glucokinase	2.10
22385	Baz1b	Bromodomain adjacent to zinc finger domain, 1B	2.10
12577	Cdkn1c	Cyclin-dependent kinase inhibitor 1C (P57)	2.10
17999	Nedd4	Neural precursor cell expressed, developmentally down-regulated	2.09
29812	Ndr3	N-myc downstream regulated gene 3	2.09
74479	Snx11	Sorting nexin 11	2.08
18538	Pcna	Proliferating cell nuclear antigen	2.08
56297	Arl6	ADP-ribosylation factor-like 6	2.08
68628	Fbxw9	F-box and WD-40 domain protein 9	2.08
22123	Psm3	Proteasome (prosome, macropain) 26S subunit, non-ATPase	2.08
27058	Srp9	Signal recognition particle 9	2.08
11789	Apc	Adenomatous polyposis coli	2.08
20104	Rps6	Ribosomal protein S6	2.08
52906	Ahi1	Abelson helper integration site	2.08
15108	Hadh2	Hydroxyacyl-Coenzyme A dehydrogenase type II	2.08
76233	Dntip1	Deoxynucleotidyltransferase, terminal, interacting protein 1	2.07
67945	Rpl41	Ribosomal protein L41	2.07
66890	Lman2	Lectin, mannose-binding 2	2.07
12268	C4b	Complement component 4B (Childo blood group)	2.07
93834	Peli2	Pellino 2	2.07
107035	Fbxo38	F-box protein 38	2.07
84113	Ptov1	Prostate tumor over expressed gene 1	2.07
22288	Utrn	Utrophin	2.07
67891	Rpl4	Ribosomal protein L4	2.06
68565	Mrps18a	Mitochondrial ribosomal protein S18A	2.06
235402	Lrrn6a	Leucine rich repeat neuronal 6A	2.06
12497	Entpd6	Ectonucleoside triphosphate diphosphohydrolase 6	2.06
21356	Tapbp	TAP binding protein	2.06
52696	Zwint	ZW10 interactor	2.05
54633	Pqbp1	Polyglutamine binding protein 1	2.05
353190	Edc3	Enhancer of mRNA decapping 3 homolog (S. cerevisiae)	2.05

382056	Crtc1	CREB regulated transcription coactivator 1	2.04
20591	Jarid1c	Jumonji, AT rich interactive domain 1C (Rbp2 like)	2.04
83701	Ars2	Arsenate resistance protein 2	2.04
22154	Tubb5	Tubulin, beta 5	2.04
66383	Iscu	IscU iron-sulfur cluster scaffold homolog (E. coli)	2.04
11740	Slc25a5	Solute carrier family 25 (mitochondrial carrier, adenine nucleo	2.04
105559	Mbnl2	Muscleblind-like 2	2.03
22763	Zfr	Zinc finger RNA binding protein	2.03
110147	Ehmt2	Euchromatic histone lysine N-methyltransferase 2	2.03
21413	Tcf4	Transcription factor 4	2.03
68342	Ndufb10	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 10	2.03
12988	Csk	C-src tyrosine kinase	2.03
21849	Trim28	Tripartite motif protein 28	2.03
26895	Cops7b	COP9 (constitutive photomorphogenic) homolog, subunit 7b (u	2.02
269788	Lhfp14	Lipoma HMGIC fusion partner-like protein 4	2.02
54161	Copg	Coatomer protein complex, subunit gamma	2.02
17191	Mbd2	Methyl-CpG binding domain protein 2	2.02
67155	Smarca2	SWI/SNF related, matrix associated, actin dependent regulato	2.02
209446	Tcf3	Transcription factor E3	2.02
12444	Ccnd2	Cyclin D2	2.02
18039	Nefl	Neurofilament, light polypeptide	2.02
20321	Frrs1	Ferric-chelate reductase 1	2.02
13039	Ctsl	Cathepsin L	2.02
18542	Pcolce	Procollagen C-endopeptidase enhancer protein	2.01
20501	Slc16a1	Solute carrier family 16 (monocarboxylic acid transporters), m	2.01
76477	Pcolce2	Procollagen C-endopeptidase enhancer 2	2.01
12168	Bmpr2	Bone morphogenic protein receptor, type II (serine/threonine k	2.01
12833	Col6a1	Procollagen, type VI, alpha 1	2.01
71207	Nudt4	Nudix (nucleoside diphosphate linked moiety X)-type motif 4	2.01
67501	Ccdc50	Coiled-coil domain containing 50	2.01
11987	Slc7a1	Solute carrier family 7 (cationic amino acid transporter, y+ sys	2.01
74142	Lonp1	Lon peptidase 1, mitochondrial	2.01
50795	Sh3bgr	SH3-binding domain glutamic acid-rich protein	2.00
71732	Vps11	Vacuolar protein sorting 11 (yeast)	2.00
98402	Sh3bp4	SH3-domain binding protein 4	2.00



**Supplementary Table S2-BCC Transcripts**

Entrez GeneID	Gene Symbol	Gene Description	fold change
21333	Tac1	Tachykinin 1	13.8
13175	Dcamk1	Doublecortin and calcium/calmodulin-dependent protein kinase-like 1	6.53
68730	Dus1l	Dihydrouridine synthase 1-like ( <i>S. cerevisiae</i> )	5.88
16451	Jak1	Janus kinase 1	4.12
215351	Senp6	SUMO/sentrin specific peptidase 6	3.82
216618	Ccdc104	Coiled-coil domain containing 104	3.53
13205	Ddx3x	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 3, X-linked	3.49
15251	Hif1a	Hypoxia inducible factor 1, alpha subunit	3.26
51810	Hnrpu	Heterogeneous nuclear ribonucleoprotein U	3.16
21808	Tgfb2	Transforming growth factor, beta 2	3.13
12916	Crem	CAMP responsive element modulator	3.09
101490	Inpp5f	Inositol polyphosphate-5-phosphatase F	3.05
66912	Bzw2	Basic leucine zipper and W2 domains 2	3.02
11938	Atp2a2	ATPase, Ca <sup>++</sup> transporting, cardiac muscle, slow twitch 2	3.01
16573	Kif5b	Kinesin family member 5B	3
52502	Carhsp1	Calcium regulated heat stable protein 1	2.99
72289	Malat1	Metastasis associated lung adenocarcinoma transcript 1 (non-coding RNA)	2.98
17112	Tm4sf1	Transmembrane 4 superfamily member 1	2.96
26950	Vsnl1	Visinin-like 1	2.94
18619	Enk	Enk	2.94
170719	Oxr1	Oxidation resistance 1	2.94
15519	Hsp90aa1	Heat shock protein 90kDa alpha (cytosolic), class A member 1	2.88
218952	Plekhc1	Pleckstrin homology domain containing, family C (with FERM domain) member 1	2.88
93762	Smarca5	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subf	2.85
19983	Rpl5	Ribosomal protein L5	2.82
18148	Npm1	Nucleophosmin 1	2.78
53379	Hnrpa2b1	Heterogeneous nuclear ribonucleoprotein A2/B1	2.77
215449	Rap1b	RAS related protein 1b	2.77
319448	Fndc3a	Fibronectin type III domain containing 3a	2.75
13684	Eif4e	Eukaryotic translation initiation factor 4E	2.75

20254	Scg2	Secretogranin II	2.74
13690	Eif4g2	Eukaryotic translation initiation factor 4, gamma 2	2.74
19346	Rab6	RAB6, member RAS oncogene family	2.73
15481	Hspa8	Heat shock protein 8	2.73
71799	Ptcd1	Pentatricopeptide repeat domain 1	2.71
76299	Txndc4	Thioredoxin domain containing 4 (endoplasmic reticulum)	2.7
380684	Nefh	Neurofilament, heavy polypeptide	2.67
67154	Mtdh	Metadherin	2.67
74117	Actr3	ARP3 actin-related protein 3 homolog (yeast)	2.66
22027	Hsp90b1	Heat shock protein 90kDa beta (Grp94), member 1	2.66
217869	Eif5	Eukaryotic translation initiation factor 5	2.61
56397	Morf4l2	Mortality factor 4 like 2	2.6
12653	Chgb	Chromogranin B	2.59
16412	Itgb1	Integrin beta 1 (fibronectin receptor beta)	2.59
57377	Gcs1	Glucosidase 1	2.59
67437	Ssr3	Signal sequence receptor, gamma	2.57
56258	Hnrph2	Heterogeneous nuclear ribonucleoprotein H2	2.57
71514	Sfpq	Splicing factor proline/glutamine rich (polypyrimidine tract binding protein associat	2.56
19244	Ptp4a2	Protein tyrosine phosphatase 4a2	2.55
17149	Magoh	Mago-nashi homolog, proliferation-associated (Drosophila)	2.55
12313	Calm1	Calmodulin 1	2.54
52666	D10Ert610e	DNA segment, Chr 10, ERATO Doi 610, expressed	2.53
20102	Rps4x	Ribosomal protein S4, X-linked	2.53
75423	Arl5a	ADP-ribosylation factor-like 5A	2.53
110960	Tars	Threonyl-tRNA synthetase	2.51
212712	Satb2	Special AT-rich sequence binding protein 2	2.5
20005	Rpl9	Ribosomal protein L9	2.5
13681	Eif4a1	Eukaryotic translation initiation factor 4A1	2.49
18458	Pabpc1	Poly A binding protein, cytoplasmic 1	2.49
50771	Atp9b	ATPas, class II, type 9B	2.49
50933	Uchl3	Ubiquitin carboxyl-terminal esterase L3 (ubiquitin thiolesterase)	2.47
71994	Cnn3	Calponin 3, acidic	2.47

