Enrichment of Phosphorylated Tau (Thr181) and Functionally Interacting Molecules in Chronic Traumatic Encephalopathy Brain-derived Extracellular Vesicles

Satoshi Muraoka¹, Weiwei Lin²,³, Kayo Takamatsu-Yukawa¹, Jianqiao Hu¹, Seiko Ikezu¹, Michael A. DeTure⁴, Dennis W. Dickson⁴, Andrew Emili²,³, Tsuneya Ikezu¹,⁵,⁶*
Supplementary Figure 1. Gene Ontology (GO) analysis of CTE brain-derived EV proteins using DAVID Bioinformatics Resources 6.8. The GO term of Top5 Cellular Component A), Molecular Function B), Biological process C), Tissue Expression Ontology D), Disease Ontology E), and KEGG Pathway F) with -log10(FDR p-value).

Supplementary Figure 2. Networks generated by Ingenuity pathway analysis. The canonical pathways that were up - and down - regulated in CTE compared to controls. Upregulated or down regulated pathway are denoted in red or blue.
Supplementary Figure 3. A box plot of TMT-reporter intensity normalized by pooled sample as a standard control. The t-test was calculated by Welch’s test. A) The 19 proteins were up-regulated in CTE compared to CTRL groups. B) The four proteins were down-regulated in CTE compared to CTRL groups.
**Supplementary Figure 4.** Comparison of CTE brain-derived EV proteome and AD brain-derived EV proteome. 

A) The AD brain-derived EV proteome were identified 1080 proteins [1]. The 613 proteins were common between CTE brain-derived EV and AD brain-derived EV proteins. 

B) Scattered plot of CTE brain-derived EV and AD brain-derived EV proteins ($r = -0.0514$, $p = 0.2397$ using two-tailed t-test).

**Supplementary Figure 5.** Comparison of CTE brain-derived EV proteome and CTE brain tissue homogenates proteome. The CTE brain tissue homogenates proteomics data, which was published by Bi et al. was identified 6218 proteins [2]. The 843 proteins were common between CTE brain-derived EV and CTE brain tissue homogenate proteins.
**Supplementary Table 1.** Assessment of the degree of purity of EV preparation.

| Category | Gene name          | Uniprot ID |
|----------|--------------------|------------|
| 1a       | GNAI2              | P04899     |
|          | GNAO1              | P09471     |
|          | GNAZ               | P19086     |
|          | GNA11              | P29992     |
|          | GNAQ               | P50148     |
|          | GNAS               | P63092     |
|          | GNAI1              | P63096     |
|          | GNA13              | Q14344     |
|          | HLA-B              | P01889     |
|          | ITGAV              | P06756     |
|          | ITGA6              | P23229     |
|          | ITGB1              | P05556     |
|          | EMMPRIN (BSG)      | P35613     |
|          | ADAM10             | O14672     |
|          | CD73 (NT5E)        | P21589     |
|          | CD59               | P13987     |
| 1b       | CD90 (THY1)        | P04216     |
|          | APP                | P05067     |
| 2a       | ALIX (PDCD6IP)     | Q8WUM4     |
|          | FLOT1              | Q075955    |
|          | FLOT2              | Q14254     |
|          | EHD1               | Q9H4M9     |
|          | EHD3               | Q9NZN3     |
|          | EHD2               | Q9NZN4     |
|          | RHOA               | P0483      |
|          | ANXA1              | P07355     |
|          | ANXA2              | P08133     |
|          | ANXA5              | P08758     |
### SUPPLEMENTARY DATA

| Protein | PDB ID |
|---------|--------|
| ANXA7   | P20073 |
| ANXA11  | P50995 |
| HSPA8   | P11142 |
| HSP90AB1| P08238 |
| SDCBP   | O00560 |
| Tau (MAPT) | P10636 |
| ACTG1   | P63261 |
| TUBAL3  | A6NHL2 |
| TPPP    | Q94811 |
| TUBB4A  | P04350 |
| TUBB    | P07437 |
| TUBA1A  | Q71U36 |
| TUBA4A  | P68366 |
| TUBB4B  | P68371 |
| TUBB3   | Q13509 |
| TUBB2B  | Q9BVA1 |
| TUBB8   | Q3ZCM7 |
| GAPDH   | P04406 |

#### Major components of non-EV co-isolated structures

| For non-EV (contaminant) |
|--------------------------|
| ALB (contaminant)        |
| P02768                   |

#### Analysis of protein of this category is required when claiming specific analysis of small EVs

| Evs (large oncosomes, large EVs) |
|-----------------------------------|
| For small EVs                     |

#### Functional activites

| For functional component |
|--------------------------|
| ACTN1                    |
| P12814                   |
| MFGE8                    |
| Q08431                   |

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### Tetraspanin TSPAN7 P41732

| Protein names | Ave_CTRL | Ave_CTE | log₂(CTE/CTR LFC) | p-value* |
|---------------|----------|---------|-------------------|----------|
| Rab4A         | 0.982612065 | 1.082613861 | 0.139824906 | 0.03017023 |
| Rab4B         | 1.085606193 | 1.235035538 | 0.186051699 | 0.00798276 |
| Rab5b         | 1.062220295 | 0.785712598 | -0.435009401 | 0.02676405 |
| Rab5c         | 0.918166614 | 1.026720028 | 0.161214955 | 0.0177589  |
| Rab11b        | 0.916464824 | 1.071238358 | 0.225128112 | 0.03529199 |
| Rab7a         | 0.904892386 | 1.155341546 | 0.352501273 | 0.01836626 |
| VPS28         | 1.055683554 | 1.235843659 | 0.2273188  | 0.00948977 |
| VPS36         | 1.015761905 | 1.145433765 | 0.173331764 | 0.0160733  |

**ESCRT machinery**
- Snf7-2(CHMP4B,VPS32B)
- Rab27b
- Rab35

**syntenin-1(SDCBP)**
- O00560

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**Supplementary Table 2.** Identification and quantification of EVs separated from CTE and controls brain tissue.

| Protein IDs | Gene names | Protein names | Ave_CTRL | Ave_CTE | log₂(CTE/CTR LFC) | p-value* |
|-------------|------------|---------------|----------|---------|-------------------|----------|
| P10599      | TXN        | Thioredoxin   | 0.982612065 | 1.082613861 | 0.139824906 | 0.03017023 |
| Q01813      | PFKP       | ATP-dependent 6-phosphofructokinase, platelet type | 1.085606193 | 1.235035538 | 0.186051699 | 0.00798276 |
| P05408      | SCG5       | Neuroendocrine protein 7B2 | 1.062220295 | 0.785712598 | -0.435009401 | 0.02676405 |
| P19784      | CSNK2A2    | Casein kinase II subunit alpha | 0.918166614 | 1.026720028 | 0.161214955 | 0.0177589  |
| Q7Z6L0      | PRRT2      | Proline-rich transmembrane protein 2 | 0.904892386 | 1.155341546 | 0.352501273 | 0.01836626 |
| Q14194      | CRMP1      | Dihydropyrimidinase-related protein 1 | 1.055683554 | 1.235843659 | 0.2273188  | 0.00948977 |
| Q2M1P5      | KIF7       | Kinesin-like protein KIF7 | 1.015761905 | 1.145433765 | 0.173331764 | 0.0160733  |
| P30101      | PDIA3      | Protein disulfide-isomerase A3 | 1.02330167 | 0.915955765 | -0.159881684 | 0.0160897 |
| P28482      | MAPK1      | Mitogen-activated protein kinase 1 | 0.954403551 | 1.147871841 | 0.26629026 | 0.02040801 |
| P45974      | USP5       | Ubiquitin carboxyl-terminal hydrolase 5 | 0.916464824 | 1.071238358 | 0.225128112 | 0.03529199 |
| P60880      | SNAP25     | Synaptosomal-associated protein 25 | 0.981106094 | 1.065253762 | 0.118716088 | 0.03648962 |
| P9471      | GNAO1      | Guanine nucleotide-binding protein G(o) subunit alpha | 0.948644336 | 1.09302717 | 0.204390062 | 0.03885183 |
| Q13303      | KCNAB2     | Voltage-gated potassium channel subunit beta-2 | 0.930639255 | 1.094655054 | 0.234182357 | 0.0408079 |
| Q9HCH3      | CPNE5      | Copine-5 | 0.939261395 | 1.050479096 | 0.161448835 | 0.03133789 |
| P05023      | ATP1A1     | Sodium/potassium-transporting ATPase subunit alpha-1 | 1.020500163 | 1.095769097 | 0.10266741 | 0.04086187 |
| P50991      | CCT4       | T-complex protein 1 subunit delta Ubiquitin-like modifier-activating enzyme 1 | 1.135414227 | 1.389039333 | 0.29068728 | 0.04180259 |
| P22314      | UBA1       | Ubiquitin-like modifier-activating enzyme 1 | 0.959177128 | 1.052764798 | 0.134313993 | 0.01668341 |
| P31946      | YWHAB      | 14-3-3 protein beta/alpha | 0.579359454 | 0.448843351 | -0.368246697 | 0.02909462 |

