Supplemental Information:

SFPQ and Tau: critical factors contributing to rapid progression of Alzheimer’s disease

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2 Materials and methods

2.1 Quantitative real-time PCR (qRT-PCR)

cDNA was synthesized from brain-derived total RNA (1 µg), using High Capacity cDNA Reverse Transcription Kit (Thermo Fisher Scientific). All primer pairs for qRT-PCR assays were designed with Primer 3 (Table 1).

Reaction mixtures for RT-PCR were prepared by mixing 1 µL of 10x PCR reaction buffer (Roche), 1 µL of dimethylsulphoxide (DMSO) (Sigma), 0.5 µL of 1:1000 dilutions of SYBR Green (Sigma), 0.2 mmol of each dNTP (Roche), 0.15 units of Taq-polymerase, 10 pm/µL of forward and reverse primers and 1 µL of cDNA (1:10 diluted); the volume was increased to 20 µL with RNase-free water. Amplification was performed using Light Cycler 480 (Roche), with an initial denaturation at 95°C for 2 min, followed by 40-PCR cycles [(denaturation at 95°C for 30 seconds (sec), annealing at 56°C for 30 sec and extension at 72°C for 30 sec)]. Reactions were done in triplicates. No template controls were used to ensure reaction specificity. The data were analysed with Light Cycler 480 software SW1.5.1 (Roche) and values were normalised with GAPDH. The relative expression was calculated by comparative Ct method ($2^{-\Delta\Delta C_T}$) [45].

Table 1: List of primer pairs used in the study

| Gene  | Direction | Sequence                        |
|-------|-----------|---------------------------------|
| GAPDH | Forward   | TGGGTGTGAACCATGAGAAGTA          |
|       | Reverse   | GAGTCCTTCCACGATACCAAAG          |
|       | Forward   | TGGGAAGTGACATGCGTACT            |
| SFPQ  | Reverse   | TGTTTGGGCCTTCGTACTCT            |
|       | Forward   | AGTTCCTGGCCTGCAATTC             |
| TIA-1 | Reverse   | AACTCGAGCTGTCTTCTC              |

2.2 Immunoblotting

Frontal cortex tissues were lysed from spAD, rpAD, sCJD (-MM1 & -VV2 subtypes) and non-demented control subjects, along with cortical tissues from mouse brains, as published previously [91]. Equal amounts of proteins (30-50 µg) from each brain lysate or cell lysate were resolved by molecular weight on a 12% SDS-PAGE polyacrylamide gel (prepared in house) or 4-12% Bis-Tris gels (NuPAGE™ 4-12% Bis-Tris Protein Gels, Invitrogen). The protein marker (Precision plus protein dual color standards, Bio-Rad, Germany) was used to visualize the correct separation of the proteins and to confirm the correct protein band sizes. After separation on the gel, proteins were transferred onto a polyvinylidene difluoride (PVDF) membrane, with a 0.45 µm pore size, using a semi-dry blot chamber (Bio-Rad, Hercules, USA) for one hr. The membranes were blocked for 1 hr at RT in blocking reagent (5% non-fat dry milk in 1x TBS-T or PBS-T), followed by incubation with primary antibodies at 4°C overnight. All the primary antibodies (total-tau, phospho-tau (S199), SFPQ, TIA-1, β-actin, and GAPDH) were diluted in blocking buffer. Dilution of all the primary antibodies is given in table (see Table 2). Next, the membranes were washed in 1x PBS-T/TBS-T and incubated with secondary antibodies coupled to horseradish peroxidase (HRP) for 60 min at RT. Protein bands were detected using the enhanced chemiluminescent (ECL) method with Chemi-Doc (Bio-Rad). The densitometric analysis was performed with Image Lab software (3.0.1).
Table 2: List of primary antibodies used in the study