67529	Fgfr1op2	FGFR1 oncogene partner 2	2.46
330938	Dixdc1	DIX domain containing 1	2.46
326618	Tpm4	Tropomyosin 4	2.45
12469	Cct8	Chaperonin subunit 8 (theta)	2.44
21761	Morf4l1	Mortality factor 4 like 1	2.44
76709	Arpc2	Actin related protein 2/3 complex, subunit 2	2.44
15289	Hmgb1	High mobility group box 1	2.42
21873	Tjp2	Tight junction protein 2	2.42
50926	Hnrpd1	Heterogeneous nuclear ribonucleoprotein D-like	2.42
226757	Wdr26	WD repeat domain 26	2.41
53324	Narp	Narp	2.41
54375	Azin1	Antizyme inhibitor 1	2.41
226982	Eif5b	Eukaryotic translation initiation factor 5B	2.38
66882	Bzw1	Basic leucine zipper and W2 domains 1	2.38
56543	Kcnd3	Potassium voltage-gated channel, Shal-related family, member 3	2.38
13207	Ddx5	DEAD (Asp-Glu-Ala-Asp) box polypeptide 5	2.37
67160	Eef1g	Eukaryotic translation elongation factor 1 gamma	2.37
20848	Stat3	Signal transducer and activator of transcription 3	2.36
107508	Eprs	Glutamyl-prolyl-tRNA synthetase	2.36
66645	Pspc1	Paraspeckle protein 1	2.34
11843	Arf4	ADP-ribosylation factor 4	2.33
74838	Narg1	NMDA receptor-regulated gene 1	2.33
12314	Calm2	Calmodulin 2	2.32
67891	Rpl4	Ribosomal protein L4	2.31
15502	Dnaja1	DnaJ (Hsp40) homolog, subfamily A, member 1	2.31
22712	Zfp54	Zinc finger protein 54	2.31
59069	Tpm3	Tropomyosin 3, gamma	2.3
16211	Kpnb1	Karyopherin (importin) beta 1	2.28
13627	Eef1a1	Eukaryotic translation elongation factor 1 alpha 1	2.28
15382	Hnrpa1	Heterogeneous nuclear ribonucleoprotein A1	2.28
57874	Ptplad1	Protein tyrosine phosphatase-like A domain containing 1	2.28
19877	Rock1	Rho-associated coiled-coil containing protein kinase 1	2.27

14827	Pdia3	Protein disulfide isomerase associated 3	2.27
14852	Gspt1	G1 to S phase transition 1	2.27
13669	Eif3s10	Eukaryotic translation initiation factor 3, subunit 10 (theta)	2.26
18139	Zfml	Zinc finger, matrin-like	2.26
69276	Tloc1	Translocation protein 1	2.26
67302	Zc3h13	Zinc finger CCCH type containing 13	2.25
640703	EG640703	Predicted gene, EG640703	2.24
12461	Cct2	Chaperonin subunit 2 (beta)	2.24
66870	Serbp1	Serpine1 mRNA binding protein 1	2.23
76295	Atp11b	ATPase, Class VI, type 11B	2.22
78257	Lrrc9	Leucine rich repeat containing 9	2.22
15526	Hspa9a	Heat shock protein 9A	2.22
68240	Rpa3	Replication protein A3	2.22
56354	Dnajc7	DnaJ (Hsp40) homolog, subfamily C, member 7	2.21
19046	Ppp1cb	Protein phosphatase 1, catalytic subunit, beta isoform	2.21
13665	Eif2s1	Eukaryotic translation initiation factor 2, subunit 1 alpha	2.2
667666	LOC667666	Similar to reduced expression 2	2.19
26900	Ddx3y	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, Y-linked	2.19
66105	Ube2d3	Ubiquitin-conjugating enzyme E2D 3 (UBC4/5 homolog, yeast)	2.19
19921	Rpl19	Ribosomal protein L19	2.18
108989	Tpr	Translocated promoter region	2.18
353172	Gars	Glycyl-tRNA synthetase	2.18
56445	Dnaja2	DnaJ (Hsp40) homolog, subfamily A, member 2	2.18
20384	Sfrs5	Splicing factor, arginine/serine-rich 5 (SRp40, HRS)	2.18
81898	Sf3b1	Splicing factor 3b, subunit 1	2.18
75302	Asxl2	Additional sex combs like 2 (Drosophila)	2.18
66244	Sdccag1	Serologically defined colon cancer antigen 1	2.17
66335	Atp6v1c1	VATPase, H+ transporting, lysosomal V1 subunit C1	2.17
232087	Mat2a	Methionine adenosyltransferase II, alpha	2.17
19652	Rbm3	RNA binding motif protein 3	2.17
28030	Gfm1	G elongation factor, mitochondrial 1	2.16
56403	Syncrip	Synaptotagmin binding, cytoplasmic RNA interacting protein	2.16

19896	Rpl10a	Ribosomal protein L10A	2.16
66177	Ubl5	Ubiquitin-like 5	2.15
216739	Acsl6	Acyl-CoA synthetase long-chain family member 6	2.15
276770	Eif5a	Eukaryotic translation initiation factor 5A	2.14
67869	Paip2	Polyadenylate-binding protein-interacting protein 2	2.14
22134	Tgoln1	Trans-golgi network protein	2.14
18738	Pitpna	Phosphatidylinositol transfer protein, alpha	2.13
17975	Ncl	Nucleolin	2.13
14618	Gjb1	Gap junction membrane channel protein beta 1	2.12
26413	Mapk1	Mitogen activated protein kinase 1	2.12
20191	Ryr2	Ryanodine receptor 2, cardiac	2.12
22589	Atrx	Alpha thalassemia/mental retardation syndrome X-linked homolog (human)	2.12
59027	Pbef1	Pre-B-cell colony-enhancing factor 1	2.11
12038	Bche	Butyrylcholinesterase	2.11
239528	Eif2c2	Eukaryotic translation initiation factor 2C, 2	2.1
381199	Tmem151	Transmembrane protein 151	2.09
26554	Cul3	Cullin 3	2.09
170763	Zfp87	Zinc finger protein 87	2.09
224902	Safb2	Scaffold attachment factor B2	2.09
17463	Psmc7	Proteasome (prosome, macropain) 26S subunit, non-ATPase, 7	2.09
11787	Apbb2	Amyloid beta (A4) precursor protein-binding, family B, member 2	2.08
76815	Ndp52	Nuclear domain 10 protein 52	2.08
12306	Anxa2	Annexin A2	2.08
69020	Zfp707	Zinc finger protein 707	2.08
67533	Ppfibp1	PTPRF interacting protein, binding protein 1 (liprin beta 1)	2.08
117198	Ivns1abp	Influenza virus NS1A binding protein	2.08
666841	LOC666841	Hypothetical protein LOC666841	2.08
19330	Rab18	RAB18, member RAS oncogene family	2.07
54214	Golga4	Golgi autoantigen, golgin subfamily a, 4	2.06
73274	Gppb1	GC-rich promoter binding protein 1	2.06
22413	Wnt2	Wingless-related MMTV integration site 2	2.06
24109	Ubl3	Ubiquitin-like 3	2.06

240753	Plekha6	Pleckstrin homology domain containing, family A member 6	2.05
19876	Robo1	Roundabout homolog 1 (Drosophila)	2.05
269593	Luzp1	Leucine zipper protein 1	2.04
19656	Rbmxrt	RNA binding motif protein, X chromosome retrogene	2.04
22631	Ywhaz	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta	2.04
65960	Twsg1	Twisted gastrulation homolog 1 (Drosophila)	2.04
22004	Tpm2	Tropomyosin 2, beta	2.04
226757	Wdr26	WD repeat domain 26	2.03
12724	Clcn2	Chloride channel 2	2.03
229663	Csde1	Cold shock domain containing E1, RNA binding	2.03
71912	Jsrp1	Junctional sarcoplasmic reticulum protein 1	2.02
18412	Sqstm1	Sequestosome 1	2.02
54633	Pqbp1	Polyglutamine binding protein 1	2.02
12818	Col14a1	Procollagen, type XIV, alpha 1	2.02
22003	Tpm1	Tropomyosin 1, alpha	2.01
70356	St13	Suppression of tumorigenicity 13	2.01
66661	Srp72	Signal recognition particle 72	2.01
17755	Mtap1b	Microtubule-associated protein 1 B	2.01
19317	Qk	Quaking	2.01
22223	Uchl1	Ubiquitin carboxy-terminal hydrolase L1	2.01
319939	Tns3	Tensin 3	2.01
78134	Gpr23	G protein-coupled receptor 23	2.01
21857	Timp1	Tissue inhibitor of metalloproteinase 1	2.01
20226	Sars	Seryl-aminoacyl-tRNA synthetase	2.01
56347	Eif3s8	Eukaryotic translation initiation factor 3, subunit 8	2
101861	Ints4	Integrator complex subunit 4	2
24128	Xrn2	5'-3' exoribonuclease 2	2
56307	Metap2	Methionine aminopeptidase 2	1.99
12798	Cnn2	Calponin 2	1.99