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SUPPLEMENTARY DATA

Q99747  NAPG  Gamma-soluble NSF attachment protein  1.008103  1.16837079  0.212855146  0.03915817
Q6PLU2  NCEH1  Neutral cholesterol ester hydrolase 1  1.272657073  1.649581262  0.374256124  0.06161237
P09104  ENO2  Gamma-enolase  0.935193492  1.03839098  0.151010321  0.09073574
Q99962  SHHGL2  Endophilin-A1  0.981358666  1.116447738  0.186063307  0.04359349
Q09470  KCNA1  Potassium voltage-gated channel subfamily A member 1  0.98083712  1.117297332  0.187927678  0.06794857
P53396  ALCY  ATP-citrate synthase  1.038903882  1.088062233  0.066698893  0.09044608
Q96P70  IPO9  Importin-9  0.917206873  1.064370374  0.214681189  0.09865718
P23229  ITGA6  Integrin alpha-6  1.036748536  0.937558972  -0.145084666  0.10187327
Q9HCM2  PLXNA4  Plexin-A4  0.976464483  1.078772247  0.143750837  0.1171458
P31150  GDI1  Rab GDP dissociation inhibitor alpha  0.968822602  1.034160218  0.094155285  0.02791495
P27338  MAOB  Amine oxidase [flavin-containing] B  1.061473482  0.904472061  -0.230920487  0.04984126
Q13362  PPP2R5C  56 kDa regulatory subunit gamma isoform  0.914288685  0.794451496  -0.202696025  0.05915672
Q9BSJ8  ESYT1  Extended synaptotagmin-1  1.006426227  1.122747054  0.157791514  0.06115764
O60716  CTNNB1  Catenin delta-1  0.925113386  1.054007254  0.188182692  0.08825566
P15880  RPS2  40S ribosomal protein S2  1.230793478  1.069881313  -0.202137944  0.09545186
Q9Y368  CAB39  Calcium-binding protein 39  0.900883951  1.043832341  0.21246425  0.05279138
P09417  QDPR  Dihydropyridine reductase  1.023302823  1.248821499  0.28298544  0.07424693
P16152  CBR1  Carboxyl reductase [NADPH] 1  1.043462464  1.138211357  0.125389781  0.07705886
P69905  HBA1  Hemoglobin subunit alpha  1.041767463  0.85982004  -0.276926642  0.08199897
Q01518  CAP1  Adenyl cyclase-associated protein 1  1.046756571  1.1705398  0.161248014  0.09537515
Q95248  SBF1  Myotubularin-related protein 5  1.07777102  1.195061915  0.149034664  0.09680421
P12277  CKB  Creatine kinase B-type  0.946818517  1.006695022  0.088466859  0.11105851
P30086  PEBP1  Phosphatidylethanolamine-binding protein 1  1.032470494  1.130739277  0.131165762  0.11139839
P28907  CD38  ADP-ribosyl cyclase/cyclo ADP-ribose hydrolase 1  1.075662815  1.213208895  0.17360207  0.11399442
P61266  STXB1  Syntaxin-1B  1.005289032  1.080905445  0.10448647  0.13824936
P63027  VAMP2  Vesicle-associated membrane protein 2  0.973884224  1.048020207  0.10584355  0.24635526
Q4GF0F  VPS26B  Vacuolar protein sorting-associated protein 26B  0.984501705  1.117332971  0.18259357  0.04534982
Q9BWFD1  ACAT2  Acetyl-CoA acetyltransferase, cytosolic  0.817494164  1.001671045  0.293128459  0.10507972
Q69BM9  ARL8A  ADP-ribosylation factor-like protein 8A  1.087184702  1.02393186  -0.086477349  0.30395439
O75340  PDCD6  Programmed cell death protein 6  0.920825818  0.876528617  -0.07130053  0.35708879
Q16555  DPYSL2  Dihydropyrimidinase-related protein 2  0.910871991  0.991544663  0.122429439  0.36340199
P02794  FTH1  Ferritin heavy chain  0.448145549  0.3317706  -0.433781321  0.17193684
P10636  MAPT  Microtubule-associated protein tau  1.003851757  1.325966891  0.401500474  0.0683613
Q14515  SPARCL1  SPARC-like protein 1  0.980948044  0.839278509  -0.225072088  0.08457788
P06744  GPI  Glucose-6-phosphate isomerase  1.056091552  1.123245997  0.088934096  0.1103881
Q05193  DNM1  Dynamin-1  1.017043852  1.098685602  0.11139672  0.1112133
Q25958  HSPH1  Heat shock protein 105 kDa  1.015918343  1.145246733  0.172874001  0.1132252
O75110  ATP9A  Probable phospholipid-transporting ATPase IIa  0.956898483  0.824094438  -0.215556204  0.11877693

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## SUPPLEMENTARY DATA

| Gene Symbol | Gene Name                        | Description                                                                 | Fold Change |
|-------------|----------------------------------|-----------------------------------------------------------------------------|-------------|
| Q9Y2A7      | NCKAP1                           | Nck-associated protein 1                                                   | 0.938191141 |
| Q86UW7      | CADPS2                           | Calcium-dependent secretion activator 2                                    | 1.006201695 |
| P50914      | RPL14                            | 60S ribosomal protein L14                                                   | 1.051315187 |
| Q13618      | CUL3                             | Cullin-3                                                                    | 1.059081126 |
| Q14203      | DCTN1                            | Dynactin subunit 1                                                          | 0.90548381  |
| Q9PJ0       | NDUFA13                          | NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 13              | 1.138406559 |
| Q43169      | CYB5B                            | Cytochrome b5 type B                                                        | 2.13416317  |
| P17252      | PRKCA                            | Protein kinase C alpha type                                                  | 0.970330001 |
| A1L0T0      | ILVBL                            | Acetolactate synthase-like protein                                          | 1.21368749  |
| P26232      | CTNNA2                           | Catenin alpha-2                                                             | 0.940720149 |
| Q9Y7Q0      | ATP8A1                           | Phospholipid-transporting ATPase IA                                        | 0.937532877 |
| O75781      | PALM                             | Parallemnin-1                                                               | 0.967723659 |
| P14174      | MIF                              | Macrophage migration inhibition factor                                      | 1.043939213 |
| P84085      | ARF5                             | ADP-ribosylation factor 5                                                   | 0.906290002 |
| Q9NS86      | LANCL2                           | LanC-like protein 2                                                          | 1.148146464 |
| Q9NP79      | VTA1                             | Vacuolar protein sorting-associated protein VTA1 homolog                   | 0.951069703 |
| P08237      | PFKM                             | ATP-dependent 6-phosphofructokinase, muscle type                            | 1.017346303 |
| Q13424      | SNTA1                            | Alpha-1-syntrophin                                                          | 1.02142877  |
| Q86Y82      | STX12                            | Syntaxin-12                                                                 | 1.107764005 |
| Q9Y4I1      | MYO5A                            | Unconventional myosin-Va                                                    | 0.95545354  |
| P48147      | PREP                             | Prolyl endopeptidase                                                         | 0.903409501 |
| P04271      | S100B                            | Protein S100-B                                                              | 0.776861888 |
| P49720      | PSMB3                            | Proteasome subunit beta type-3                                              | 0.906371267 |
| P17600      | SYN1                             | Synapsin-1                                                                  | 0.967258858 |
| Q99798      | ACO2                             | Aconitate hydratase, mitochondrial                                           | 1.025601632 |
| O43175      | PHGDH                            | D-3-phosphoglycerate dehydrogenase                                          | 0.968996428 |
| P40925      | MDH1                             | Malate dehydrogenase, cytoplasmian                                          | 0.942095378 |
| P63261      | ACTG1                            | Actin                                                                       | 0.943728435 |
| O00410      | IPO5                             | Importin-5                                                                  | 1.024037665 |
| Q8NEV1      | CSNK2A3                          | Casein kinase II subunit alpha 3                                            | 0.869727732 |
| P55786      | NPEPPS                           | Puromycin-sensitive aminopeptidase                                          | 0.9585094   |
| Q9UQM7      | CAMK2A                           | Calcium/calmodulin-dependent protein kinase type II subunit alpha 3         | 0.970873153 |
| Q9NZN3      | EHD3                             | EH domain-containing protein 3                                              | 0.962597273 |
| O75915      | ARL6IP5                          | Rho1 family protein 3                                                        | 0.976972165 |
| P07195      | LDHB                             | L-lactate dehydrogenase B chain                                             | 1.065088813 |
| P63000      | RAC1                             | Ras-related C3 botulinum toxin substrate 1                                 | 1.068890274 |
| P05026      | ATP1B1                           | Sodium/potassium-transporting ATPase subunit beta-1                         | 0.988942486 |
| P09382      | LGALS1                           | Galectin-1                                                                  | 1.063676163 |
| O00483      | NDUFA4                           | Cytochrome c oxidase subunit NDUFA4                                         | 1.009674672 |

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| Protein ID | Description | Expression Values | qValues |
|-----------|-------------|------------------|---------|
| O60268    | KIAA0513    | Uncharacterized protein KIAA0513 | 1.10507927 | 0.133620856 | 0.1015544 |
| Q7Z3U7    | MON2        | Protein MON2 homolog | 1.009095705 | -0.23151882 | 0.12748011 |
| Q15041    | ARL6IP1     | GDP-ribosylation-factor-like protein 6-interacting protein 1 | 1.045849723 | -0.250999693 | 0.13160171 |
| P00533    | EGFR        | Epidermal growth factor receptor | 1.008166123 | 0.173423456 | 0.13194395 |
| Q9UBQ0    | VPS29       | Vacuolar protein-sorting-associated protein 29 | 1.132090478 | 0.271097136 | 0.15286866 |
| A6NH2L    | TUBAL3      | Tubulin alpha chain-like 3 | 1.06315508 | 0.217980253 | 0.16816353 |
| Q96GG9    | DCUN1D1     | DCN1-like protein 1 | 1.052848964 | -0.16869529 | 0.18367177 |
| P04264    | KRT1        | Keratin, type II cytoskeletal 1 | 0.967086869 | 0.077385241 | 0.18741636 |
| O43301    | HSPA12A     | Heat shock 70 kDa protein 12A | 0.978804694 | 0.048619767 | 0.20479927 |
| P60842    | EIF4A1      | Eukaryotic initiation factor 4A-1 | 0.920698886 | 0.048956559 | 0.20801122 |
| Q9NZ32    | ACTR10      | Actin-related protein 10 | 1.010337044 | -0.130186633 | 0.23345782 |
| Q9ULP9    | TBC1D24     | TBC1 domain family member 24 | 0.945830879 | 0.151967984 | 0.2433588 |
| P21283    | ATP6VC1C    | V-type proton ATPase subunit C1 | 1.08091819 | -0.210421008 | 0.24516676 |
| P04350    | TUBB4A      | Tubulin beta-4A chain | 0.950169562 | 0.078632377 | 0.27197948 |
| Q96CS3    | FAF2        | FAS-associated factor 2 | 1.102912551 | 0.096850758 | 0.27388793 |
| P29401    | TKT         | Transketolase | 0.96871469 | 0.083390834 | 0.28544996 |
| Q15102    | PAFAH1B3    | Platelet-activating factor acetylcholinesterase IB subunit gamma | 1.06372751 | 0.098729847 | 0.29555027 |
| Q96JE9    | MAP6        | Microtubule-associated protein 6 | 1.039625288 | 0.120631164 | 0.31691167 |
| P61604    | HSPE1       | 10 kDa heat shock protein, mitochondrial protein kinase C and casein kinase substrate in neurons protein 1 | 1.088189971 | -0.196265467 | 0.32533134 |
| Q9BY11    | PACSIN1     | Flotillin-1 | 1.008453522 | 0.064218245 | 0.36144783 |
| Q14254    | FLOT2       | Plasma membrane calcium-transporting ATPase 4 | 0.886905268 | 0.097179154 | 0.3659768 |
| P23634    | ATP2B4      | Fatty acid synthase | 1.056499538 | 0.081765267 | 0.37063832 |
| P49327    | FASN        | Mitochondrial protein 6 | 1.038945777 | 0.126620167 | 0.43807416 |
| O14807    | MRAS        | Ras-related protein M-Ras | 0.960028369 | 0.104055588 | 0.55636199 |
| O43426    | SYNJ1       | Synaptotaginin-1 | 1.078981344 | -0.173833551 | 0.14135747 |
| Q9GZ7N    | ROGDI       | Protein rogdi homolog | 0.899988277 | 0.138633595 | 0.14620629 |
| P22695    | UQCR2C      | Cytochrome b-1 complex subunit 2, mitochondrial | 1.083186817 | -0.103672255 | 0.21223858 |
| Q13363    | CTBP1       | C-terminal-binding protein 1 | 0.949848538 | -0.109231511 | 0.22483683 |
| P00568    | AK1         | Adenylyl kinase isoenzyme 1 | 1.031381874 | -0.092673959 | 0.2258126 |
| Q02818    | NUCB1       | Nucleobindin-1 | 0.921189388 | 0.087689111 | 0.24823236 |
| P78352    | DLG4        | Disks large homolog 4 | 0.960874935 | 0.317823706 | 0.26082387 |
| P19367    | HK1         | Hexokinase-1 | 1.082296633 | 0.100887352 | 0.26160237 |
| P07437    | TUBB        | Tubulin beta chain | 0.900858568 | 0.07245779 | 0.26635224 |
| Q92597    | NDRG1       | Protein NDRG1 | 1.055256837 | 0.185801198 | 0.26654388 |
| P60891    | PRPS1       | Ribose-phosphate pyrophosphokinase 1 | 0.942363461 | 0.068068251 | 0.28672437 |
| Q04837    | SSBP1       | Single-stranded DNA-binding protein, mitochondrial | 1.179058055 | 0.168268598 | 0.29628889 |
| P61421    | ATP6V0D1    | V-type proton ATPase subunit d1 | 1.049594628 | -0.092357776 | 0.32718953 |
| O75390    | CS          | Citrate synthase, mitochondrial | 1.015032268 | -0.147872313 | 0.34083914 |
| P50148    | GNAQ        | Guanine nucleotide-binding protein G(q) subunit alpha | 0.994836159 | -0.032432125 | 0.35508835 |