| Primary Antibody | Origin | Dilution (IB) | Dilution (IF) | Cat. No./ Company |
|------------------|--------|--------------|--------------|-------------------|
| Tau-5            | Mouse  | 1: 500       | 1: 100       | ab80579/Abcam     |
| Anti-tau (T22), oligomeric | Rabbit | 1: 1000       | 1: 250       | ABN454/Sigma-Aldrich |
| Phospho-tau (S199) | Rabbit | 1: 1000       | 1: 100       | ab81268/Abcam     |
| TIA-1            | Rabbit | 1: 500       | 1: 100       | ab140595/Abcam    |
| TIA-1            | Mouse  | 1: 500       | -            | ab40693/Abcam     |
| TIA-1(G-3)       | Rabbit | 1: 200       | 1: 100       | sc-166247/Santa Cruz |
| TIA-1 (G-3) AlexaFluor 488 | Mouse | -             | 1: 50        | sc-166247/Santa Cruz |
| SFPQ             | Rabbit | 1: 500       | 1: 100       | ab38148/Abcam     |
| GAPDH            | Mouse  | 1: 3000      | -            | G8795/Sigma-Aldrich |
| β-Actin          | Mouse  | 1: 1000      | -            | ab8227/Abcam      |

2.3 Immunocytochemistry

The cells were grown in T75 flasks with the culture medium (DMEM, 10% FBS, 1% PS). At confluency (70–90%), cells were trypsinized and seeded (5 x 10⁴) on glass coverslips (13 mm) in 24 well plates. After undergoing the stress treatment as described above, the cells were fixed with 4% PFA for 20 min at RT, followed by 3x washes with ice-cold PBS for 5 min each. Permeabilization was achieved using 0.2% Triton X-100 in PBS for 10 min, followed by 3x washes with PBS for 5 min each. To avoid non-specific binding, cells were incubated with blocking buffer (1% BSA, 10% FBS in PBS) for 30 min at RT. Primary antibodies (in case of double labelling, both antibodies) were diluted in 1% BSA in PBS, followed by overnight incubation at 4°C. The cells were washed 3x with PBS (each wash was for 5 min) followed by incubation with secondary antibodies (AlexaFlour 488 and AlexaFlour 546) diluted in 1% BSA in PBS for two hrs at RT in the dark. The cells were washed 3x with PBS for 5 min each in the dark to remove the nonspecific binding. The cells were then counterstained with DAPI (one min) or a RedDot 2 Far red nuclear stain (20 min). After nuclear staining, the cells were washed 3x with PBS, followed by mounting with one drop of mounting medium (immuno-mount, Thermo Fisher Scientific). The slides were stored in the dark at -20°C or +4°C. Detail procedure for imaging the slides has been provided in the Co-immunoprecipitation protocol described in the main Manuscript. The average number of stress granules in each cell was calculated using FIJI software.

2.4 Cell lysis and protein extraction

Total protein extracts were prepared from 70-90% confluent HeLa, HEK-293 and SH-SY5Y cells. After stress treatment, all the cell lines were washed with 1x PBS, scraped and resuspended in lysis buffer ([50 mM Tris-HCl, pH 8, 1% Triton X-100, 0.5% CHAPS, 1mM DTT, protease, and phosphatase inhibitors (Roche, Germany)]. Lysates were sonicated using an ultrasonicator on ice, followed by incubation for one hr at 4°C with shaking. The lysates were centrifuged at 14000 rpm for 30 min at 4°C. The supernatants were transferred to new tubes. To harvest cells after transient transfections, cells were trypsinized and washed with 1x PBS followed by centrifugation at 400xg for 5 min at 4°C. The washed cell pellets were lysed, and protein quantification was performed with Bradford assay.
2.5 MTS assay

Cells were grown in T75 flasks with the culture medium (DMEM, 10% FBS, 1% PS). At confluency (70–90%), cells were trypsinized and then washed with 1x PBS, and seeded (10 x 10^3) in 96-well plates and incubated for 18-24 hours at 37°C. Transfections were performed with WT-tau and P301L-tau plasmids for variable periods of time (24 and 48 hours). To measure cell viability, MTS assay (ab197010, Abcam) was used according to the manufacturer’s instructions. The culture media was replaced with a fresh medium before treatment with MTS [3-(4, 5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2Htetrazolium, inner salt]. To estimate the effect of tau-expression on cell viability, reduced MTS tetrazolium complex (colored formazan product) was measured. This conversion is a property of metabolically active cells. For color development, cells were incubated at 37°C for one hour and the absorbance measurement was taken at 490 nm using a Perkin Elmer Wallac 1420 Victor microplate reader (GMI, USA). Absorbance from the control wells (background) was subtracted from the experimental sample wells.