**Supplementary Table S3-PC12 Transcripts**

GeneID	Gene Name	Gene Symbol	PC12-0to6h	PC12-6h	PC12-48h
76408	ATP-binding cassette, sub-family C (CFTR/MRP), member 3	Abcc3			
295305	Acid phosphatase 6, lysophosphatidic	Acp6			
109711	Actinin, alpha 1	Actn1			
77559	Amylo-1,6-glucosidase, 4-alpha-glucanotransferase	Agl			
11677	Aldo-keto reductase family 1, member B3 (aldose reductase)	Akr1b3			
14187	Aldo-keto reductase family 1, member B8	Akr1b8			
11658	Activated leukocyte cell adhesion molecule	Alcam			
380959	Asparagine-linked glycosylation 10 homolog B (yeast, alpha-1,2-glucosyltransferase)	Alg10b			
25284	Alpha-methylacyl-CoA racemase	Amacr			
12306	Annexin A2	Anxa2			
108012	Adaptor-related protein complex 1, sigma 2 subunit	Ap1s2			
11789	Adenomatous polyposis coli	Apc			
11843	ADP-ribosylation factor 4	Arf4			
11865	Aryl hydrocarbon receptor nuclear translocator-like	Arntl			
56378	Actin related protein 2/3 complex, subunit 3	Arpc3			
57344	Arsenic (+3 oxidation state) methyltransferase	As3mt			
11911	Activating transcription factor 4	Atf4			
50770	ATPase, class VI, type 11A	Atp11a			
227648	Expressed sequence AU024582	AU024582			
215418	AXIN1 up-regulated 1	Axud1			
54375	Antizyme inhibitor 1	Azin1			
57370	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 3	B4galt3			
29810	Bcl2-associated athanogene 3	Bag3			
12227	B-cell translocation gene 2, anti-proliferative	Btg2			
12512	Cd63 antigen	Cd63			
66440	Cell division cycle 26	Cdc26			
68916	CDK5 regulatory subunit associated protein 1-like 1	Cdkal1			
12611	CCAAT/enhancer binding protein (C/EBP), gamma	Cebpg			
24259	Chromogranin B	Chgb			
12705	Cbp/p300-interacting transactivator with Glu/Asp-rich carboxy-terminal domain 1	Cited1			

54321	Calponin 3, acidic	Cnn3			
67876	Coenzyme Q10 homolog B ( <i>S. cerevisiae</i> )	Coq10b			
67579	Cytoplasmic polyadenylation element binding protein 4	Cpeb4			
208647	CAMP responsive element binding protein 3-like 2	Creb3l2			
13007	Cysteine and glycine-rich protein 1	Csrp1			
228410	Cleavage stimulation factor, 3' pre-RNA, subunit 3	Cstf3			
28146	DNA segment, Chr 3, University of California at Los Angeles 1	D3Ucla1			
114874	DDHD domain containing 1	Ddhd1			
13205	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 3, X-linked	Ddx3x			
67800	Diacylglycerol O-acyltransferase 2	Dgat2			
114125	Delta-like 3 ( <i>Drosophila</i> )	Dll3			
58233	DnaJ (Hsp40) homolog, subfamily A, member 4	Dnaja4			
105638	DPH3 homolog (KTI11, <i>S. cerevisiae</i> )	Dph3			
93838	DEAQ RNA-dependent ATPase	Dqx1			
66143	Eukaryotic translation elongation factor 1 epsilon 1	Eef1e1			
98878	EH-domain containing 4	Ehd4			
20918	Eukaryotic translation initiation factor 1	Eif1			
13664	Eukaryotic translation initiation factor 1A	Eif1a			
239528	Eukaryotic translation initiation factor 2C, 2	Eif2c2			
13684	Eukaryotic translation initiation factor 4E	Eif4e			
192657	Elongation factor RNA polymerase II 2	Eli2			
13723	Embigin	Emb			
13836	Eph receptor A2	Epha2			
107508	Glutamyl-prolyl-tRNA synthetase	Eprs			
300519	Endothelial cell adhesion molecule	Esam			
363460	FYVE, RhoGEF and PH domain containing 1	Fgd1			
319448	Fibronectin type III domain containing 3a	Fndc3a			
14284	Fos-like antigen 2	Fosl2			
20321	Ferric-chelate reductase 1	Frrs1			
108150	UDP-N-acetyl-alpha-D-galactosamine: polypeptide N-acetylgalactosaminyltransferase 7	Galnt7			
14451	Growth arrest specific 1	Gas1			
14461	GATA binding protein 2	Gata2			



29244	GTP cyclohydrolase 1	Gch				
29739	Glutamate cysteine ligase, modifier subunit	Gclm				
93692	Glutaredoxin	Glrx				
70231	Golgi reassembly stacking protein 2	Gorasp2				
94189	Golgi SNAP receptor complex member 1	Gosr1				
14783	Growth factor receptor bound protein 10	Grb10				
67345	Hect domain and RLD 4	Herc4				
15463	HIV-1 Rev binding protein	Hrb				
292155	Heparan sulfate 2-O-sulfotransferase 1	Hs2st1				
14828	Heat shock 70kD protein 5 (glucose-regulated protein)	Hspa5				
15507	Heat shock protein 1	Hspb1				
80888	Heat shock protein 8	Hspb8				
15902	Inhibitor of DNA binding 2	Id2				
15903	Inhibitor of DNA binding 3	Id3				
15937	Immediate early response 3	Ier3				
55978	Intraflagellar transport 20 homolog (Chlamydomonas)	Ift20				
66989	Potassium channel tetramerisation domain containing 20	Kctd20				
16600	Kruppel-like factor 4 (gut)	Klf4				
16776	Laminin, alpha 5	Lama5				
16854	Lectin, galactose binding, soluble 3	Lgals3				
109594	LIM domain only 1	Lmo1				
299282	Serine protease inhibitor	LOC299282				
116565	Low density lipoprotein receptor-related protein associated protein 1	Lrpap1				
50772	Mitogen-activated protein kinase 6	Mapk6				
30957	Mitogen-activated protein kinase 8 interacting protein 3	Mapk8ip3				
17164	MAP kinase-activated protein kinase 2	Mapkapk2				
212679	Methionine-tRNA synthetase 2 (mitochondrial)	Mars2				
84004	Melanoma cell adhesion molecule	Mcam				
17210	Myeloid cell leukemia sequence 1	Mcl1				
54387	Minichromosome maintenance deficient 3 (S. cerevisiae) associated protein	Mcm3ap				
17308	Mannoside acetylglucosaminyltransferase 1	Mgat1				
499934	Similar to mannosidase, beta A, lysosomal-like	MGC109145				

17768	Methylenetetrahydrofolate dehydrogenase (NAD+ dependent), methenyltetrahydrofolate cyclohydrolase	Mthfd2			
298075	Nuclear cap binding protein subunit 1, 80kDa	Ncbp1			
314648	Nicalin homolog (zebrafish)	Ncln			
83431	Nuclear distribution gene E-like homolog 1 (A. nidulans)	Ndel1			
18081	Ninjurin 1	Ninj1			
18148	Nucleophosmin 1	Npm1			
18194	NAD(P) dependent steroid dehydrogenase-like	Nsdhl			
109019	Oligonucleotide/oligosaccharide-binding fold containing 2A	Obfc2a			
18263	Ornithine decarboxylase, structural 1	Odc1			
99543	Olfactomedin-like 3	Olfml3			
18472	Platelet-activating factor acetylhydrolase, isoform 1b, beta1 subunit	Pafah1b1			
72333	Palladin, cytoskeletal associated protein	Palld			
63885	Phosphodiesterase 10A	Pde10a			
236900	Pyruvate dehydrogenase kinase, isoenzyme 3	Pdk3			
18791	Plasminogen activator, tissue	Plat			
18810	Plectin 1	Plec1			
18845	Plexin A2	Plxna2			
18984	P450 (cytochrome) oxidoreductase	Por			
19052	Protein phosphatase 2 (formerly 2A), catalytic subunit, alpha isoform	Ppp2ca			
72930	Protein phosphatase 2 (formerly 2A), regulatory subunit B (PR 52), beta isoform	Ppp2r2b			
94167	Peroxiredoxin 6	Prdx6			
106042	Prickle like 1 (Drosophila)	Prickle1			
19084	Protein kinase, cAMP dependent regulatory, type I, alpha	Prkar1a			
19124	Protein C receptor, endothelial	Procr			
100678	Phosphoserine phosphatase	Psph			
19243	Protein tyrosine phosphatase 4a1	Ptp4a1			
108705	Pituitary tumor-transforming 1 interacting protein	Pttg1ip			
52118	Poliovirus receptor	Pvr			
58235	Poliovirus receptor-related 1	Pvr1			
110391	Quinoid dihydropteridine reductase	Qdpr			
29885	RAB3A interacting protein	Rab3ip			
217944	Rap guanine nucleotide exchange factor (GEF) 5	Rapgef5			

300996	RNA binding motif protein 5	Rbm5			
108911	Regulator of chromosome condensation 2	Rcc2			
19735	Regulator of G-protein signaling 2	Rgs2			
11852	Ras homolog gene family, member B	Rhob			
80751	Ring finger protein 34	Rnf34			
29236	Ribosomal protein SA	Rpsa			
81778	S100 calcium binding protein A10 (calpactin)	S100a10			
65169	Secretory carrier membrane protein 3	Scamp3			
29871	Sex comb on midleg homolog 1	Scmh1			
230779	Serine incorporator 2	Serinc2			
66222	Serine (or cysteine) peptidase inhibitor, clade B, member 1a	Serpib1a			
306376	SH2 domain containing 4A	Sh2d4a			
93759	Sirtuin 1 ((silent mating type information regulation 2, homolog) 1 (S. cerevisiae)	Sirt1			
105727	Solute carrier family 38, member 1	Slc38a1			
50934	Solute carrier family 7 (cationic amino acid transporter, y+ system), member 8	Slc7a8			
25671	MAD homolog 1 (Drosophila)	Smad1			
25012	Synaptosomal-associated protein 25	Snap25			
20848	Signal transducer and activator of transcription 3	Stat3			
74178	Serine/threonine kinase 40	Stk40			
77097	Tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 2	Tanc2			
76281	Tax1 (human T-cell leukemia virus type I) binding protein 3	Tax1bp3			
21753	Testis derived transcript	Tes			
21823	Tyrosine hydroxylase	Th			
75909	Transmembrane protein 49	Tmem49			
19240	Thymosin, beta 10	Tmsb10			
326618	Tropomyosin 4	Tpm4			
21807	TSC22 domain family, member 1	Tsc22d1			
22141	Tubby candidate gene	Tub			
73710	Tubulin, beta 2b	Tubb2b			
105245	Thioredoxin domain containing 5	Txndc5			
53382	Thioredoxin-like 1	Txn1			
58819	Thioredoxin reductase 1	Txnrd1			