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| ID     | Gene Name | Protein Name                                                                 | Log2 fold change |
|--------|-----------|-------------------------------------------------------------------------------|------------------|
| Q9UB6  | NCDN      | Neurochondrin, Cytosolic acyl coenzyme A thioloester hydrolase                | 0.948435753      |
| O00154 | ACOT7     | 78 kDa glucose-regulated protein                                             | 1.096986762      |
| P11021 | HSPA5     | Lambda-crystallin homolog Serine/threonine-protein phosphatase 2B            | 0.871894902      |
| Q9Y2S2 | CRYL1     | Catalytic subunit beta isoform                                               | 0.896143137      |
| P16298 | PPP3CB    | Glutamate receptor 2                                                          | 1.068507713      |
| P42262 | GRIA2     | Cadherin-1                                                                    | 0.979055581      |
| P55290 | CDH13     | Ubiquitin carboxyl-terminal hydrolase 7                                      | 0.933782714      |
| P18124 | RPL7      | Protein S100-A13                                                              | 1.07982596       |
| P08133 | ANXA6     | Protein S100-A13                                                              | 0.951975329      |
| Q13098 | GPS1      | COP9 signalosome complex subunit 1                                            | 0.906389945      |
| O00764 | PDKX      | Pyridoxal kinase, Transitional endoplasmic reticulum ATPase                  | 0.955383873      |
| P55072 | VCP       | 60S ribosomal protein L7                                                       | 1.07982596       |
| Q99584 | S100A13   | Protein S100-A13                                                              | 0.6458782       |
| A6NDG6 | PGP       | Ras-related protein Rab-4A                                                   | 0.992020117      |
| P20338 | RAB4A     | Ras-related protein Rab-2A                                                    | 1.072468489      |
| Q15165 | PON2      | Heterogeneous nuclear ribonucleoproteins                                    | 0.842950473      |
| P22626 | HNRNPA2   | V-type proton ATPase subunit S1                                               | 1.091338869      |
| Q15904 | ATP6AP1   | Ras-related protein Rab-2A                                                    | 0.924466387      |
| P61019 | RAB2A     | Endoplasmic reticulum ATPase                                                  | 1.062987138      |
| P14625 | HSP90B1   | Abl interactor 2                                                               | 1.064803692      |
| Q9NYB9 | ABI2      | EH domain-containing protein 1                                                | 1.049537017      |
| Q9H4M9 | EHD1      | Fascin                                                                        | 0.989422084      |
| Q16658 | FSCN1     | GTPase Hras                                                                   | 0.980252166      |
| P01112 | HRAS      | Guanine nucleotide-binding protein Gi(Gi/Si(G(T) subunit beta-1               | 0.934628809      |
| P62873 | GNB1      | Ras-related protein Rab-11B                                                   | 1.100931985      |
| Q15907 | RAB11B    | Neuroplastin                                                                  | 1.001427377      |
| Q9Y639 | NPTN      | V-type proton ATPase subunit H                                                | 1.00046187       |
| Q9U12  | ATP6V1H   | CD59, CD59 glycoprotein, Methylmalonate-semialdehyde dehydrogenase [acylating], mitochondrial | 1.164275237      |
| P1987  | CDS9      | Immunoglobulin superfamily member 8                                           | 1.035068381      |
| Q02252 | ALDH6A1   | Synapsin-2                                                                    | 1.058763213      |
| Q9990  | IGSF8     | Metallo-beta-lactamase domain-containing protein 2                            | 1.004608816      |
| Q92777 | SYN2      | Protein S100-A13                                                              | 0.984080806      |
| Q68D91 | MBLAC2    | Interleukin 5                                                                  | 1.039406458      |
| Q9UMF0 | ICAM5     | Importin subunit beta-1                                                        | 1.132658096      |
| Q14974 | KPNB1     | Serine/threonine-protein phosphatase 2A                                        | 1.004274614      |
| Q96OK1 | VPS35     | 65 kDa regulatory subunit A alpha isoform                                      | 1.004270969      |
| P30153 | PPP2R1A   | ATPase ASNA1                                                                  | 0.976618888      |

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SUPPLEMENTARY DATA

| Gene | Description | Fold Change |
|------|-------------|-------------|
| ATP6V1E1 | V-type proton ATPase subunit E 1 | 0.979193465 1.044858678 0.093639504 0.45905423 |
| CCK | Cholecystokinin | 0.945642365 1.002434054 0.084140756 0.47454806 |
| PITPN | Phosphatidylinositol transfer protein alpha isoform | 0.961544989 0.906658997 -0.084794319 0.4904622 |
| LDHA | L-lactate dehydrogenase A chain | 1.002538966 1.051793753 0.076507801 0.50792775 |
| ARPC3 | Gamma-aminobutyric acid receptor subunit alpha-1 | 0.904668054 0.93573508 0.048156465 0.65199394 |
| GABRA1 | Alpha-crystallin B chain | 1.075324764 1.104784871 0.038993027 0.6709687 |
| CRYAB | AP-2 complex subunit alpha-2 | 0.97885472 1.04475526 0.093998364 0.31642722 |
| MDH2 | Malate dehydrogenase, mitochondrial | 1.125728337 1.15043926 0.031326099 0.91394278 |
| TAGLN3 | Transgelin-3 | 0.989068773 1.092579991 0.143596164 0.24885081 |
| NDUFS2 | NADH dehydrogenase [ubiquinone] iron-sulfur protein 2, mitochondrial | 1.009081191 0.873070612 -0.208872014 0.27176613 |
| AP2A1 | Clathrin heavy chain 1 | 0.97885472 1.04475526 0.093998364 0.31642722 |
| UCHL1 | Ubiquitin carboxy-terminal hydrolase isozyme L1 | 1.021488333 1.098110274 0.104350213 0.33481606 |
| SLC30A3 | Zinc transporter 3 | 1.093242001 0.98066695 -0.156763294 0.36369731 |
| CLTC | Clathrin heavy chain | 0.940812436 0.973041608 0.048594367 0.38505677 |
| ATP5A1 | ATP synthase subunit alpha, mitochondrial | 0.937375411 0.889773907 -0.075181859 0.39437362 |
| NDUFS1 | NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial | 1.038732187 1.109483411 0.095018718 0.40660574 |
| SRI | Sorcin | 1.15060291 1.25359238 0.123515394 0.4189102 |
| RALB | Ras-related protein Rab-B | 0.915068856 0.843421702 -0.117626162 0.42193721 |
| GNB2 | Guanine nucleotide-binding protein Gi(1)/Gi(2)/Gi(3) beta-2 | 0.983512541 0.103009991 0.042632946 0.49294396 |
| PGAM1 | Phosphoglycerate mutase 1 | 0.823186131 0.741772538 -0.150241819 0.44530493 |
| EB4L1 | Band 4.1-like protein 1 | 1.090579283 1.13168407 0.053384939 0.5269328 |
| NAPA | Alpha-soluble NSF attachment protein | 0.98052614 0.935752876 -0.067428515 0.56524083 |
| PLD3 | Phospholipase D3 | 1.090965671 1.073146052 -0.02375927 0.6862825 |
| DPYSL3 | Dihydropyrimidinase-related protein 3 | 1.165931701 1.191346192 0.031109426 0.82900167 |
| HAGH | Hydroxyacylglutathione hydrolase, mitochondrial | 0.934539968 1.099600061 0.234659884 0.21458832 |
| HSPA4 | Heat shock 70 kDa protein 4 | 0.987829215 0.925242389 -0.094430274 0.21733314 |
| ATP6V1A | V-type proton ATPase catalytic subunit A | 0.992606478 1.035235146 0.060664727 0.22177073 |
| CAPZA2 | F-actin-capping protein subunit alpha-2 | 1.02801848 1.119073588 0.122443818 0.24712946 |
| CYCS | Cytochrome c | 0.89444553 0.82668266 -0.113685122 0.30235051 |
| RAB1B | Ras-related protein Rab-1B | 0.945120462 0.993153927 0.071519114 0.31475079 |
| GNA12 | Guanine nucleotide-binding protein G(i) subunit alpha-2 | 1.051655047 1.185298649 0.172589043 0.33557935 |
| VCAN | Versican core protein | 0.974697232 1.038107932 0.090930396 0.33705854 |
| FLOT1 | Flotillin-1 | 1.013383963 1.123978583 0.148680047 0.35835031 |
| PSMC5 | 26S proteasome regulatory subunit 8 | 0.990257979 0.982350721 0.113136056 0.36305189 |
| SLC8A1 | Sodium/calcium exchanger 1 | 1.108430231 1.175848325 0.085180413 0.36501147 |
| ARHGAP1 | Rho GTPase-activating protein 1 | 0.924771696 0.984733006 0.090635451 0.36655034 |
| PPP1R7 | Protein phosphatase 1 regulatory subunit 7 | 1.025136062 1.060249956 0.048589018 0.38661739 |
| RHBG | Ammonium transporter Rh type B | 0.975917126 0.928796303 -0.071396411 0.42309181 |
| PYGB | Glycogen phosphorylase, brain form | 0.980069278 1.004690174 0.035795035 0.42637202 |
| Gene symbol | Protein Name | Description |
|-------------|--------------|-------------|
| P67936      | TPM4         | Tropomyosin alpha-4 chain |
| Q9BTV4      | TMEM43       | Transmembrane protein 43 |
| P06733      | ENO1         | Alpha-enolase |
| Q5TF21      | SOGA3        | Protein SOGA3 |
| O15484      | CAPN5        | Calpain-5 |
| P13489      | RNH1         | Ribonuclease inhibitor |
| Q9UHY7      | ENOPH1       | Enolase-phosphatase E1 |
| P04075      | ALDOA        | Fructose-bisphosphate aldolase A |
| Q9UM19      | HPCAL4       | Hippocalcin-like protein 4 |
| Q9UQB3      | CTNND2       | Catenin delta-2 |
| Q9UPR5      | SLC8A2       | Sodium/calcium exchanger 2 |
| Q9ULX5      | RNF112       | RING finger protein 112 |
| P6286       | RAN          | GTP-binding nuclear protein Ran |
| O43581      | SYT7         | Synaptotagmin-7 |
| P20073      | ANXA7        | Annexin A7 |
| P09972      | ALDOC        | Fructose-bisphosphate aldolase C |
| P61106      | RAB14        | Ras-related protein Rab-14 |
| P14927      | UQCRB        | Cytochrome b-1 complex subunit 7 |
| P63104      | YWHAZ        | 14-3-3 protein zeta/delta |
| P08758      | ANXA5        | Annexin A5 |
| Q01814      | ATPB2        | Plasma membrane calcium-transporting ATPase 2 |
| P68366      | TUBA4A       | Tubulin alpha-4A chain |
| Q06124      | PTPN11       | Tyrosine-protein phosphatase non-receptor type 11 |
| P63010      | AP2B1        | AP-2 complex subunit beta |
| Q9NRW1      | RAB6B        | Ras-related protein Rab-6B |
| P10768      | ESD          | S-formylglutathione hydrolase 1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase beta-1 |
| Q9NQ66      | PLCB1        | |
| Q9ULU8      | CADPS        | Calcium-dependent secretion activator 1 |
| P21266      | GSTM3        | Glutathione S-transferase Mu 3 |
| P05091      | ALDH2        | Aldehyde dehydrogenase, mitochondrial |
| P48163      | ME1          | NADP-dependent malic enzyme |
| P15311      | EZR          | Ezrin |
| Q7Z6G3      | NECAB2       | N-terminal EF-hand calcium-binding protein 2 |
| O60531      | PIP5KC1      | Phosphatidylinositol 4-phosphate 5-kinase type-1 gamma |
| P54289      | CAMK2        | CaM kinase-like vesicle-associated protein |
| Q8NCB2      | CN1          | Contactin-1 |
| P07990      | HSP90AA1     | Heat shock protein HSP 90-alpha |
| O60641      | SNAP91       | Clathrin coat assembly protein PA180 |