2.6 Trypan blue exclusion assay

Cell viability was also assessed through the trypan blue exclusion dye test. Briefly, the cell suspension in the culture medium (25 µL) after trypsinization was mixed with 25 µL of 0.4% trypan blue. After mixing, the 10 µL of cell suspension was loaded onto hemocytometer. Both viable (colorless) and dead (blue) cells were counted in each large square of the haemocytometer under (40x) objective for both untreated (control) and sodium arsenite treated (stress) cells.

2.7 SWATH-MS (Sequential Windowed Acquisition of All Theoretical Fragment Ion Mass Spectra) for global proteomics

2.7.1. Library preparation

Analytical-grade reagents were used for protein extraction and digestion. Ampuwa water (Ampuwa sterile water, Handels GmbH, Germany) was used to prepare all buffers and solutions. To prepare spectral peptide library, digested protein extracts (normalized for protein amounts) from each sample were pooled to a total amount of 220 µg and separated into fourteen staggered pooled fractions, using an Aekta pure (GE Healthcare) with a Hypersil Gold C18 column (Diam. 150x2,1 mm, Particle size: 3 µ). Digested proteins were analyzed on an Eksigent nanoLC425 nanoflow chromatography system associated with TripleTOF 5600+, a hybrid triple quadrupole TOF mass spectrometer with a Nanospray III ionization source (Ionspray voltage 2400V, Interface heater temperature 150°C, Sheath gas setting 12). The peptides were dissolved in loading buffer (0.1% formic acid, 2% acetonitrile in optima water (Thermo Scientific) to a final concentration of 0.3 µg/µL and spiked with a synthetic peptide standard used for retention time alignment (iRT Standard, Schlieren, Schweiz). For every measurement, digested proteins (1.5 µg) were enriched on a precolumn (PharmFluidics µPAC Trapping Column) and separated on a PharmaFluidics µPAC micro Chip based separations analytical column with 50 cm length) using a 120 min linear gradient of 5%-45% ACN, 0.1% FA) at a flow rate of 300 nL/min. Qualitative LC-MS/MS measurement was carried out using a Top 20 data-dependent acquisition (DDA) mode with a mass range of m/z 350–1250 for 250 milliseconds (ms). For every measurement, digested proteins (1.5 µg) were enriched on a precolumn (PharmFluidics µPAC Trapping Column) and separated on a PharmaFluidics µPAC micro Chip based separations analytical column with 50 cm length) using a 120 min linear gradient of 5%-45% ACN, 0.1% FA) at a flow rate of 300 nL/min. Qualitative LC-MS/MS measurement was carried out using a Top 20 data-dependent acquisition (DDA) mode with a mass range of m/z 350–1250 for 250 milliseconds (ms). The resolution for data extraction was 30,000 full width at half maximum (FWHM). MS/MS scans of mass range m/z 180–1600 at a resolution of 17,500 FWHM for 85 ms and a precursor isolation width of 0.7 FWHM with a cycle time of 2.9 sec was used. For MS/MS, the criteria for precursor ions selection was: a
threshold intensity of more than 125 cps with charge states of 2+, 3+, and 4+, and the dynamic exclusion of 30 sec. In every reversed-phase fraction, two technical replicates were analyzed for the construction of the spectral library.

### 2.7.2 Quantitative SWATH measurement

For the SWATH measurement, MS/MS data was obtained using windows of 65 variable sizes across a mass range of 400-900 m/z. For each biological sample, two technical replicates were performed. Protein identifications were obtained using ProteinPilot Software version 5.0 build 4769 (AB Sciex) at “thorough” settings. MS/MS spectra were searched in the UniProtKB using *Homo sapiens* as reference proteome (revision 04/2018, 93661 entries) at a false discovery rate (FDR) of 1%. Spectral library and SWATH peak extraction were obtained in PeakView Software version 2.1 build 11041 (AB Sciex). Following retention time correction using the iRT standard, peak areas were extracted using information from the MS/MS library at 1% FDR. The peak areas were summed up to peptide and finally corresponding protein area values that were used for downstream statistical and functional analysis.

### 2.8 Bioinformatics Analysis

#### 2.8.1 Differential enrichment analysis of RBPome

For a detailed analysis of the isolated RNA-binding proteomic candidates, two different approaches were used, here labeled approach A and B.