300968	Ubiquitin-activating enzyme E1-domain containing 1	Ube1dc1			
56228	Ubiquitin-conjugating enzyme E2, J1	Ube2j1			
22195	Ubiquitin-conjugating enzyme E2L 3	Ube2l3			
17847	Ubiquitin specific peptidase 34	Usp34			
78787	Ubiquitin specific peptidase 54	Usp54			
22350	Villin 2	Vil2			
232341	WNK lysine deficient protein kinase 1	Wnk1			
78903	Werner helicase interacting protein 1	Wrnip1			
22628	3-monooxygenase/tryptophan 5-monooxygenase activation protein, gamma polypeptide	Ywhag			
22680	Zinc finger protein 207	Zfp207			

**Supplementary Table S4-MCAO Transcripts**

Gene ID	Gene symbol	Gene Description	Time Post-MCAO
232370	Clstn3	Calsyntenin 3	1hr
105501	Abhd4	Abhydrolase domain containing 4	1hr
108100	Baiap2	BAI1 associated protein 2	1hr
27267	Cars	Cysteinyln tRNA synthetase	1hr
12465	Cct5	Chaperonin subunit 5 (epsilon)	1hr
105859	Csdc2	Cold shock domain containing C2, RNA binding	1hr
13179	Dcn	Decorin	1hr
83768	Dpp7	Dipeptidylpeptidase 7	1hr
252864	Dusp15	Dual specificity phosphatase like 15	1hr
107035	Fbxo38	F box protein 38	1hr
23882	Gadd45g	Growth arrest and DNA damage inducible, gamma	1hr
78926	Gas2l1	Growth arrest specific 2 like 1	1hr
14590	Ggh	Gamma glutamyl hydrolase	1hr
14694	Gnb2l1	Guanine nucleotide binding protein (G protein), beta polypeptide 2 like 1	1hr
64378	Gpr88	G protein coupled receptor 88	1hr
108073	Grm7	Glutamate receptor, metabotropic 7	1hr
15127	Hbb	Hemoglobin beta chain complex	1hr
15937	Ier3	Immediate early response 3	1hr
16362	Irf1	Interferon regulatory factor 1	1hr
245049	Myrip	Myosin VIIA and Rab interacting protein	1hr
228961	Npepl1	Aminopeptidase like 1	1hr
18619	Penk1	Preproenkephalin 1	1hr
71726	Smug1	Single strand selective monofunctional uracil DNA glycosylase	1hr
21333	Tac1	Tachykinin 1	1hr

75909	Tmem49	Transmembrane protein 49	1hr
103573	Xpo1	Exportin 1, CRM1 homolog (yeast)	1hr
329693	Fcrl5	Fc receptor like protein 5	1hr
22139	Ttr	Transthyretin	1hr
16476	Jun	Jun oncogene	1hr
19225	Ptgs2	Prostaglandin endoperoxide synthase 2	1hr
20620	Plk2	Polo like kinase 2 (Drosophila)	1hr
219024	Tmem55b	Transmembrane protein 55b	1hr
78818	Mbnl2	MKIAA4072 protein	1hr
53324	Nptx2	Neuronal pentraxin 2	1hr
11472	Actn2	Actinin alpha 2	1hr
15387	Hnrpk	Heterogeneous nuclear ribonucleoprotein K	1hr
319520	Dusp4	Dual specificity phosphatase 4	1hr
64011	Nrgn	Neurogranin	1hr
19744	Rheb	RAS homolog enriched in brain	1hr
19049	Ppp1r1b	Protein phosphatase 1	1hr
19259	Ptpn5	Protein tyrosine phosphatase, non receptor type 5	1hr
56405	Dusp14	Dual specificity phosphatase 14	1hr
76690	Map3k10	Mitogen activated protein kinase kinase kinase 10	1hr
278795	Gm705	Gene model 705, (NCBI)	1hr
67603	Dusp6	Dual specificity phosphatase 6	1hr
59046	Arpp19	cAMP regulated phosphoprotein 19	1hr
56323	Dnajb5	DnaJ (Hsp40)	1hr
74365	Lonrf3	LON peptidase N terminal domain and ring finger 3	1hr
64294	Itm2c	Integral membrane protein 2C	1hr
23872	Ets2	E26 avian leukemia oncogene 2, 3 domain	1hr

11838	Arc	Activity regulated cytoskeletal associated protein	1hr
380928	Lmo7	LIM domain only 7	1hr
67405	Nts	Neurotensin	1hr
72124	Seh1l	SEH1 like	1hr
219228	Pcdh17	Protocadherin 17	1hr
71853	Pdia6	Protein disulfide isomerase associated 6	1hr
67252	Cap2	Adenylate cyclase associated protein, 2	1hr
15370	Nr4a1	Nuclear receptor subfamily 4, group A, member 1	1hr
13803	Enc1	Ectodermal neural cortex 1	1hr
18574	Pde1b	Phosphodiesterase 1B	1hr
67245	Peli1	Pellino 1	1hr
105171	Arrdc3	Arrestin domain containing 3	1hr
19107	Dnajc3	DnaJ (Hsp40) homolog	1hr
14284	Fosl2	fos like antigen 2	1hr
30939	Pttg1	Pituitary tumor transforming 1	1hr
13190	Dct	Dopachrome tautomerase	24 hr
11815	Apod	Apolipoprotein D	24 hr
11772	Ap2a2	Adaptor protein complex AP 2, alpha 2 subunit	24 hr
12508	Cd53	CD53 antigen	24 hr
12842	Col1a1	Procollagen, type I, alpha 1	24 hr
13627	Eef1a1	Eukaryotic translation elongation factor 1 alpha 1	24 hr
11475	Acta2	Actin, alpha 2, smooth muscle, aorta	24 hr
14325	Ftl1	Ferritin light chain 1	24 hr
67126	Atp5e	ATP synthase, epsilon subunit	24 hr
192176	Flna	Filamin, alpha	24 hr
11465	Actg1	Actin, gamma, cytoplasmic 1	24 hr

12466	Cct6a	Chaperonin subunit 6a (zeta)	24 hr
12306	Anxa2	Annexin A2	24 hr
12419	Cbx5	Chromobox homolog 5 (Drosophila HP1a)	24 hr
20877	Aurkb	Aurora kinase B	24 hr
13806	Eno1	Enolase 1, alpha non neuron	24 hr
12512	Cd63	Cd63 antigen	24 hr
11949	Atp5c1	ATP synthase, gamma polypeptide 1	24 hr
52502	Carhsp1	Calcium regulated heat stable protein 1	24 hr
319945	Flad1	Flavin adenine dinucleotide synthetase, homolog	24 hr
12260	C1qb	Complement component 1	24 hr
67239	Bxdc1	Brix domain containing 1	24 hr
12305	Ddr1	Discoidin domain receptor family, member 1	24 hr
13681	Eif4a1	Eukaryotic translation initiation factor 4A1	24 hr
69823	Fytd1	Forty two three domain containing 1	24 hr
75302	Asx12	Additional sex combs like 2 (Drosophila)	24 hr
78885	Coro7	Coronin 7	24 hr
226414	Dars	Aspartyl tRNA synthetase	24 hr
12468	Cct7	Chaperonin subunit 7 (eta)	24 hr
13628	Eef1a2	Eukaryotic translation elongation factor 1 alpha 2	24 hr
11829	Aqp4	Aquaporin 4	24 hr
11837	Arbp	Acidic ribosomal phosphoprotein P0	24 hr
29876	Clic4	Chloride intracellular channel 4 (mitochondrial)	24 hr
12387	Ctnnb1	Catenin	24 hr
13039	Ctsl	Cathepsin L	24 hr
12330	Canx	Calnexin	24 hr
12462	Cct3	Chaperonin subunit 3 (gamma)	24 hr



12505	Cd44	CD44 antigen	24 hr
12785	Cnbp1	Cellular nucleic acid binding protein 1	24 hr
13033	Ctsd	Cathepsin D	24 hr
72584	Cul4b	Cullin 4B	24 hr
55935	Fnbp4	Formin binding protein 4	24 hr
54208	Arl6ip1	ADP ribosylation factor like 6 interacting protein 1	24 hr
27053	Asns	Asparagine synthetase	24 hr
50770	Atp11a	ATPase, class VI, type 11A	24 hr
12010	B2m	Beta 2 microglobulin	24 hr
67789	Dalrd3	DALR anticodon binding domain containing 3	24 hr
12848	Cops2	Constitutive photomorphogenic homolog, subunit 2	24 hr
232370	Clstn 3	Calsyntenin 3	24 hr
105501	Abhd4	Abhydrolase domain containing 4	24 hr
108100	Baiap2	BAI1 associated protein 2	24 hr
27267	Cars	Cysteinyl tRNA synthetase	24 hr
12465	Cct5	Chaperonin subunit 5 (epsilon)	24 hr
105859	Csdc2	Cold shock domain containing C2, RNA binding	24 hr
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252864	Dusp15	Dual specificity phosphatase like 15	24 hr
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78926	Gas2l1	Growth arrest specific 2 like 1	24 hr
14590	Ggh	Gamma glutamyl hydrolase	24 hr
14694	Gnb2l1	Guanine nucleotide binding protein (G protein), beta polypeptide 2 like 1	24 hr
64378	Gpr88	G protein coupled receptor 88	24 hr