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### SUPPLEMENTARY DATA

| Gene ID | Gene Name | Description | Log2 Fold Change |
|---------|-----------|-------------|-----------------|
| P29218  | IMPA1     | Inositol monophosphatase 1 | 1.013256326 |
| Q15293  | RCN1      | Reticulocalbin-1 | 0.999113874 |
| P63096  | GNAI1     | Guanine nucleotide-binding protein G(i) subunit alpha-1 | 0.824243486 |
| O00533  | CHL1      | Neural cell adhesion molecule L1-like protein | 1.127638455 |
| P18505  | GABRB1    | Gamma-aminobutyric acid receptor subunit beta-1 | 1.051258716 |
| O60675  | MAFK      | Transcription factor MaK | 1.120955325 |
| P56134  | ATP5J2    | ATP synthase subunit f, mitochondrial | 1.054582398 |
| Q7L099  | RUFY3     | Protein RUFY3 | 1.007708686 |
| O14531  | DPYSL4    | Dihydropyrimidinase-related protein 4 | 1.144671132 |
| P28472  | GABRB3    | Gamma-aminobutyric acid receptor subunit beta-3 | 1.080940046 |
| Q14416  | GRM2      | Metabotropic glutamate receptor 2 | 0.982905043 |
| P13637  | ATP1A3    | Sodium/potassium-transporting ATPase subunit alpha-3 | 1.019379219 |
| O75935  | DCTN3     | Dynactin subunit 3 | 1.091329041 |
| Q71U36  | TUBA1A    | Tubulin alpha-1A chain | 0.850296406 |
| Q05639  | EEF1A2    | Elongation factor 1-alpha 2 | 0.999168965 |
| P35611  | ADD1      | Alpha-2aducin | 1.019064647 |
| O95336  | PGLS      | 6-phosphogluconolactonase | 0.982855309 |
| Q9NV96  | TMEM30A   | Cell cycle control protein 50A | 1.213342244 |
| P08559  | PDHA1     | Pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial | 1.072963199 |
| P14618  | PKM       | Pyruvate kinase PKM | 0.960259815 |
| P52306  | RAP1GDS1  | Rap1 GTPase-GDP dissociation stimulator 1 | 0.89167333 |
| Q9YSK8  | ATP6V1D   | V-type proton ATPase subunit D | 1.082684824 |
| P20020  | ATP2B1    | Plasma membrane calcium-transporting ATPase 1 | 0.915296617 |
| O00429  | DNM1L     | Dynamin-1-like protein | 0.961251902 |
| Q13367  | AP3B2     | AP-3 complex subunit beta-2 | 0.916066309 |
| P36915  | GNL1      | Guanine nucleotide-binding protein-like 1 | 0.964288328 |
| P21579  | SYT1      | Synaptotagmin-1 | 0.974276183 |
| P53680  | AP2S1     | AP-2 complex subunit sigma | 1.032645787 |
| P09543  | CNP       | 2,3-cyclic-nucleotide 3-phosphodiesterase | 1.016460548 |
| P05186  | ALPL      | Alkaline phosphatase, tissue-nonspecific isozyme | 1.029721628 |
| Q16348  | SLC15A2   | Solute carrier family 15 member 2 | 0.986415479 |
| O94811  | TPPP      | Tubulin polymerization-promoting protein | 0.976087947 |
| P78356  | PIP4K2B   | Prolin-density lipoprotein receptor-related protein 1 | 0.95421541 |
| Q07954  | LRP1      | | 1.049626453 |
| O14576  | DYNC1H1   | Cytoplasmic dynein 1 intermediate chain 1 | 0.779951023 |
| P32119  | PRDX2     | Peroxiredoxin-2 | 1.004467875 |
| P14136  | GFAP      | Gial fibriallar acidic protein | 0.952405631 |
| P14406  | COX7A2    | Cytochrome c oxidase subunit 7A2, mitochondrial | 1.074166439 |
### SUPPLEMENTARY DATA

| Gene ID | Gene Name | Description | Fold Change |
|---------|-----------|-------------|-------------|
| Q14773 | TPP1 | Tripeptidyl-peptidase 1 | 1.107076431 |
| Q9NQR4 | NIT2 | Omega-amidase NIT2 | 0.86976434 |
| Q8N608 | DPP10 | Inactive dipeptidyl peptidase 10 | 0.98962906 |
| Q8N372 | ZNF33B | Zinc finger protein 33B | 1.16440304 |
| P11217 | PYGM | Glycogen phosphorylase, muscle form | 1.04165211 |
| P05067 | APP | Amyloid beta A4 protein | 1.122867851 |
| Q15008 | PSMD6 | 26S proteasome non-ATPase regulatory subunit 6 | 1.022462811 |
| Q9UP7V | KIAA1045 | Protein KIAA1045 | 0.956361807 |
| P50351 | SLC6A1 | 26S proteasome non-ATPase regulatory subunit 2 | 0.970004558 |
| Q13200 | PSMD2 | 26S proteasome non-ATPase regulatory subunit 2 | 0.897208744 |
| P60174 | TPPI | Triosephosphate isomerase | 0.919803266 |
| Q99880 | HIST1H2B | Histone H2B type 1-L | 0.966033672 |
| P12532 | CKMT1A | Creatine kinase U-type, mitochondrial | 1.01082866 |
| Q14204 | DYNC1H1 | Cytoplasmic dynein 1 heavy chain 1 | 0.978198527 |
| P17174 | GOT1 | Aspartate aminotransferase, cytoplasmic | 1.289030011 |
| Q13561 | DCTN2 | Dynactin subunit 2 | 0.995030054 |
| Q8WUW | BRK1 | Protein BRICK1 | 1.055724289 |
| Q92752 | TNR | Tenascin-R | 1.007799191 |
| P63151 | PPP2R2A | Serine/threonine-protein phosphatase 2A | 0.944883718 |
| Q8WUM4 | PDCD6IP | Programmed cell death 6-interacting protein | 0.916261065 |
| P10909 | CLU | Clusterin | 0.981728166 |
| Q13554 | CAMK2B | Calcium/calmodulin-dependent protein kinase type II subunit beta | 0.932571744 |
| Q92599 | SEP8 | Septin-8 | 1.039827314 |
| Q8N9R8 | SCAI | Protein SCA1 | 0.996070085 |
| P15104 | GLUL | Glutamine synthetase | 0.964303509 |
| Q9UHG2 | PCSK1N | ProSAAS | 1.098536034 |
| Q14894 | CRYM | Kinetine reductase mu-crystallin | 1.032169198 |
| P05771 | PRKCB | Protein kinase C beta type | 0.809437161 |
| Q9H2X9 | SLC12A5 | Solute carrier family 12 member 5 | 1.002439378 |
| P14854 | COX6B1 | Cytochrome c oxidase subunit 6B1 | 1.231708994 |
| Q9H2M9 | RAB3GAP2 | Gamma-aminobutyric acid receptor subunit alpha-4 | 0.952531499 |
| P48163 | GABRA4 | Presynaptic glutamate receptor | 0.921257111 |
| Q9UHG3 | PCYOX1 | ATP-dependent 6-phosphofructokinase, liver type | 1.040791749 |
| P17858 | PFKL | 6-phosphofructokinase, liver type | 0.958664012 |
| Q7L03 | SV2A | Synaptic vesicle glycoprotein 2A | 1.02958064 |
| P51674 | GP56A | Neuronal membrane glycoprotein M6-a | 1.1030152758 |
| P07203 | GPX1 | Glutathione peroxidase 1 | 0.947108894 |
| P31948 | STIP1 | Stress-induced-6-phosphophosphate 1 | 0.996412493 |