**Approach A:** to find out differentially enriched proteins in disease groups, pairwise t-tests (two-sided) were performed for all disease group combinations using Perseus software (version 1.5.0.31). Missing or Zero values are observed in the data for several proteins in MS-based proteomics data. These values appear when the mass spectrometer cannot detect peptides having abundances below the censoring cutoff of the mass spectrometer. Such values are informative because they are below the lowest abundance observed for a peptide. In such situations, when quantitative values are missing in one group but are present in other groups, this more likely represents differences in abundance between groups, which might indicate interesting features specific to that group. Therefore, zero values were imputed by half of the minimum value of total spectrum count values, to have statistical analysis of the proteomic candidates (Approach A). Fold change (FC) for all comparisons was set at ±1.5 and a p-value < 0.05 for significance. Proteins which were identified as significantly enriched were used to make heatmaps using Perseus software (version 1.5.0.31). Volcano plots were also calculated using Perseus software, where FC was log2-transformed, so that the data are centered on zero, while the p-values were transformed into −log10.

**Approach B:** given the exploratory nature of this discovery-based proteomics work-flow, the criteria were relaxed and proteins with a single quantitative value were included in the analysis to compare all the disease groups. To find similar and unique proteins, venn diagram was prepared using functional enrichment and analysis tool (FunRich).

#### 2.8.2 Gene Ontology analysis and functional network mapping

To gain functional insights from proteomics data, three different enrichment strategies were used. Functional enrichment analysis was initially performed using Perseus software for significantly-enriched Gene Ontology
(GO) processes including the Biological Process and Molecular Function by Fisher’s exact-test. Then, overrepresentation enrichment analysis was performed using the web-based Gene Set Analysis Toolkit (WebGestalt), in the domains of Biological and Molecular Functions to have a GO Slim summary of enriched terms. Finally, an Ingenuity Pathway Analysis (IPA, Qiagen, USA) was performed to find out canonical pathways associated with up- and down-regulated proteins after tau-expression as described below.

2.8.3 Ingenuity Pathway Analysis (IPA)

The proteomic dataset containing the fold change and p-values of significantly regulated proteins was uploaded to IPA for core analysis (Qiagen, USA). The protein candidates from the submitted dataset generated top molecular networks based on Molecular and Biological Functions including canonical pathways, potential upstream regulators, and disease-based networks. The settings for analysis were based on direct and indirect relationships between differentially expressed proteins (DEPs), and were supported by experimentally reported data from human, mouse and rat studies [27]. Potential upstream regulators were designated as inhibited or activated according to the fold change and p-values (-log10-p-values) [65] of the DEPs.

Table 3: Prion-like domain prediction score of RBPs from PLAAC database

| Experimental group | SEQid       | COREscore | PAPAprop |
|--------------------|-------------|-----------|----------|
| Cont., sCJD        | sp|Q12906|ILF3     | 30.688   | 0.092    |
| Cont. rpAD, sCJD   | sp|P08247|SYPH    | 25.009   | -0.105   |
| Cont. spAD, sCJD   | sp|Q5D862|FILA2   | 24.633   | 0.109    |
| Cont., spAD, rpAD, sCJD | sp|P17600|SYN1   | 20.311   | -0.054   |
| Cont, sCJD         | sp|O43390|HNRPR  | 17.059   | -0.049   |
| Cont., sCJD        | sp|P09012|SNRPA  | 11.165   | -0.146   |
| rpAD, rpAD         | sp|Q9UPA5|BSN    | 22.864   | -0.044   |
| spAD, rpAD, sCJD   | sp|P20073|ANXA7  | 17.868   | -0.033   |
| spAD, sCJD         | sp|Q92943|FUBP2  | 15.926   | -0.065   |
| spAD, rpAD, sCJD   | sp|P02671|FIBA   | 12.12    | 0.033    |
| rpAD, sCJD         | sp|Q14103|HNRPD  | 30.124   | 0.164    |
| rpAD, sCJD         | sp|P23246|SPPQ   | 28.671   | -0.1     |
| rpAD               | sp|P04156|PRIO   | 14.844   | 0.02     |
| sCJD               | sp|Q92734|TFG    | 38.015   | -0.005   |
| sCJD               | sp|Q01844|EWS    | 34.368   | 0.057    |
| sCJD               | sp|P22626|ROA2   | 30.362   | 0.043    |
| sCJD               | sp|P09651|ROA1   | 28.381   | 0.093    |
| sCJD               | sp|Q8WUM4|PDC6   | 26.882   | 0.049    |
| sCJD               | sp|P50995|ANX11  | 19.803   | -0.059   |
| sCJD     | sp|P9UBV8|PEFI |   19.787 |  0.005 |
|---------|-----------------|-------|--------|----------|--------|
| sCJD     | sp|P17931|LEG3 |   17.868 | -0.033 |
| sCJD     | sp|P49840|GSK3A|   11.251 | -0.103 |
| sCJD     | sp|P14678|RSMB |   10.958 | -0.121 |
| sCJD     | sp|O60506|HNRPQ|    8.799 | -0.019 |