108073	Grm7	Glutamate receptor, metabotropic 7	24 hr
15127	Hbb	Hemoglobin beta chain complex	24 hr
15937	Ier3	Immediate early response 3	24 hr
16362	Irf1	Interferon regulatory factor 1	24 hr
245049	Myrip	Myosin VIIA and Rab interacting protein	24 hr
228961	Npepl1	Aminopeptidase like 1	24 hr
18619	Penk1	Preproenkephalin 1	24 hr
71726	Smug1	Single strand selective monofunctional uracil DNA glycosylase	24 hr
21333	Tac1	Tachykinin 1	24 hr
75909	Tmem49	Transmembrane protein 49	24 hr
103573	Xpo1	Exportin 1, CRM1 homolog (yeast)	24 hr

**Supplementary Table S5-Gene Glossary**

Gene Symbol	Gene Description	Encoded Protein Location	Family	GeneID for Human	GeneID for Mouse	GeneID for Rat
ABCC3	ATP-binding cassette, sub-family C (CFTR/MRP), member 3	Plasma Membrane	transporter	<a href="#">8714</a>	<a href="#">76408</a>	<a href="#">140668</a>
ACTR2	ARP2 actin-related protein 2 homolog (yeast)	Plasma Membrane	other	<a href="#">10097</a>	<a href="#">66713</a>	<a href="#">289820</a>
ACTR3	ARP3 actin-related protein 3 homolog (yeast)	Plasma Membrane	other	<a href="#">10096</a>	<a href="#">74117</a>	<a href="#">81732</a>
ADCYAP1	adenylate cyclase activating polypeptide 1 (pituitary)	Extracellular Space	other	<a href="#">116</a>	<a href="#">11516</a>	<a href="#">24166</a>
ADORA2B	adenosine A2b receptor	Plasma Membrane	G-protein coupled receptor	<a href="#">136</a>	<a href="#">11541</a>	<a href="#">29316</a>
AKR1C2	aldo-keto reductase family 1, member C2	Cytoplasm	enzyme	<a href="#">1646</a>	<a href="#">83702</a>	<a href="#">307092</a>
ANXA2	annexin A2	Plasma Membrane	other	<a href="#">302</a>	<a href="#">12306</a>	<a href="#">56611</a>
AP1S2	adaptor-related protein complex 1, sigma 2 subunit	Cytoplasm	transporter	<a href="#">8905</a>	<a href="#">108012</a>	<a href="#">na</a>
APC	adenomatosis polyposis coli	Nucleus	enzyme	<a href="#">324</a>	<a href="#">11789</a>	<a href="#">24205</a>
APOD	apolipoprotein D	Extracellular Space	transporter	<a href="#">347</a>	<a href="#">11815</a>	<a href="#">25239</a>
AQP4	aquaporin 4	Plasma Membrane	transporter	<a href="#">361</a>	<a href="#">11829</a>	<a href="#">25293</a>
ARC	activity-regulated cytoskeleton-associated protein	Cytoplasm	other	<a href="#">23237</a>	<a href="#">11838</a>	<a href="#">54323</a>
ARF4	ADP-ribosylation factor 4	Cytoplasm	enzyme	<a href="#">378</a>	<a href="#">11843</a>	<a href="#">79120</a>
ARHGEF1	Rho guanine nucleotide exchange factor (GEF) 1	Cytoplasm	other	<a href="#">9138</a>	<a href="#">16801</a>	<a href="#">60323</a>
ARPC1A	actin related protein 2/3 complex, subunit 1A, 41kDa	Cytoplasm	other	<a href="#">10552</a>	<a href="#">56443</a>	<a href="#">81824</a>
ARPC1B	actin related protein 2/3 complex, subunit 1B, 41kDa	Cytoplasm	other	<a href="#">10095</a>	<a href="#">11867</a>	<a href="#">54227</a>
ARPC2	actin related protein 2/3 complex, subunit 2, 34kDa	Cytoplasm	other	<a href="#">10109</a>	<a href="#">76709</a>	<a href="#">301511</a>
ARPC3	actin related protein 2/3 complex, subunit 3, 21kDa	Cytoplasm	other	<a href="#">10094</a>	<a href="#">56378</a>	<a href="#">288669</a>
ARPC4	actin related protein 2/3 complex, subunit 4, 20kDa	Unknown	other	<a href="#">10093</a>	<a href="#">68089</a>	<a href="#">297518</a>
ARPC5	actin related protein 2/3 complex, subunit 5, 16kDa	Cytoplasm	other	<a href="#">10092</a>	<a href="#">67771</a>	<a href="#">360854</a>
ASGR2	asialoglycoprotein receptor 2	Plasma Membrane	transmembrane receptor	<a href="#">433</a>	<a href="#">11890</a>	<a href="#">29403</a>
AZIN1	antizyme inhibitor 1	Cytoplasm	enzyme	<a href="#">51582</a>	<a href="#">54375</a>	<a href="#">58961</a>
B2M	beta-2-microglobulin	Plasma Membrane	transmembrane receptor	<a href="#">567</a>	<a href="#">12010</a>	<a href="#">24223</a>
BATF	basic leucine zipper transcription factor, ATF-like	Nucleus	transcription regulator	<a href="#">10538</a>	<a href="#">53314</a>	<a href="#">299206</a>
BDNF	brain-derived neurotrophic factor	Extracellular Space	growth factor	<a href="#">627</a>	<a href="#">12064</a>	<a href="#">24225</a>
BTG2	BTG family, member 2	Nucleus	transcription regulator	<a href="#">7832</a>	<a href="#">12227</a>	<a href="#">29619</a>
CALD1	caldesmon 1	Cytoplasm	other	<a href="#">800</a>	<a href="#">109624</a>	<a href="#">25687</a>
CALM2	calmodulin 2 (phosphorylase kinase, delta)	Plasma Membrane	other	<a href="#">805</a>	<a href="#">12314</a>	<a href="#">50663</a>
CANX	calnexin	Cytoplasm	other	<a href="#">821</a>	<a href="#">12330</a>	<a href="#">29144</a>
CAPNS1	calpain, small subunit 1	Cytoplasm	peptidase	<a href="#">826</a>	<a href="#">12336</a>	<a href="#">29156</a>
CARHSP1	calcium regulated heat stable protein 1, 24kDa	Cytoplasm	other	<a href="#">23589</a>	<a href="#">52502</a>	<a href="#">260416</a>
CARS	cysteinyl-tRNA synthetase	Cytoplasm	enzyme	<a href="#">833</a>	<a href="#">27267</a>	<a href="#">293638</a>