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**SUPPLEMENTARY DATA**

| Gene ID | Description | Expression Values |
|---------|-------------|-------------------|
| Q9HCJ6  | VAT1L Synaptic vesicle membrane protein VAT-1 homolog-like | 0.911806266 0.981699392 0.106553999 0.53802028 |
| P20936  | RASA1 Ras GTPase-activating protein 1 | 0.890787208 0.847194246 -0.072388049 0.54634391 |
| P13591  | NCAM1 Neural cell adhesion molecule 1 | 0.993409613 0.957820113 -0.052633977 0.57148215 |
| P10182  | SPTBN1 Spectrin beta chain, non-erythrocytic | 0.93079878 0.95445119 0.036206529 0.59819432 |
| Q9BT78  | COP9 Signalosome complex subunit 4 | 0.93544429 0.977835631 0.06394024 0.60184186 |
| P37235  | HPCAL1 Hippocalcin-like protein 1 | 1.00026747 0.979248618 -0.03068735 0.60877553 |
| P49418  | AMPH Amphiphysin | 1.024006302 1.002636635 -0.03042574 0.61869004 |
| Q9Y4L1  | HYOU1 Hypoxia up-regulated protein 1 | 1.112171623 1.164693189 0.066570529 0.62072056 |
| P30085  | CMPK1 UMP-CMP kinase | 0.938234674 0.909608532 -0.044703023 0.62275204 |
| Q8N126  | CADM3 Cell adhesion molecule 3 | 1.168014695 1.224526923 0.069256367 0.65339034 |
| Q3ZC2W  | LGALSL Galectin-related protein Gamma-aminobutyric acid type B receptor subunit 1 | 0.852977963 0.830143319 -0.039148038 0.65886861 |
| Q9UBS5  | GABBR1 | 0.80401649 0.75456763 -0.091519233 0.69627777 |
| Q9H313  | TTYHI Protein tweety homolog 1 | 1.030797588 1.043525108 0.017704247 0.71956656 |
| P61981  | YWHAG 14-3-3 protein gamma | 0.834126926 0.865798611 0.035764557 0.73332067 |
| P11142  | HSPA8 Heat shock cognate 71 kDa protein | 0.990712162 1.009929979 0.027717402 0.74204 |
| P61457  | PCBD1 Peroxired 4-alpha-carbinolamine dehydratase | 0.808948434 0.770082293 -0.071035118 0.75505012 |
| O14880  | MGST3 Microsomal glutathione S-transferase 3 | 1.001311781 0.968050468 -0.048737093 0.75734069 |
| P02792  | FTL Ferritin light chain | 0.920053581 0.940534434 0.031853394 0.75839999 |
| P60201  | PLP1 Myelin proteolipid protein | 1.14096735 1.219244393 0.09572983 0.76312129 |
| Q14697  | GANAB Neutral alpha-glucosidase AB Receptor-type tyrosine-protein phosphatase delta | 1.021144731 1.058810327 0.052256812 0.76514817 |
| P23468  | PTPRD | 0.949359812 0.938318144 -0.016779879 0.79489169 |
| Q15365  | PCBP1 Poly(C)-binding protein 1 | 0.967369182 0.990186639 0.033593639 0.79940571 |
| P10301  | RRAS Ras-related protein R-Ras | 1.008558946 0.992779698 -0.022749898 0.83478561 |
| Q15149  | PLEC | 0.988876192 0.997648167 0.01259533 0.85390603 |
| O15075  | DCLK1 Serine/threonine-protein kinase DCLK1 26S proteasome non-ATPase regulatory subunit 1 | 0.982567392 0.972142077 -0.015389186 0.83780497 |
| Q99460  | PSMD1 Glyceraldehyde-3-phosphate dehydrogenase | 1.011509099 0.989317931 -0.032003166 0.84707522 |
| P04046  | GAPDH | 0.86574965 0.874414774 0.014373974 0.85318067 |
| Q9UM22  | EPDR1 Mammalian ependymin-related protein 1 | 1.018741997 1.005737511 -0.018769938 0.85681383 |
| P61586  | RHOA | 0.998470237 0.992450981 0.011308209 0.85984902 |
| Q9H299  | SH3BGL3 | 0.89880585 0.884415853 -0.023284629 0.87851704 |
| P07355  | ANXA2 Annexin A2 | 0.971459233 0.957196685 -0.021330855 0.8800228 |
| Q14156  | EFR3A Protein EFR3 homolog A | 0.936935662 0.958195505 0.032370061 0.91289581 |
| Q9Y2J2  | EPB41L3 | 0.929865326 0.943622901 0.021188649 0.91381151 |
| Q14642  | INPP5A | 0.810181066 0.798436114 -0.021063794 0.91867531 |
| Q8IZP0  | ABO Abl interactor 1 | 0.951560688 0.958001961 0.009732938 0.93046303 |
| O62602  | GNG7 G1(G)/G(S)/G(O) subunit gamma-7 | 0.947616073 0.94161513 -0.009170684 0.93126266 |
| Q9UU6   | DBNL Drehrin-like protein 6-phosphoglucuronate dehydrogenase, decarboxylating | 0.945229485 1.029726086 0.123524084 0.44060201 |
| P52209  | PGD | 1.292823708 1.140773512 -0.18051317 0.47506953 |
| Q9BTU6  | PI4K2A Phosphatidylinositol 4-kinase type 2-alpha | 1.065005342 0.99406144 -0.09945562 0.4831287 |

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SUPPLEMENTARY DATA

P36405  ARL3  ADP-ribosylation factor-like protein 3  0.963812012  0.913266921  -0.077715204  0.49119433
P61026  RAB10  Ras-related protein Rab-10  0.946309031  1.015582999  0.101924851  0.50002155
P60953  CDC42  Cell division control protein 42 homolog  0.917981303  0.96466487  0.071563059  0.51760713
Q94919  ENDO1  Endonuclease domain-containing 1 protein  1.044258623  1.018992427  -0.035368546  0.54433035
Q9HAV0  GNB4  Guanine nucleotide-binding protein subunit beta-4  1.073580933  1.139255067  0.085659834  0.57190596
O75899  GABBR2  Guanine nucleotide-binding protein (g) subunit 2  1.148058154  1.102220692  -0.058782606  0.59045737
P19086  GNAZ  Guanine nucleotide-binding protein (g) subunit alpha  1.074511939  1.150658583  0.098778315  0.59793368
P07339  CTSD  Cathepsin D  1.046750254  1.12846248  0.108441183  0.60239163
Q7LS76  CYFIP1  Cytoplasmic FMR1-interacting protein 1  0.998871506  1.016754055  0.025599736  0.62240015
Q8TDJ6  DMXL2  DmX-like protein 2  0.960961268  0.931175442  -0.045425274  0.68558407
Q9NP72  RAB18  Ras-related protein Rab-18  0.923265166  0.893403304  -0.047433465  0.68615736
Q9Y617  PSAT1  Phosphoserine aminotransferase  0.940009991  0.977354333  0.056205605  0.68901764
P68871  HBB  Hemoglobin subunit beta  0.9588764  0.993274866  0.050848142  0.7241499
P17066  HSPA6  Heat shock 70 kDa protein 6  0.972789266  1.000462038  0.04046721  0.73199415
P59998  ARPC4  Actin-related protein 2/3 complex subunit 4  0.952682165  0.962224364  0.014378349  0.73294665
P42858  HTT  Huntingtin  1.002084531  1.020473286  0.026234203  0.77643219
O43266  SEP4  Septin-4  0.769291041  0.744168396  -0.047900384  0.84175599
Q99RR4  CAMKK2  Calcium/calmodulin-dependent protein kinase kinase 2  1.129474512  1.104787425  -0.031882911  0.84613301
Q9UPN3  MACF1  Microtubule-actin cross-linking factor 1, isoforms 1/2/3/5  0.958740373  0.967511217  0.013138202  0.87336973
Q99878  HIST1H2AJ  Histone H2A type 1-J  1.332816669  1.308013123  -0.027101353  0.9027415
Q9H115  NAPB  Beta-soluble NSF attachment protein  0.931806865  0.939377159  0.011673555  0.90684385
O75353  PPFA4  Liprin-alpha-4  0.940347345  0.948951878  0.013141172  0.91005623
Q15811  ITSN1  Intersectin-1  1.05431105  1.046784433  -0.010336188  0.91903675
Q13813  SPTAN1  Spectrin alpha chain, non-erythrocytic 1  0.962086266  0.965991974  0.005844943  0.92401978
Q9H8M5  CNNM2  Metal transporter CNNM2  0.999401799  0.990098791  -0.013492331  0.92841731
Q9PZU7  SLIC1A7  Vesicular glutamate transporter 1  1.035672868  1.038831513  0.004393305  0.95221595
P68036  UBE2L3  Ubiquitin-conjugating enzyme E2 L3  1.058887314  1.063960304  0.006895258  0.95665174
P62987  UBA52  Ubiquitin-60S ribosomal protein L40  0.858148109  0.861358893  0.005387808  0.97853762
P00558  PGK1  Phosphoglycerate kinase 1  1.033152528  1.035360774  0.003080306  0.97885264
P43003  SLIC1A3  Excitatory amino acid transporter 1  1.028235952  1.024516641  -0.005227944  0.98220054
P23381  WARS  Tryptophan--tRNA ligase, cytoplasmic  1.01901396  1.020404304  0.002018023  0.98589982
P78559  MAP1A  Microtubule-associated protein 1A  1.112493303  1.040165261  -0.09698389  0.33024439
P30041  PRDX6  Peroxiredoxin-6  0.961720348  1.00625808  0.06531093  0.38750031
P78371  CCT2  T-complex protein 1 subunit beta  1.030798714  1.058393519  0.038113491  0.45070568
P01303  NPY  Pro-neuropeptide Y  0.998079186  0.935574818  -0.093301251  0.45154191
Q16653  MOG  Myelin-oligodendrocyte glycoprotein  1.084757152  1.383163323  0.350599327  0.46081655
Q01484  ANK2  Ankyrin-2  0.998836428  0.970429158  -0.04162554  0.51835986
P40123  CAP2  Adenylyl cyclase-associated protein 2  0.978821128  1.033048223  0.077785705  0.53413401
P31939  ATIC  Bifunctional purine biosynthesis protein 0.980328447  1.017623104  0.053866237  0.55312712