PLAAC: Prion-like amino acid composition, SEQid: sequence id from fasta file, COREscore: max sum of PLAAC LLRs, PAPAprop: max score of PAPA prion propensities [81]. Cont.: control, spAD: sporadic Alzheimer's disease, rpAD: rapidly progressive Alzheimer's disease, sCJD: sporadic Creutzfeldt-Jakob disease.
Table 4: Summary of cases. rpAD: rapid Alzheimer disease; spAD: sporadic AD; Cont: control; CJD: Creutzfeldt-Jakob disease; N: normal; Braak NFT: Braak neurofibrillary tangle pathology (0-VI); TAP: Thal αB phase (1-5); CERAD: Consortium to Establish a Registry for Alzheimer disease (C0-C3); NIA score: National Institute on Aging (A0-A3); PMI: post-mortem delay. ABC categorization: A: TAP: amyloid score; B: Baak NFT pathology; C: CERAD (CERAD-NIA-AA score)

| No. | Case  | Clinical diagnosis | Age  | Gender | Disease duration (y) | PMI (hr) | TAP | Braak NFT | CERAD-(NIA-AA score) | NIA-AA score |
|-----|-------|--------------------|------|--------|----------------------|----------|-----|-----------|----------------------|--------------|
| 1   | rpAD1 | CJD                | 70   | Male   | < 4                  | 11:30    | 3   | VI        | C (C3)               | A2, B3, C3  |
| 2   | rpAD2 | CJD                | 76   | Female | < 4                  | 18       | 4   | VI        | C (C3)               | A3, B3, C3  |
| 3   | rpAD3 | CJD                | 79   | Female | < 4                  | 05:30    | 3   | V         | C (C3)               | A2, B3, C3  |
| 4   | rpAD4 | CJD                | 83   | Male   | < 4                  | 05:30    | 5   | VI        | C (C3)               | A3, B3, C3  |
| 5   | rpAD5 | CJD                | 83   | Male   | < 4                  | 08:20    | 3   | V         | C (C3)               | A2, B3, C3  |
| 6   | rpAD6 | CJD                | 76   | Male   | < 4                  | 06:30    | 4   | VI        | C (C3)               | A3, B3, C3  |
| 7   | rpAD7 | CJD                | 78   | Male   | < 4                  | 03:30    | 5   | VI        | C (C3)               | A3, B3, C3  |
| 8   | spAD1 | AD                 | 78   | Male   | > 4                  | 09:30    | 4   | V         | C (C3)               | A3, B3, C3  |
| 9   | spAD2 | AD                 | 72   | Female | > 4                  | 09:30    | 3   | V         | C (C3)               | A2, B3, C3  |
| 10  | spAD3 | AD                 | 82   | Female | > 4                  | 01:45    | 4   | VI        | C (C3)               | A3, B3, C3  |
| 11  | spAD4 | AD-mixed dementia  | 56   | Female | > 4                  | 07       | 4   | VI        | C (C3)               | A3, B3, C3  |
| 12  | spAD5 | AD                 | 87   | Male   | > 4                  | 07:05    | 3   | V         | C (C3)               | A2, B3, C3  |
| 13  | spAD6 | AD-mixed dementia  | 75   | Female | > 4                  | 04:15    | 4   | V         | C (C3)               | A3, B3, C3  |
| 14  | spAD7 | AD                 | 93   | Male   | > 4                  | 03       | 3   | V         | C (C3)               | A2, B3, C3  |
| 15  | spAD8 | AD                 | 74   | Female | -                   | 5:30     | 4   | V         | C (C3)               | A3, B3, C3  |
| 16  | spAD9 | AD                 | 82   | Male   | -                   | 3:45     | 4   | V         | C (C3)               | A3, B3, C3  |
| 17  | Cont1 | N                  | 69   | Male   | -                   | 03:45    | 1   | II        | A (C1)               | A1, B1, C1  |
Table 5: Details of sporadic Creutzfeldt Jakob disease subtype cases; neuropathological examination of all these cases was performed in the context of suspected prion disease in all cases. When PrPSc positivity was observed, additional pathologies such as amyloid deposits were described briefly.