CASP3	caspase 3, apoptosis-related cysteine peptidase	Cytoplasm	peptidase	<a href="#">836</a>	<a href="#">12367</a>	<a href="#">25402</a>
CCK	cholecystokinin	Extracellular Space	other	<a href="#">885</a>	<a href="#">12424</a>	<a href="#">25298</a>
CD247	CD247 molecule	Plasma Membrane	transmembrane receptor	<a href="#">919</a>	<a href="#">12503</a>	<a href="#">25300</a>
CD44	CD44 molecule (Indian blood group)	Plasma Membrane	other	<a href="#">960</a>	<a href="#">12505</a>	<a href="#">25406</a>
CD63	CD63 molecule	Plasma Membrane	other	<a href="#">967</a>	<a href="#">12512</a>	<a href="#">29186</a>
CD68	CD68 molecule	Plasma Membrane	other	<a href="#">968</a>	<a href="#">12514</a>	<a href="#">287435</a>
CHGB	chromogranin B (secretogranin 1)	Extracellular Space	other	<a href="#">1114</a>	<a href="#">12653</a>	<a href="#">24259</a>
CITED1	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 1	Nucleus	transcription regulator	<a href="#">4435</a>	<a href="#">12705</a>	<a href="#">64466</a>
CLDN4	claudin 4	Plasma Membrane	transmembrane receptor	<a href="#">1364</a>	<a href="#">12740</a>	<a href="#">304407</a>
CNN2	calponin 2	Cytoplasm	other	<a href="#">1265</a>	<a href="#">12798</a>	<a href="#">na</a>
CNN3	calponin 3, acidic	Cytoplasm	other	<a href="#">1266</a>	<a href="#">71994</a>	<a href="#">54321</a>
COL24A1	collagen, type XXIV, alpha 1	Extracellular Space	other	<a href="#">255631</a>	<a href="#">71355</a>	<a href="#">na</a>
COL8A1	collagen, type VIII, alpha 1	Extracellular Space	other	<a href="#">1295</a>	<a href="#">12837</a>	<a href="#">304021</a>
COPS2	COP9 constitutive photomorphogenic homolog subunit 2 (Arabidopsis)	Cytoplasm	transcription regulator	<a href="#">9318</a>	<a href="#">12848</a>	<a href="#">261736</a>
CREB1	cAMP responsive element binding protein 1	Nucleus	transcription regulator	<a href="#">1385</a>	<a href="#">12912</a>	<a href="#">81646</a>
CSDE1	cold shock domain containing E1, RNA-binding	Cytoplasm	other	<a href="#">7812</a>	<a href="#">229663</a>	<a href="#">117180</a>
CSRP1	cysteine and glycine-rich protein 1	Nucleus	other	<a href="#">1465</a>	<a href="#">13007</a>	<a href="#">29276</a>
CTNNB1	catenin (cadherin-associated protein), beta 1, 88kDa	Nucleus	transcription regulator	<a href="#">1499</a>	<a href="#">12387</a>	<a href="#">84353</a>
DARS	aspartyl-tRNA synthetase	Cytoplasm	enzyme	<a href="#">1615</a>	<a href="#">226414</a>	<a href="#">116483</a>
DBH	dopamine beta-hydroxylase (dopamine beta-monooxygenase)	Cytoplasm	enzyme	<a href="#">1621</a>	<a href="#">13166</a>	<a href="#">25699</a>
DCT	dopachrome tautomerase (dopachrome delta-isomerase, tyrosine-related protein 2)	Cytoplasm	enzyme	<a href="#">1638</a>	<a href="#">13190</a>	<a href="#">290484</a>
DDX3X	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, X-linked	Nucleus	enzyme	<a href="#">1654</a>	<a href="#">13205</a>	<a href="#">317335</a>
DDX5	DEAD (Asp-Glu-Ala-Asp) box polypeptide 5	Nucleus	enzyme	<a href="#">1655</a>	<a href="#">13207</a>	<a href="#">287765</a>
DKK1	dickkopf homolog 1 (Xenopus laevis)	Extracellular Space	growth factor	<a href="#">22943</a>	<a href="#">13380</a>	<a href="#">293897</a>
DNAJA1	DnaJ (Hsp40) homolog, subfamily A, member 1	Nucleus	other	<a href="#">3301</a>	<a href="#">15502</a>	<a href="#">65028</a>
DNAJA4	DnaJ (Hsp40) homolog, subfamily A, member 4	Nucleus	other	<a href="#">55466</a>	<a href="#">58233</a>	<a href="#">300721</a>
DNAJC3	DnaJ (Hsp40) homolog, subfamily C, member 3	Nucleus	other	<a href="#">5611</a>	<a href="#">19107</a>	<a href="#">63880</a>
ECE1	endothelin converting enzyme 1	Plasma Membrane	peptidase	<a href="#">1889</a>	<a href="#">230857</a>	<a href="#">94204</a>
EDN1	endothelin 1	Extracellular Space	other	<a href="#">1906</a>	<a href="#">13614</a>	<a href="#">24323</a>
EEF1A1	eukaryotic translation elongation factor 1 alpha 1	Cytoplasm	translation regulator	<a href="#">1915</a>	<a href="#">13627</a>	<a href="#">171361</a>
EEF1G	eukaryotic translation elongation factor 1 gamma	Cytoplasm	translation regulator	<a href="#">1937</a>	<a href="#">67160</a>	<a href="#">293725</a>
EFNA2	ephrin-A2	Plasma Membrane	kinase	<a href="#">1943</a>	<a href="#">13637</a>	<a href="#">84358</a>
EIF2S1	eukaryotic translation initiation factor 2, subunit 1 alpha, 35kDa	Cytoplasm	translation regulator	<a href="#">1965</a>	<a href="#">13665</a>	<a href="#">54318</a>
EIF3S10	eukaryotic translation initiation factor 3, subunit 10 theta, 150/170kDa	Cytoplasm	translation regulator	<a href="#">8661</a>	<a href="#">13669</a>	<a href="#">292148</a>
EIF3S8	eukaryotic translation initiation factor 3, subunit 8, 110kDa	Cytoplasm	translation regulator	<a href="#">8663</a>	<a href="#">56347</a>	<a href="#">293484</a>

EIF4A1	eukaryotic translation initiation factor 4A, isoform 1	Cytoplasm	translation regulator	<a href="#">1973</a>	<a href="#">13681</a>	<a href="#">287436</a>
EIF4E	eukaryotic translation initiation factor 4E	Cytoplasm	translation regulator	<a href="#">1977</a>	<a href="#">13684</a>	<a href="#">117045</a>
EIF4G2 (includes	eukaryotic translation initiation factor 4 gamma, 2	Cytoplasm	translation regulator	<a href="#">1982</a>	<a href="#">13690</a>	<a href="#">361628</a>
EIF5	eukaryotic translation initiation factor 5	Cytoplasm	translation regulator	<a href="#">1983</a>	<a href="#">217869</a>	<a href="#">56783</a>
EP300	E1A binding protein p300	Nucleus	transcription regulator	<a href="#">2033</a>	<a href="#">328572</a>	<a href="#">170915</a>
EPHA2	EPH receptor A2	Plasma Membrane	kinase	<a href="#">1969</a>	<a href="#">13836</a>	<a href="#">366492</a>
EPRS	glutamyl-prolyl-tRNA synthetase	Cytoplasm	enzyme	<a href="#">2058</a>	<a href="#">107508</a>	<a href="#">289352</a>
ERBB2	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog (avian)	Plasma Membrane	kinase	<a href="#">2064</a>	<a href="#">13866</a>	<a href="#">24337</a>
ETS2	v-ets erythroblastosis virus E26 oncogene homolog 2 (avian)	Nucleus	transcription regulator	<a href="#">2114</a>	<a href="#">23872</a>	<a href="#">304063</a>
FCGRT	Fc fragment of IgG, receptor, transporter, alpha	Plasma Membrane	transmembrane receptor	<a href="#">2217</a>	<a href="#">14132</a>	<a href="#">29558</a>
FOLR2	folate receptor 2 (fetal)	Plasma Membrane	transporter	<a href="#">2350</a>	<a href="#">14276</a>	<a href="#">293154</a>
FOSL2	FOS-like antigen 2	Nucleus	transcription regulator	<a href="#">2355</a>	<a href="#">14284</a>	<a href="#">25446</a>
FRAT1	frequently rearranged in advanced T-cell lymphomas	Cytoplasm	other	<a href="#">10023</a>	<a href="#">14296</a>	<a href="#">na</a>
FRRS1	ferric-chelate reductase 1	Plasma Membrane	transmembrane receptor	<a href="#">391059</a>	<a href="#">20321</a>	<a href="#">310810</a>
FYN	FYN oncogene related to SRC, FGR, YES	Plasma Membrane	kinase	<a href="#">2534</a>	<a href="#">14360</a>	<a href="#">25150</a>
FZD9	frizzled homolog 9 (Drosophila)	Plasma Membrane	G-protein coupled receptor	<a href="#">8326</a>	<a href="#">14371</a>	<a href="#">266608</a>
GARS	glycyl-tRNA synthetase	Cytoplasm	enzyme	<a href="#">2617</a>	<a href="#">353172</a>	<a href="#">297113</a>
GAS1	growth arrest-specific 1	Plasma Membrane	other	<a href="#">2619</a>	<a href="#">14451</a>	<a href="#">83818</a>
GCLM	glutamate-cysteine ligase, modifier subunit	Cytoplasm	enzyme	<a href="#">2730</a>	<a href="#">14630</a>	<a href="#">29739</a>
GCS1	glucosidase I	Cytoplasm	enzyme	<a href="#">7841</a>	<a href="#">57377</a>	<a href="#">78947</a>
GLP109	--	Unknown	other	<a href="#">na</a>	<a href="#">na</a>	<a href="#">na</a>
GLRX	glutaredoxin (thioltransferase)	Cytoplasm	enzyme	<a href="#">2745</a>	<a href="#">93692</a>	<a href="#">64045</a>
GNB2L1	guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1	Cytoplasm	enzyme	<a href="#">10399</a>	<a href="#">14694</a>	<a href="#">83427</a>
GSPT1	G1 to S phase transition 1	Cytoplasm	translation regulator	<a href="#">2935</a>	<a href="#">14852</a>	<a href="#">24420</a>
H2-LD	histocompatibility 2, D region	Plasma Membrane	other	<a href="#">na</a>	<a href="#">14980</a>	<a href="#">na</a>
HERPUD1	homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	Cytoplasm	other	<a href="#">9709</a>	<a href="#">64209</a>	<a href="#">85430</a>
HLA-G	HLA-G histocompatibility antigen, class I, G	Plasma Membrane	transmembrane receptor	<a href="#">3135</a>	<a href="#">15007</a>	<a href="#">368153</a>
HMGB1	high-mobility group box 1	Nucleus	other	<a href="#">3146</a>	<a href="#">15289</a>	<a href="#">25459</a>
HNRPH2	heterogeneous nuclear ribonucleoprotein H2 (H')	Nucleus	other	<a href="#">3188</a>	<a href="#">56258</a>	<a href="#">na</a>
HOXA9	homeobox A9	Nucleus	transcription regulator	<a href="#">3205</a>	<a href="#">15405</a>	<a href="#">297099</a>
HSP90AA1	heat shock protein 90kDa alpha (cytosolic), class A member 1	Cytoplasm	other	<a href="#">3320</a>	<a href="#">15519</a>	<a href="#">299331</a>
HSP90B1	heat shock protein 90kDa beta (Grp94), member 1	Plasma Membrane	other	<a href="#">7184</a>	<a href="#">22027</a>	<a href="#">362862</a>
HSPA5	heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa)	Cytoplasm	other	<a href="#">3309</a>	<a href="#">14828</a>	<a href="#">25617</a>
HSPA8	heat shock 70kDa protein 8	Cytoplasm	enzyme	<a href="#">3312</a>	<a href="#">15481</a>	<a href="#">24468</a>
HSPA9B (includes	heat shock 70kDa protein 9B (mortalin-2)	Cytoplasm	other	<a href="#">3313</a>	<a href="#">15526</a>	<a href="#">291671</a>