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## SUPPLEMENTARY DATA

| Gene ID | Gene Name                  | Protein Description                                      | Log2 Fold Change |
|---------|----------------------------|----------------------------------------------------------|-----------------|
| P62937  | PPLA                       | Peptidyl-prolyl cis-trans isomerase A                    | 0.905235278     |
| P00492  | HPRT1                      | Hypoxanthine-guanine phosphoribosyltransferase           | 0.906136569     |
| O43157  | PLXNB1                     | Flexin-B                                                 | 1.221430029     |
| P22694  | PRKACB                     | cAMP-dependent protein kinase catalytic subunit beta     | 0.967288783     |
| P02763  | ORM1                       | Alpha-1-acid glycoprotein 1                             | 0.923236093     |
| P43034  | PAFAH1B1                   | Platelet-activating factor acetylhydrolase subunit alpha | 1.016259638     |
| P31323  | PRKARB2                    | cAMP-dependent protein kinase type II beta regulatory subunit | 0.989608188     |
| Q13153  | PAK1                       | Serine/threonine-protein kinase PAK 1                   | 1.13897777      |
| P04792  | HSPB1                      | Heat shock protein beta-1                               | 0.984682974     |
| P50993  | ATP1A2                     | Sodium/potassium-transporting ATPase subunit alpha-2    | 0.963949532     |
| Q16643  | DBN1                       | Drebrin                                                  | 0.894020478     |
| Q9BQ5   | SGIP1                      | SH3-containing GRB2-like protein 3-interacting protein 1 | 1.20898475     |
| P61764  | STXB1P                     | Syntaxin-binding protein 1                              | 0.990141814     |
| Q15084  | PDA6                       | Protein disulfide-isomerase A6                          | 1.021879509     |
| P43007  | SLC1A4                     | Neutral amino acid transporter A                         | 1.041828939     |
| Q9NZQ3  | NCKIPSD                    | NCK-interacting protein with SH3 domain                 | 0.901403555     |
| Q9P035  | HACD3                      | Very-long-chain (3R)-3-hydroxyacyl-CoA dehydratase 3     | 0.916254637     |
| Q15286  | RAB35                      | Solute carrier family 2, facilitated glucose transporter member 1 | 0.872231359   |
| P11166  | SLC2A1                     | V-type proton ATPase subunit B, brain isomorph           | 0.907652445     |
| P21281  | ATP6V1B2                   | Sodium- and chloride-dependent GABA transporter 3        | 0.907360379     |
| P48066  | SLC6A11                    | V-type proton ATPase subunit B, brain isomorph           | 0.943605725     |
| P08238  | HSP90AB1                   | Heat shock protein HSP 90-beta                          | 1.040270779     |
| P18507  | GABRG2                     | Vacuolar protein sorting-associated protein 26A          | 1.060311656     |
| O75436  | VPS26A                     | NCK-interacting protein with SH3 domain                 | 0.966015407     |
| Q00139  | KIF2A                      | Kinesin-like protein KIF2A                              | 1.198737893     |
| O95670  | ATP6V1G2                   | V-type proton ATPase subunit G 2                         | 0.987562097     |
| P42263  | GRIA3                      | Serine/threonine-protein phosphatase 2A                  | 0.904582967     |
| Q16537  | PPP2R5E                    | 56 kDa regulatory subunit epsilon isoform                | 0.904582967     |
| Q92871  | PMM1                       | Phosphomannosutase 1                                    | 0.934420912     |
| P14415  | ATP1B2                     | Phosphomannosutase 1                                    | 1.069908231     |
| P26885  | FKBP2                      | Peptidyl-prolyl cis-trans isomerase FKBP2                | 0.888062899     |
| Q8TCU6  | PREX1                      | Phosphatidylinositol 3,4,5-trisphosphate-dependent Rac exchanger 1 protein | 1.12825646     |
| Q9UUK0  | ACSL6                      | Long-chain-fatty-acid-CoA ligase 6                       | 1.06710595      |
| Q32851  | HNRNPA1 L2                 | Heterogeneous nuclear ribonucleoprotein A1-like 2        | 1.006811938     |
| P13716  | ALAD                       | Delta-aminolevulinic acid dehydratase                    | 0.95092069      |
| Q9UH03  | SEP3                       | Neuronal-specific septin-3                              | 0.885545487     |
| P21397  | MAOA                       | Aminolevulinic acid [flavin-containing] A                | 1.124450195     |
| P42658  | DPP6                       | Dipeptidyl aminopeptidase-like protein 6                 | 1.021298587     |

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| Protein ID | Name | Function/Description |
|-----------|------|----------------------|
| P62333    | SMC6 | 26S protease regulatory subunit 10B |
| Q01469    | FABP5 | Fatty acid-binding protein, epidermal |
| P02686    | MBP  | Myelin basic protein |
| Q10567    | APIB1 | AP-1 complex subunit beta-1 |
| P62258    | YWHAE | 14-3-3 protein epsilon |
| Q15121    | PEA15 | Astrocytic phosphoprotein PEA-15 |
| P50995    | ANXA11 | Annexin A11 |
| Q86YS7    | C2CD5 | C2 domain-containing protein 5 |
| P23763    | VAMP1 | Vesicle-associated membrane protein 1 |
| P04083    | ANXA1 | Annexin A1 |
| Q15019    | SEPII | Septin-2 |
| Q04179    | SOD2 | Superoxide dismutase [Mn], mitochondrial |
| P63092    | GNAS | Guanine nucleotide-binding protein G(s) subunit alpha isoforms short |
| P68402    | PAFAH1B2 | Platelet-activating factor acylhydrolase IB subunit beta |
| P05129    | PRKCG | Protein kinase C gamma type |
| Q9Y2R8    | PADI2 | Protein-arginine deiminase type-2 |
| P38646    | HSPA9 | Stress-70 protein, mitochondrial |
| P16949    | STMN1 | Stathmin |
| P23526    | AHCY | Adenosylhomocysteinase |
| Q96CX2    | KCTD12 | BTB/POZ domain-containing protein KCTD12 |
| Q16623    | STX1A | Syntaxin-1A |
| Q9Y218    | WD3R | WD repeat-containing protein 37 |
| P67775    | PPP2CA | Serine/threonine-protein phosphatase 2A catalytic subunit alpha isoform |
| P08195    | SLC3A2 | 4F2 cell-surface antigen heavy chain |
| P11177    | PDHB | Pyruvate dehydrogenase E1 component subunit beta, mitochondrial |
| Q14832    | GRM3 | Metabotropic glutamate receptor 3 |
| P46821    | MAP1B | Microtubule-associated protein 1B |
| P11137    | MAP2 | Microtubule-associated protein 2 |
| P55580    | MYH10 | Myosin-10 |
| P78357    | CNTNAP1 | Contactin-associated protein 1 |
| Q08209    | PPP3CA | Serine/threonine-protein phosphatase 2B catalytic subunit alpha isoform |
| Q86VP6    | CAND1 | Cullin-associated NEDD8-associated protein 1 |
| P00441    | SOD1 | Superoxide dismutase [Cu-Zn] |
| Q86TV6    | TCT7B | Tetratricopeptide repeat protein 7B |
| P62760    | VSNL1 | Visinin-like protein 1 |
| P61225    | RAP2B | Ras-related protein Rap-2b |
| Q9QU16    | DNMs | Dynamin-3 |
| Q9HDC9    | APMAP | Adipocyte plasma membrane-associated protein |
| Q13636    | RAB31 | Ras-related protein Rab-31 |

**Note:** The table includes protein IDs, names, and functional descriptions relevant to various cellular processes and functions. The data likely represents a subset of proteins involved in specific biological pathways or cellular activities.
**SUPPLEMENTARY DATA**

| ID     | Gene   | Description                                                                 | Value 1 | Value 2 | Value 3 | Value 4 | Value 5 | Value 6 |
|--------|--------|------------------------------------------------------------------------------|---------|---------|---------|---------|---------|---------|
| Q9UN36 | NDRG2  | Protein NDRG2                                                                | 1.029203441 | 1.13567917 | 0.142027144 | 0.52831519 |
| P47870 | GABRB2 | Gamma-aminobutyric acid receptor subunit beta-2                              | 1.01207298 | 0.980894119 | -0.045144005 | 0.56020987 |
| P02730 | SLC4A1 | Band 3 anion transport protein                                               | 0.856358244 | 0.930426148 | 0.11967719 | 0.61205964 |
| Q9Y5R1 | SLC4A4 | Electrogenic sodium bicarbonate transporter 1                                | 1.06449283 | 1.146650603 | 0.10725963 | 0.64472437 |
| P08247 | SYP    | Synaptophysin                                                                | 0.887832049 | 0.854574139 | -0.05058113 | 0.65864621 |
| O15254 | ACOX3  | Peroxisomal acyl-coenzyme A oxidase 3 Ubiquitin-conjugating enzyme E2 variant | 1.000599934 | 0.958502959 | -0.062010471 | 0.66490175 |
| Q15819 | UBE2V2 | Mitochondrial 2-oxoglutarate/malate carrier protein                           | 0.975344246 | 0.947673604 | -0.041821252 | 0.70780844 |
| Q02978 | SLC25A11| Peroxisomal multifunctional enzyme type 2                                     | 0.963906197 | 1.03202288 | 0.098510293 | 0.71527695 |
| P51659 | HSD17B4|                                                               | 1.058454395 | 1.075463874 | 0.022999954 | 0.72242897 |
| P28070 | PSMB4  | Proteasome subunit beta type-4                                               | 1.063424648 | 1.032268481 | -0.042899563 | 0.75709851 |
| O95782 | AP2A1  | AP-2 complex subunit alpha-1                                                | 0.92836649 | 0.914387164 | -0.021889297 | 0.79491297 |
| O43813 | LANCL1 | LanC-like protein 1 Glycerol-3-phosphate dehydrogenase, mitochondrial        | 0.943812406 | 0.951796571 | 0.012153122 | 0.81454551 |
| P43304 | GPD2   | T-complex protein 1 subunit theta                                             | 1.035389291 | 1.018219697 | -0.02411694 | 0.84977161 |
| P50990 | CCT8   |                                                                   | 0.992624702 | 1.000709114 | 0.01170241 | 0.85054918 |
| P35222 | CTNNB1 | Catenin beta-1                                                               | 1.091721863 | 1.082127359 | -0.012735044 | 0.85416796 |
| Q9P2D8 | UNC79  | Protein unc-79 homolog                                                       | 0.99844361 | 1.016003001 | 0.025295225 | 0.86611321 |
| P04216 | THY1   | Thy-1 membrane glycoprotein Phytanoyl-CoA hydroxylase-interacting protein   | 1.006659544 | 0.993087095 | -0.019583687 | 0.87289031 |
| Q92561 | PHYHIP |                                                                   | 1.08054586 | 1.104677305 | 0.031865057 | 0.87337719 |
| Q9BVA1 | TUBB2B | Tubulin beta-2B chain                                                        | 1.026531076 | 1.011804398 | -0.020846887 | 0.87936217 |
| P46459 | NSF    | Vesicle-fusing ATPase                                                        | 0.945293777 | 0.939662383 | -0.008620262 | 0.88147444 |
| Q96CW1 | AP2M1  | AP-2 complex subunit mu                                                      | 0.98146203 | 0.987904766 | 0.009439518 | 0.88298737 |
| P06576 | ATP5B  | ATP synthase subunit beta, mitochondrial                                     | 0.91695938 | 0.904300059 | -0.020056269 | 0.89829292 |
| Q16181 | SEP7   |                                                                  | 0.909586776 | 0.918058423 | 0.013374687 | 0.90205094 |
| Q9BR01 | SULT4A1| Sulfotransferase 4A1 V-type proton ATPase 116 kDa subunit a isofrom 1         | 1.102940515 | 1.093372696 | -0.01256973 | 0.92549859 |
| Q93050 | ATP6V0A|                                                                   | 0.99630315 | 0.999878115 | 0.005167456 | 0.93055833 |
| Q92686 | NGN    | Neurogranin                                                                  | 0.920984454 | 0.931787822 | 0.016824671 | 0.93390678 |
| O75396 | SEC22B | Vesicle-trafficking protein SEC22b                                            | 0.907143586 | 0.901979947 | -0.008235563 | 0.95655172 |
| Q13509 | TUBB3  | Tubulin beta-3 chain                                                         | 0.989483476 | 0.99495836 | 0.007962675 | 0.96048068 |
| P0DMV9 | HSPA1B | Heat shock 70 kDa protein 1 BS                                                | 0.967748099 | 0.970947646 | 0.004761939 | 0.96483137 |
| P68371 | TUBB4B | Tubulin beta-4 chain 4-aminobutyrate aminotransferase, mitochondrial         | 0.78403983 | 0.782465481 | -0.002899839 | 0.97884856 |
| P80404 | ABAT   |                                                                   | 0.905620367 | 0.908633002 | 0.0047913 | 0.98132064 |
| P06756 | ITGAV  | Integrin alpha-V                                                             | 0.942189607 | 0.942576981 | 0.000579256 | 0.99566391 |
| Q9H0E2 | TOLLIP | Toll-interacting protein                                                     | 0.990113296 | 0.989982271 | -0.000190928 | 0.99873511 |

* The p value was calculated by student's t. test.