IARS (includes E	isoleucine-tRNA synthetase	Cytoplasm	enzyme	<a href="#">3376</a>	<a href="#">105148</a>	<a href="#">306804</a>
ID2	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein	Nucleus	transcription regulator	<a href="#">3398</a>	<a href="#">15902</a>	<a href="#">25587</a>
IDI1	isopentenyl-diphosphate delta isomerase 1	Cytoplasm	enzyme	<a href="#">3422</a>	<a href="#">319554</a>	<a href="#">89784</a>
IER3	immediate early response 3	Cytoplasm	other	<a href="#">8870</a>	<a href="#">15937</a>	<a href="#">294235</a>
IL13	interleukin 13	Extracellular Space	cytokine	<a href="#">3596</a>	<a href="#">16163</a>	<a href="#">116553</a>
IL8RA	interleukin 8 receptor, alpha	Plasma Membrane	G-protein coupled receptor	<a href="#">3577</a>	<a href="#">227288</a>	<a href="#">54258</a>
IRF1	interferon regulatory factor 1	Nucleus	transcription regulator	<a href="#">3659</a>	<a href="#">16362</a>	<a href="#">24508</a>
ITGB1	integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)	Plasma Membrane	transmembrane receptor	<a href="#">3688</a>	<a href="#">16412</a>	<a href="#">24511</a>
ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	Plasma Membrane	transmembrane receptor	<a href="#">3690</a>	<a href="#">16416</a>	<a href="#">29302</a>
JUN	v-jun sarcoma virus 17 oncogene homolog (avian)	Nucleus	transcription regulator	<a href="#">3725</a>	<a href="#">16476</a>	<a href="#">24516</a>
KLRC3	killer cell lectin-like receptor subfamily C, member 3	Plasma Membrane	transmembrane receptor	<a href="#">3823</a>	<a href="#">58179</a>	<a href="#">na</a>
KPNB1	karyopherin (importin) beta 1	Nucleus	transporter	<a href="#">3837</a>	<a href="#">16211</a>	<a href="#">24917</a>
LAMA5	laminin, alpha 5	Extracellular Space	other	<a href="#">3911</a>	<a href="#">16776</a>	<a href="#">140433</a>
LIF	leukemia inhibitory factor (cholinergic differentiation factor)	Extracellular Space	cytokine	<a href="#">3976</a>	<a href="#">16878</a>	<a href="#">60584</a>
MAFF	v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)	Nucleus	transcription regulator	<a href="#">23764</a>	<a href="#">17133</a>	<a href="#">366960</a>
MAP4	microtubule-associated protein 4	Cytoplasm	other	<a href="#">4134</a>	<a href="#">17758</a>	<a href="#">367171</a>
MAPK1	mitogen-activated protein kinase 1	Cytoplasm	kinase	<a href="#">5594</a>	<a href="#">26413</a>	<a href="#">116590</a>
MAT2A	methionine adenosyltransferase II, alpha	Cytoplasm	enzyme	<a href="#">4144</a>	<a href="#">232087</a>	<a href="#">171347</a>
METAP2	methionyl aminopeptidase 2	Cytoplasm	peptidase	<a href="#">10988</a>	<a href="#">56307</a>	<a href="#">64370</a>
MST1R	macrophage stimulating 1 receptor (c-met-related tyrosine kinase)	Plasma Membrane	kinase	<a href="#">4486</a>	<a href="#">19882</a>	<a href="#">300999</a>
MTHFD2	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	Cytoplasm	enzyme	<a href="#">10797</a>	<a href="#">17768</a>	<a href="#">na</a>
MYC	v-myc myelocytomatosis viral oncogene homolog (avian)	Nucleus	transcription regulator	<a href="#">4609</a>	<a href="#">17869</a>	<a href="#">24577</a>
MYCN	v-myc myelocytomatosis viral related oncogene, neuroblastoma derived (avian)	Nucleus	transcription regulator	<a href="#">4613</a>	<a href="#">18109</a>	<a href="#">298894</a>
MYLPF	fast skeletal myosin light chain 2	Cytoplasm	other	<a href="#">29895</a>	<a href="#">17907</a>	<a href="#">24584</a>
MYO7A	myosin VIIA	Cytoplasm	enzyme	<a href="#">4647</a>	<a href="#">17921</a>	<a href="#">266714</a>
MYRIP	myosin VIIA and Rab interacting protein	Cytoplasm	other	<a href="#">25924</a>	<a href="#">245049</a>	<a href="#">360034</a>
NCLN	nicalin homolog (zebrafish)	Unknown	peptidase	<a href="#">56926</a>	<a href="#">103425</a>	<a href="#">314648</a>
NEDD8	neural precursor cell expressed, developmentally down-regulated 8	Nucleus	enzyme	<a href="#">4738</a>	<a href="#">18002</a>	<a href="#">25490</a>
NEFH	neurofilament, heavy polypeptide 200kDa	Cytoplasm	other	<a href="#">4744</a>	<a href="#">380684</a>	<a href="#">24587</a>
NEFL (includes E	neurofilament protein-like (mapped)	Unknown	other	<a href="#">na</a>	<a href="#">na</a>	<a href="#">24589</a>
NET1	neuroepithelial cell transforming gene 1	Nucleus	other	<a href="#">10276</a>	<a href="#">56349</a>	<a href="#">307098</a>
NFE2L2	nuclear factor (erythroid-derived 2)-like 2	Nucleus	transcription regulator	<a href="#">4780</a>	<a href="#">18024</a>	<a href="#">83619</a>
NINJ1	ninjurin 1	Plasma Membrane	other	<a href="#">4814</a>	<a href="#">18081</a>	<a href="#">25338</a>
NKX6-2	NK6 transcription factor related, locus 2 (Drosophila)	Nucleus	transcription regulator	<a href="#">84504</a>	<a href="#">14912</a>	<a href="#">309095</a>
NPM1	nucleophosmin (nucleolar phosphoprotein B23, numatrin)	Nucleus	transcription regulator	<a href="#">4869</a>	<a href="#">18148</a>	<a href="#">25498</a>

NR4A1	nuclear receptor subfamily 4, group A, member 1	Nucleus	ligand-dependent nuclear receptor	<a href="#">3164</a>	<a href="#">15370</a>	<a href="#">79240</a>
NUP98	nucleoporin 98kDa	Nucleus	transporter	<a href="#">4928</a>	<a href="#">269966</a>	<a href="#">81738</a>
PABPC1	poly(A) binding protein, cytoplasmic 1	Cytoplasm	translation regulator	<a href="#">26986</a>	<a href="#">18458</a>	<a href="#">171350</a>
PAIP2	poly(A) binding protein interacting protein 2	Cytoplasm	translation regulator	<a href="#">51247</a>	<a href="#">67869</a>	<a href="#">293469</a>
PALLD	palladin, cytoskeletal associated protein	Cytoplasm	other	<a href="#">23022</a>	<a href="#">72333</a>	<a href="#">290704</a>
PAX8	paired box gene 8	Nucleus	transcription regulator	<a href="#">7849</a>	<a href="#">18510</a>	<a href="#">81819</a>
PDIA3	protein disulfide isomerase family A, member 3	Cytoplasm	peptidase	<a href="#">2923</a>	<a href="#">14827</a>	<a href="#">29468</a>
PDIA6	protein disulfide isomerase family A, member 6	Cytoplasm	enzyme	<a href="#">10130</a>	<a href="#">71853</a>	<a href="#">286906</a>
PEL1	pellino homolog 1 (Drosophila)	Cytoplasm	other	<a href="#">57162</a>	<a href="#">67245</a>	<a href="#">305549</a>
PENK	proenkephalin	Extracellular Space	other	<a href="#">5179</a>	<a href="#">18619</a>	<a href="#">29237</a>
PLEKHC1	pleckstrin homology domain containing, family C (with FERM domain) member 1	Cytoplasm	other	<a href="#">10979</a>	<a href="#">218952</a>	<a href="#">289992</a>
PPFIBP1	PTPRF interacting protein, binding protein 1 (liprin beta 1)	Plasma Membrane	other	<a href="#">8496</a>	<a href="#">67533</a>	<a href="#">312855</a>
PPID	peptidylprolyl isomerase D (cyclophilin D)	Cytoplasm	enzyme	<a href="#">5481</a>	<a href="#">67738</a>	<a href="#">361967</a>
PPP1CB	protein phosphatase 1, catalytic subunit, beta isoform	Cytoplasm	phosphatase	<a href="#">5500</a>	<a href="#">19046</a>	<a href="#">25594</a>
PPP1R1B	protein phosphatase 1, regulatory (inhibitor) subunit 1B (dopamine and cAMP regulated phosphoprotein, DARPP-32)	Cytoplasm	phosphatase	<a href="#">84152</a>	<a href="#">19049</a>	<a href="#">360616</a>
PTGS2	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	Cytoplasm	enzyme	<a href="#">5743</a>	<a href="#">19225</a>	<a href="#">29527</a>
PTPN5	protein tyrosine phosphatase, non-receptor type 5 (striatum-enriched)	Cytoplasm	phosphatase	<a href="#">84867</a>	<a href="#">19259</a>	<a href="#">29644</a>
PVR	poliovirus receptor	Plasma Membrane	G-protein coupled receptor	<a href="#">5817</a>	<a href="#">52118</a>	<a href="#">25066</a>
RAP1B	RAP1B, member of RAS oncogene family	Cytoplasm	enzyme	<a href="#">5908</a>	<a href="#">215449</a>	<a href="#">171337</a>
RAPGEF5	Rap guanine nucleotide exchange factor (GEF) 5	Unknown	other	<a href="#">9771</a>	<a href="#">217944</a>	<a href="#">500748</a>
RBM3	RNA binding motif (RNP1, RRM) protein 3	Nucleus	other	<a href="#">5935</a>	<a href="#">19652</a>	<a href="#">114488</a>
RBM5	RNA binding motif protein 5	Nucleus	other	<a href="#">10181</a>	<a href="#">83486</a>	<a href="#">300996</a>
RET	ret proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, Hirschsprung disease)	Plasma Membrane	kinase	<a href="#">5979</a>	<a href="#">19713</a>	<a href="#">24716</a>
RGS2	regulator of G-protein signalling 2, 24kDa	Nucleus	other	<a href="#">5997</a>	<a href="#">19735</a>	<a href="#">84583</a>
ROCK1	Rho-associated, coiled-coil containing protein kinase 1	Cytoplasm	kinase	<a href="#">6093</a>	<a href="#">19877</a>	<a href="#">81762</a>
RPL10	ribosomal protein L10	Cytoplasm	other	<a href="#">6134</a>	<a href="#">110954</a>	<a href="#">81764</a>
RPL10A	ribosomal protein L10a	Cytoplasm	other	<a href="#">4736</a>	<a href="#">19896</a>	<a href="#">81729</a>
RPL19	ribosomal protein L19	Cytoplasm	other	<a href="#">6143</a>	<a href="#">19921</a>	<a href="#">81767</a>
RPL22	ribosomal protein L22	Nucleus	other	<a href="#">6146</a>	<a href="#">19934</a>	<a href="#">81768</a>
RPL35	ribosomal protein L35	Cytoplasm	other	<a href="#">11224</a>	<a href="#">66489</a>	<a href="#">296709</a>
RPL7	ribosomal protein L7	Cytoplasm	transcription regulator	<a href="#">6129</a>	<a href="#">19989</a>	<a href="#">297755</a>
RPS13	ribosomal protein S13	Cytoplasm	other	<a href="#">6207</a>	<a href="#">68052</a>	<a href="#">161477</a>
RPS18	ribosomal protein S18	Cytoplasm	other	<a href="#">6222</a>	<a href="#">20084</a>	<a href="#">294282</a>
RPS19	ribosomal protein S19	Cytoplasm	other	<a href="#">6223</a>	<a href="#">20085</a>	<a href="#">29287</a>
RPS4X	ribosomal protein S4, X-linked	Cytoplasm	other	<a href="#">6191</a>	<a href="#">20102</a>	<a href="#">29426</a>

RPS9	ribosomal protein S9	Cytoplasm	other	<a href="#">6203</a>	<a href="#">76846</a>	<a href="#">81772</a>
RPSA	ribosomal protein SA	Plasma Membrane	transmembrane receptor	<a href="#">3921</a>	<a href="#">16785</a>	<a href="#">29236</a>
SCG2	secretogranin II (chromogranin C)	Extracellular Space	other	<a href="#">7857</a>	<a href="#">20254</a>	<a href="#">24765</a>
SERP1	stress-associated endoplasmic reticulum protein 1	Cytoplasm	other	<a href="#">27230</a>	<a href="#">28146</a>	<a href="#">80881</a>
SERPINB1	serpin peptidase inhibitor, clade B (ovalbumin), member 1	Cytoplasm	other	<a href="#">1992</a>	<a href="#">66222</a>	<a href="#">291091</a>
SFTPC	surfactant, pulmonary-associated protein C	Extracellular Space	other	<a href="#">6440</a>	<a href="#">20389</a>	<a href="#">50683</a>
SLA	Src-like-adaptor	Plasma Membrane	other	<a href="#">6503</a>	<a href="#">20491</a>	<a href="#">338477</a>
SLC7A8	solute carrier family 7 (cationic amino acid transporter, y+ system), member 8	Plasma Membrane	transporter	<a href="#">23428</a>	<a href="#">50934</a>	<a href="#">84551</a>
SMAD1	SMAD, mothers against DPP homolog 1 (Drosophila)	Nucleus	transcription regulator	<a href="#">4086</a>	<a href="#">17125</a>	<a href="#">25671</a>
SNRP70	small nuclear ribonucleoprotein 70kDa polypeptide (RNP antigen)	Nucleus	other	<a href="#">6625</a>	<a href="#">20637</a>	<a href="#">361574</a>
SNX9	sorting nexin 9	Cytoplasm	transporter	<a href="#">51429</a>	<a href="#">66616</a>	<a href="#">na</a>
SP1	spleen focus forming virus (SFFV) proviral integration oncogene spi1	Nucleus	transcription regulator	<a href="#">6688</a>	<a href="#">20375</a>	<a href="#">366126</a>
SQSTM1	sequestosome 1	Cytoplasm	transcription regulator	<a href="#">8878</a>	<a href="#">18412</a>	<a href="#">113894</a>
SRC	v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog (avian)	Cytoplasm	kinase	<a href="#">6714</a>	<a href="#">20779</a>	<a href="#">83805</a>
ST13	suppression of tumorigenicity 13 (colon carcinoma) (Hsp70 interacting protein)	Cytoplasm	other	<a href="#">6767</a>	<a href="#">70356</a>	<a href="#">81800</a>
STAT3	signal transducer and activator of transcription 3 (acute-phase response factor)	Nucleus	transcription regulator	<a href="#">6774</a>	<a href="#">20848</a>	<a href="#">25125</a>
STMN3	stathmin-like 3	Unknown	other	<a href="#">50861</a>	<a href="#">20262</a>	<a href="#">29246</a>
TAC1	tachykinin, precursor 1	Extracellular Space	other	<a href="#">6863</a>	<a href="#">21333</a>	<a href="#">24806</a>
TAP2	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)	Plasma Membrane	transporter	<a href="#">6891</a>	<a href="#">21355</a>	<a href="#">24812</a>
TAPBP	TAP binding protein (tapasin)	Cytoplasm	transporter	<a href="#">6892</a>	<a href="#">21356</a>	<a href="#">25217</a>
TAX1BP3	Tax1 (human T-cell leukemia virus type I) binding protein 3	Nucleus	transcription regulator	<a href="#">30851</a>	<a href="#">76281</a>	<a href="#">360564</a>
TGFB1	transforming growth factor, beta 1 (Camurati-Engelmann disease)	Extracellular Space	growth factor	<a href="#">7040</a>	<a href="#">21803</a>	<a href="#">59086</a>
TH	tyrosine hydroxylase	Cytoplasm	enzyme	<a href="#">7054</a>	<a href="#">21823</a>	<a href="#">25085</a>
TIMP1	TIMP metalloproteinase inhibitor 1	Extracellular Space	other	<a href="#">7076</a>	<a href="#">21857</a>	<a href="#">116510</a>
TM4SF1	transmembrane 4 L six family member 1	Plasma Membrane	other	<a href="#">4071</a>	<a href="#">17112</a>	<a href="#">295061</a>
TMEM49	transmembrane protein 49	Plasma Membrane	other	<a href="#">81671</a>	<a href="#">75909</a>	<a href="#">192129</a>
TNF	tumor necrosis factor (TNF superfamily, member 2)	Extracellular Space	cytokine	<a href="#">7124</a>	<a href="#">21926</a>	<a href="#">24835</a>
TPM1	tropomyosin 1 (alpha)	Cytoplasm	other	<a href="#">7168</a>	<a href="#">22003</a>	<a href="#">24851</a>
TPM2	tropomyosin 2 (beta)	Cytoplasm	other	<a href="#">7169</a>	<a href="#">22004</a>	<a href="#">500450</a>
TPM3	tropomyosin 3	Cytoplasm	other	<a href="#">7170</a>	<a href="#">59069</a>	<a href="#">117557</a>
TPM4	tropomyosin 4	Cytoplasm	other	<a href="#">7171</a>	<a href="#">326618</a>	<a href="#">24852</a>
TPR	translocated promoter region (to activated MET oncogene)	Nucleus	other	<a href="#">7175</a>	<a href="#">108989</a>	<a href="#">304862</a>
TPSD1	tryptase delta 1	Extracellular Space	peptidase	<a href="#">23430</a>	<a href="#">na</a>	<a href="#">na</a>
UCHL1	ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)	Cytoplasm	peptidase	<a href="#">7345</a>	<a href="#">22223</a>	<a href="#">29545</a>
UCHL3	ubiquitin carboxyl-terminal esterase L3 (ubiquitin thiolesterase)	Cytoplasm	peptidase	<a href="#">7347</a>	<a href="#">50933</a>	<a href="#">114094</a>



VEZT	vezatin, adherens junctions transmembrane protein	Plasma Membrane	other	<a href="#">55591</a>	<a href="#">215008</a>	<a href="#">299738</a>
VIL2	villin 2 (ezrin)	Plasma Membrane	other	<a href="#">7430</a>	<a href="#">22350</a>	<a href="#">54319</a>
XPO1	exportin 1 (CRM1 homolog, yeast)	Nucleus	transporter	<a href="#">7514</a>	<a href="#">103573</a>	<a href="#">85252</a>
YWHAZ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide	Cytoplasm	enzyme	<a href="#">7534</a>	<a href="#">22631</a>	<a href="#">25578</a>
ZC3H13	zinc finger CCCH-type containing 13	Unknown	other	<a href="#">23091</a>	<a href="#">67302</a>	<a href="#">305955</a>