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Supplementary Table 3. Protein list of these modules which were significantly positive correlated with t-tau in WPCNA.

| Module | Uniprot ID | Gene Name | Correlation coefficient with t-tau | p-value       |
|--------|------------|-----------|-----------------------------------|---------------|
| M7     | P10599     | TXN       | 0.513                             | 0.029421737   |
| M7     | P31150     | GDI1      | 0.140                             | 0.579155302   |
| M7     | P49368     | CCT3      | 0.527                             | 0.024632834   |
| M7     | P48147     | PREP      | 0.267                             | 0.283658808   |
| M7     | Q96CS3     | FAF2      | 0.453                             | 0.059242581   |
| M7     | O00154     | ACOT7     | -0.123                            | 0.627977179   |
| M7     | O15145     | ARPC3     | 0.206                             | 0.413298627   |
| M7     | P14867     | GABRA1    | -0.215                            | 0.392357649   |
| M7     | P47755     | CAPZA2    | 0.387                             | 0.113077719   |
| M7     | P32119     | PRDX2     | 0.117                             | 0.645154981   |
| M7     | P17858     | PFKL      | 0.523                             | 0.025809951   |
| M7     | Q9BT78     | COP54     | 0.201                             | 0.423520693   |
| M7     | P10301     | RRAS      | 0.364                             | 0.137758387   |
| M7     | Q9UM22     | EPDR1     | -0.546                            | 0.019082681   |
| M7     | Q9UJU6     | DBNL      | 0.450                             | 0.060813274   |
| M7     | P60953     | CDC42     | 0.488                             | 0.039893026   |
| M7     | O75899     | GABBR2    | -0.601                            | 0.008366007   |
| M7     | P02763     | ORM1      | 0.745                             | 0.000390844   |
| M7     | Q9UH03     | SEP3      | 0.416                             | 0.085842439   |
| M8     | Q96P70     | IPO9      | 0.651                             | 0.003453692   |
| M8     | P08237     | PFKM      | 0.515                             | 0.028557577   |
| M8     | Q9GZN7     | ROGDI     | 0.531                             | 0.023209365   |
| M8     | Q92597     | NDRG1     | 0.323                             | 0.191425244   |
| M8     | O75955     | FLOT1     | 0.618                             | 0.006319354   |
| M8     | Q07960     | ARHGAP1   | 0.604                             | 0.007930549   |
| M8     | P21266     | GSTM3     | 0.541                             | 0.020427979   |
| M8     | Q16348     | SLC15A2   | -0.459                            | 0.055174269   |
| M8     | Q9Y4L1     | HYOU1     | 0.256                             | 0.304717015   |
| M8     | Q9UPN3     | MACF1     | 0.450                             | 0.060847528   |
| M8     | P68036     | UBE2L3    | 0.422                             | 0.081043724   |
| M8     | Q92871     | PMM1      | 0.635                             | 0.004657478   |
| M8     | Q01469     | FABP5     | -0.245                            | 0.327488491   |
| M8     | Q96CX2     | KCTD12    | 0.600                             | 0.008425607   |
| M8     | Q9Y218     | WDR37     | 0.414                             | 0.088023299   |
| M8     | Q9Y6R1     | SLC4A4    | 0.377                             | 0.122567177   |
| M8     | O15254     | ACOX3     | -0.577                            | 0.01214402    |
| M9     | P05023     | ATP1A1    | 0.281                             | 0.25801866    |
| Gene ID | Symbol  | Description | FDR  | p-value       |
|---------|---------|-------------|------|--------------|
| M9      | Q01518  | CAP1        | 0.764| 0.000223132  |
| M9      | P61266  | STX1B       | 0.321| 0.193597036  |
| M9      | P29401  | TKT         | 0.565| 0.01457533   |
| M9      | Q9BY11  | PACSIN1     | 0.420| 0.083062741  |
| M9      | Q14807  | MRAS        | 0.475| 0.04653766   |
| M9      | Q13098  | GPS1        | 0.574| 0.012660324  |
| M9      | P55072  | VCP         | 0.609| 0.007341998  |
| M9      | Q16658  | FSCN1       | 0.405| 0.095215109  |
| M9      | Q92777  | SYN2        | 0.298| 0.22942762   |
| M9      | P00338  | LDHA        | 0.347| 0.158116541  |
| M9      | P62879  | GNB2        | 0.504| 0.03296379   |
| M9      | Q14195  | DPYSL3      | 0.290| 0.243031543  |
| M9      | P32418  | SLC8A1      | 0.609| 0.007303928  |
| M9      | P62826  | RAN         | 0.433| 0.0725384    |
| M9      | Q01814  | ATP2B2      | 0.577| 0.012210381  |
| M9      | Q06124  | PTPN11      | -0.164| 0.515156711  |
| M9      | Q9NRW1  | RAB6B       | 0.703| 0.001145438  |
| M9      | P08559  | PDHA1       | -0.681| 0.001858551  |
| M9      | Q92599  | SEPB        | 0.533| 0.022874309  |
| M9      | P07203  | GPX1        | 0.215| 0.39063523   |
| M9      | Q01082  | SPTBN1      | 0.428| 0.076161132  |
| M9      | P61981  | YWHAG       | 0.552| 0.01769773   |
| M9      | P23468  | PTPRD       | 0.660| 0.002902167  |
| M9      | Q8IZP0  | Abl1        | 0.609| 0.0073372    |
| M9      | P42858  | HTT         | 0.496| 0.036300331  |
| M9      | Q13813  | SPTAN1      | 0.446| 0.063471629  |
| M9      | P62987  | UBA52       | 0.643| 0.003991753  |
| M9      | O43157  | PLXNB1      | 0.183| 0.466898744  |
| M9      | P31323  | PRKAR2B     | -0.343| 0.163705116  |
| M9      | Q15286  | RAB35       | 0.226| 0.366586188  |
| M9      | P48066  | SLC6A11     | -0.768| 0.000195714  |
| M9      | P16949  | STMN1       | 0.639| 0.00428614   |
| M9      | Q16623  | STX1A       | 0.385| 0.11478435   |
| M9      | P46821  | MAP1B       | 0.605| 0.007825444  |
| M9      | Q9HDC9  | APMAP       | -0.386| 0.113646658  |
| M9      | P08247  | SYP         | 0.443| 0.065458088  |
| M9      | Q15819  | UBE2V2      | 0.711| 0.000950248  |
| M9      | Q9BVA1  | TUBB2B      | -0.467| 0.050875058  |
| M9      | P46459  | NSF         | 0.544| 0.019513023  |
| M9      | Q9BR01  | SULT4A1     | 0.415| 0.086856991  |
| M9      | Q93050  | ATP6V0A1    | -0.754| 0.00030348   |
| M9      | Q92686  | NRGN        | 0.717| 0.000809369  |
**Supplementary Table 4.** Gene ontology terms enrichment for M7, M8, M9, M10 and M11 modules in WPCNA.

| Module | Rank | Enrichment p.value | Term ID | Term Ontology | Term Name | Term Definition |
|--------|------|-------------------|--------|---------------|-----------|----------------|
| M7     | 1    | 0.001297017       | GO:0090317 | BP            | negative regulation of intracellular protein transport | Any process that decreases the frequency, rate or extent of the directed movement of proteins within cells. |
| M7     | 2    | 0.003136841       | GO:0051224 | BP            | negative regulation of protein transport | Any process that stops, prevents, or reduces the frequency, rate or extent of the directed movement of a protein into, out of or within a cell, or between cells, by means of some agent such as a transporter or pore. |
| M7     | 3    | 0.004376024       | GO:1904950 | BP            | negative regulation of establishment of protein localization | NA |
| M7     | 4    | 0.004455869       | GO:0110053 | BP            | regulation of actin filament organization | Any process that modulates the frequency, rate or extent of actin filament organization. |
| M7     | 5    | 0.00757723        | GO:0032956 | BP            | regulation of actin cytoskeleton organization | Any process that modulates the frequency, rate or extent of the formation, arrangement of constituent parts, or disassembly of cytoskeletal structures comprising actin filaments and their associated proteins. |
| M7     | 6    | 0.0120714         | GO:0032147 | BP            | activation of protein kinase activity | Any process that initiates the activity of an inactive protein kinase. |
| M7     | 7    | 0.012128936       | GO:0032387 | BP            | negative regulation of intracellular transport | Any process that stops, prevents, or reduces the frequency, rate or extent of the directed movement of substances within cells. |
| M7     | 8    | 0.013638845       | GO:0032970 | BP            | regulation of actin filament-based process | Any process that modulates the frequency, rate or extent of any cellular process that depends upon or alters the actin cytoskeleton. |
| M7     | 9    | 0.017710713       | GO:0008064 | BP            | regulation of actin polymerization or depolymerization | Any process that modulates the frequency, rate or extent of the assembly or disassembly of actin filaments by the addition or removal of actin monomers from a filament. |
| M7     | 10   | 0.017710713       | GO:0030832 | BP            | regulation of actin filament length | Any process that controls the length of actin filaments in a cell. |
| M8     | 1    | 0.001031546       | GO:0005504 | MF            | fatty acid binding | Interacting selectively and non-covalently with fatty acids, aliphatic monocarboxylic acids liberated from naturally occurring fats and oils by hydrolysis. |
| M8 | 2 | 0.00972337 | GO:0007422 | BP | peripheral nervous system development |
|----|----|-------------|-------------|----|----------------------------------------|
| M8 | 3 | 0.014301096 | GO:0044242 | BP | cellular lipid catabolic process |
| M8 | 4 | 0.014301096 | GO:0031406 | MF | carboxylic acid binding |
| M8 | 5 | 0.025667733 | GO:0015293 | MF | symporter activity |
| M8 | 6 | 0.025667733 | GO:0043177 | MF | organic acid binding |
| M8 | 7 | 0.032361046 | GO:1901888 | BP | regulation of cell junction assembly |
| M8 | 8 | 0.03307393 | GO:0001963 | BP | synaptic transmission, dopaminergic |
| M8 | 9 | 0.03307393 | GO:0006013 | BP | mannose metabolic process |

The process whose specific outcome is the progression of the peripheral nervous system over time, from its formation to the mature structure. The peripheral nervous system is one of the two major divisions of the nervous system. Nerves in the PNS connect the central nervous system (CNS) with sensory organs, other organs, muscles, blood vessels and glands.

The chemical reactions and pathways resulting in the breakdown of lipids, as carried out by individual cells.

Interacting selectively and non-covalently with a carboxylic acid, any organic acid containing one or more carboxyl (COOH) groups or anions (COO⁻).

Enables the active transport of a solute across a membrane by a mechanism whereby two or more species are transported together in the same direction in a tightly coupled process not directly linked to a form of energy other than chemiosmotic energy.

Interacting selectively and non-covalently with an organic acid, any acidic compound containing carbon in covalent linkage.

The vesicular release of dopamine, from a presynapse, across a chemical synapse, the subsequent activation of dopamine receptors at the postsynapse of a target cell (neuron, muscle, or secretory cell) and the effects of this activation on the postsynaptic membrane potential and ionic composition of the postsynaptic cytosol. This process encompasses both spontaneous and evoked release of neurotransmitter and all parts of synaptic vesicle exocytosis. Evoked transmission starts with the arrival of an action potential at the presynapse.

The chemical reactions and pathways involving mannose, the aldohexose manno-hexose, the C-2 epimer of glucose. The D-(-)-form is widely distributed in mannans and hemicelluloses and is of major importance in the core oligosaccharide of N-linked oligosaccharides of glycoproteins.
The directed movement of oligopeptides into, out of or within a cell, or between cells, by means of some agent such as a transporter or pore. Oligopeptides are molecules that contain a small number (2 to 20) of amino-acid residues connected by peptide linkages.

Interacting selectively and non-covalently with a specific domain of a protein.

The junction between an axon of one neuron and a dendrite of another neuron, a muscle fiber or a glial cell. As the axon approaches the synapse it enlarges into a specialized structure, the presynaptic terminal bouton, which contains mitochondria and synaptic vesicles. At the tip of the terminal bouton is the presynaptic membrane; facing it, and separated from it by a minute cleft (the synaptic cleft) is a specialized area of membrane on the receiving cell, known as the postsynaptic membrane. In response to the arrival of nerve impulses, the presynaptic terminal bouton secretes molecules of neurotransmitters into the synaptic cleft. These diffuse across the cleft and transmit the signal to the postsynaptic membrane.

A cellular component that forms a specialized region of connection between two or more cells, or between a cell and the extracellular matrix, or between two membrane-bound components of a cell, such as flagella.

A process that is carried out at the cellular level which results in the assembly, arrangement of constituent parts, or disassembly of an organelle within a cell. An organelle is an organized structure of distinctive morphology and function. Includes the nucleus, mitochondria, plastids, vacuoles, vesicles, ribosomes and the cytoskeleton. Excludes the plasma membrane.

The conversion of DNA-damage induced single-stranded gaps into large molecular weight DNA after replication. Includes pathways that remove replication-blocking lesions in conjunction with DNA replication.

The disaggregation of a protein-containing macromolecular complex into its constituent components.
The entirety of a process in which information is transmitted within a biological system. This process begins with an active signal and ends when a cellular response has been triggered.

A process that is carried out at the cellular level which results in the assembly, arrangement of constituent parts, or disassembly of cytoskeletal structures.

The process of restoring DNA after damage. Genomes are subject to damage by chemical and physical agents in the environment (e.g. UV and ionizing radiations, chemical mutagens, fungal and bacterial toxins, etc.) and by free radicals or alkylating agents endogenously generated in metabolism. DNA is also damaged because of errors during its replication. A variety of different DNA repair pathways have been reported that include direct reversal, base excision repair, nucleotide excision repair, photoreactivation, bypass, double-strand break repair pathway, and mismatch repair pathway.

An electron dense network of proteins within and adjacent to the postsynaptic membrane of an asymmetric, neuron-neuron synapse. Its major components include neurotransmitter receptors and the proteins that spatially and functionally organize them such as anchoring and scaffolding molecules, signaling enzymes and cytoskeletal components.

Interacting selectively and non-covalently with a syntaxin, a SNAP receptor involved in the docking of synaptic vesicles at the presynaptic zone of a synapse.

Interacting selectively and non-covalently with a SNARE (soluble N-ethylmaleimide-sensitive factor attached protein receptor) protein.

A secretory organelle, typically 50 nm in diameter, of presynaptic nerve terminals; accumulates in high concentrations of neurotransmitters and secretes these into the synaptic cleft by fusion with the 'active zone' of the presynaptic plasma membrane.
| M10 | 4 | 0.000662186 | GO:0070382 | CC | exocytic vesicle | A transport vesicle that mediates transport from an intracellular compartment to the plasma membrane, and fuses with the plasma membrane to release various cargo molecules, such as proteins or hormones, by exocytosis. |
| M10 | 5 | 0.001161138 | GO:0017075 | MF | syntaxin-1 binding | Interacting selectively and non-covalently with the SNAP receptor syntaxin-1. |
| M10 | 6 | 0.002376727 | GO:0030133 | CC | transport vesicle | Any of the vesicles of the constitutive secretory pathway, which carry cargo from the endoplasmic reticulum to the Golgi, between Golgi cisternae, from the Golgi to the ER (retrograde transport) or to destinations within or outside the cell. |
| M10 | 7 | 0.003408936 | GO:0071156 | BP | regulation of cell cycle arrest | Any process that modulates the rate, frequency, or extent of cell cycle arrest, the process in which the cell cycle is halted during one of the normal phases. |
| M11 | 1 | 0.01084545 | GO:0035094 | BP | response to nicotine | A spindles that forms as part of mitosis. Mitotic and meiotic spindles contain distinctive complements of proteins associated with microtubules. |
| M11 | 2 | 0.01084545 | GO:0072686 | CC | mitotic spindle | Interacting selectively and non-covalently with profilin, an actin-binding protein that forms a complex with G-actin and prevents it from polymerizing to form F-actin. |
| M11 | 3 | 0.01084545 | GO:0005522 | MF | profilin binding | A cell junction that forms a connection between a cell and the extracellular matrix. |
| M11 | 5   | 0.020846687 | GO:0042475 | BP | odontogenesis of dentin-containing tooth |
|-----|-----|-------------|------------|----|-----------------------------------------|
|     |     |             |            |    | The process whose specific outcome is the progression of a dentin-containing tooth over time, from its formation to the mature structure. A dentin-containing tooth is a hard, bony organ borne on the jaw or other bone of a vertebrate, and is composed mainly of dentin, a dense calcified substance, covered by a layer of enamel. |
| M11 | 6   | 0.020846687 | GO:0051926 | BP | negative regulation of calcium ion transport |
|     |     |             |            |    | Any process that stops, prevents, or reduces the frequency, rate or extent of the directed movement of calcium ions into, out of or within a cell, or between cells, by means of some agent such as a transporter or pore. |
| M11 | 7   | 0.020846687 | GO:0098974 | BP | postsynaptic actin cytoskeleton organization |
|     |     |             |            |    | A process that is carried out at the cellular level which results in the assembly, arrangement of constituent parts, or disassembly of cytoskeletal structures comprising actin filaments and their associated proteins in the postsynaptic actin cytoskeleton. |
| M11 | 8   | 0.047363653 | GO:0038093 | BP | Fc receptor signaling pathway |
|     |     |             |            |    | A series of molecular signals initiated by the binding of the Fc portion of an immunoglobulin to an Fc receptor on the surface of a signal-receiving cell, and ending with regulation of a downstream cellular process, e.g. transcription. The Fc portion of an immunoglobulin is its C-terminal constant region. |
| M11 | 9   | 0.048160823 | GO:1903350 | BP | response to dopamine cellular response |
|     |     |             |            |    | NA |
| M11 | 10  | 0.048160823 | GO:1903351 | BP | response to dopamine cellular response |
|     |     |             |            |    | NA |
**Supplementary Table 5.** An area under the ROC curve (AUC) for 18 proteins included in the M10 module.

| Gene name | single | t-tau | p-tau_{181} |
|-----------|--------|-------|-------------|
| t-tau     | 0.638  |       |             |
| p-tau_{181}| 0.813  |       |             |
| VPS29     | 0.675  | 0.5   | 0.813       |
| USP7      | 0.65   | 0.5   | 0.813       |
| RNF112    | 0.613  | 0.5   | 0.813       |
| PRRT2     | 0.837  | 0.837 | 0.837       |
| NAPA      | 0.625  | 0.5   | 0.813       |
| TUBB4A    | 0.675  | 0.5   | 0.813       |
| RAB10     | 0.55   | 0.5   | 0.813       |
| ATP6V1H   | 0.638  | 0.5   | 0.813       |
| UCHL1     | 0.625  | 0.5   | 0.813       |
| PLXNA4    | 0.763  | 0.5   | 0.938       |
| MIF       | 0.7    | 0.5   | 0.813       |
| CKB       | 0.738  | 0.5   | 0.813       |
| RAB4A     | 0.65   | 0.5   | 0.813       |
| CS        | 0.662  | 0.5   | 0.813       |
| SNAP25    | 0.8    | 0.8   | 0.963       |
| EFR3A     | 0.563  | 0.5   | 0.813       |
| VAMP2     | 0.738  | 0.5   | 0.813       |
| PCBD1     | 0.563  | 0.500 | 0.813       |

**Supplementary Table 6.** An area under the ROC curve (AUC) for 32 proteins included in the M11 module.

| Gene name | single | t-tau | p-tau_{181} |
|-----------|--------|-------|-------------|
| t-tau     | 0.638  |       |             |
| p-tau_{181}| 0.813  |       |             |
| PFKP      | 0.863  | 0.863 | 0.863       |
| CSNK2A2   | 0.837  | 0.837 | 0.925       |
| MAPK1     | 0.825  | 0.825 | 0.813       |
| USP5      | 0.8    | 0.8   | 0.925       |
| GNAO1     | 0.8    | 0.8   | 0.813       |
| UBA1      | 0.775  | 0.775 | 0.938       |
| NCEH1     | 0.775  | 0.775 | 0.813       |
| SH3GL2    | 0.763  | 0.763 | 0.813       |
| ITGA6     | 0.763  | 0.5   | 0.813       |
| HSPH1     | 0.713  | 0.5   | 0.813       |

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### SUPPLEMENTARY DATA

| Gene   | Value 1 | Value 2 | Value 3 |
|--------|---------|---------|---------|
| ACTG1  | 0.688   | 0.5     | 0.813   |
| MON2   | 0.675   | 0.5     | 0.813   |
| PRPS1  | 0.663   | 0.5     | 0.813   |
| PON2   | 0.65    | 0.5     | 0.813   |
| ATP6V1E1| 0.638  | 0.5     | 0.813   |
| CLTC   | 0.625   | 0.5     | 0.813   |
| NDUFS1 | 0.625   | 0.5     | 0.813   |
| HAGH   | 0.613   | 0.5     | 0.813   |
| TUBA4A | 0.6     | 0.5     | 0.813   |
| CADPS  | 0.6     | 0.5     | 0.813   |
| CNTN1  | 0.6     | 0.5     | 0.813   |
| TUBA1A | 0.588   | 0.5     | 0.813   |
| PSMD2  | 0.575   | 0.5     | 0.813   |
| VAT1L  | 0.563   | 0.5     | 0.813   |
| NCAM1  | 0.562   | 0.5     | 0.813   |
| HBB    | 0.55    | 0.5     | 0.813   |
| PPIA   | 0.538   | 0.5     | 0.813   |
| ATP1A2 | 0.538   | 0.5     | 0.813   |
| DBN1   | 0.538   | 0.5     | 0.813   |
| NCKIPSD| 0.537   | 0.5     | 0.813   |
| VAMP1  | 0.525   | 0.5     | 0.813   |
| CNTNAP1| 0.513   | 0.5     | 0.813   |