| No. | Case          | Age | Gender | Disease duration (y) | Genotype | PMI (hr) | Amyloid deposits                                                                 |
|-----|---------------|-----|--------|----------------------|----------|----------|----------------------------------------------------------------------------------|
| 1   | sCJD (MM1)1   | 65  | Male   | <1                   | MM/MMV1  | 09:45    | “Numerous amorphous amyloid deposits in the isocortex”                           |
| 2   | sCJD (MM1)2   | 74  | Female | <1                   | MM/MMV1  | 07:50    | “Countless, mostly diffuse amyloid deposits in the isocortex and in the central gray matter” |
| 3   | sCJD (MM1)3   | 61  | Male   | <1                   | MM/MMV1  | 07       | “Diffuse amyloid deposits in frontal and occipital lobes”                         |
| 4   | sCJD (MM1)4   | 66  | Female | <1                   | MM/MMV1  | 05:05    | “No other relevant pathological findings”                                        |
| 5   | sCJD (MM1)5   | 74  | Female | <1                   | MM/MMV1  | 11       | “Numerous amyloid beta deposits in the isocortex, and in the allocortex”         |
| 6   | sCJD (MM1)6   | 74  | Male   | <1                   | MM/MMV1  | 04:50    | “Numerous amyloid deposits in the isocortex”                                     |
| 7   | sCJD (VV2)1   | 66  | Male   | <1                   | VV2      | 15:30    | “No other relevant pathological findings”                                        |
| 8   | sCJD (VV2)2   | 70  | Female | <1                   | VV2      | 11       | “Few diffuse amyloid deposits in frontal lobes”                                  |
| 9   | sCJD (VV2)3   | 72  | Female | <1                   | VV2      | 06       | “No other relevant pathological findings”                                        |
| 10  | sCJD (VV2)4   | 66  | Female | <1                   | VV2      | 04       | “No other relevant pathological findings”                                        |
| Disease Group | IDs | Uniprot Acc. No. | Protein names | Involvement in disease |
|---------------|-----|-----------------|---------------|------------------------|
| spAD         | AEDO| Q96S25          | 2-aminoethanethiol dioxygenase |                        |
|              | AL1L1| O75891          | Cytoplasmic 10-formyltetrahydrofolate dehydrogenase |                        |
|              | AL4A1| P30038          | Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial | Hyperprolinemia 2 |
|              | AP2M1| Q96CW1          | AP-2 complex subunit mu |                        |
|              | ARP2 | P61160          | Actin-related protein 2 |                        |
|              | ARRB1| P49407          | Beta-arrestin-1 |                        |
|              | ATPD | P30049          | ATP synthase subunit delta, mitochondrial | Mitochondrial complex V deficiency, nuclear type 5 |
|              | CAD13| P55290          | Cadherin-13 |                        |
|              | CADM4| Q8NFZ8          | Cell adhesion molecule 4 |                        |
|              | CANB1| P63098          | Calcineurin subunit B type 1 |                        |
|              | CAND1| Q86VP6          | Cullin-associated NEDD8-dissociated protein 1 |                        |
|              | CAPZB| P47756          | F-actin-capping protein subunit beta |                        |
|              | CASA1| P47710          | Alpha-S1-casein [Cleaved into: Casxin-D] |                        |
|              | CAZA1| P52907          | F-actin-capping protein subunit alpha-1 |                        |
|              | CC50A| Q9NV96          | Cell cycle control protein 50A |                        |
|              | CD47 | Q08722          | Leukocyte surface antigen CD47 |                        |
|              | CLCA | P09496          | Clathrin light chain A |                        |
|              | CLH2 | P53675          | Clathrin heavy chain 2 |                        |
|              | CPLX2| Q6PUV4          | Complexin-2 |                        |
|              | CSN2 | P61201          | COP9 signalosome complex subunit 2 |                        |
|              | CYFP2| Q96F07          | Cytoplasmic FMR1-interacting protein 2 | Epileptic encephalopathy, early infantile, 65 |
|              | DBNL | Q9UJU6          | Drebrin-like protein |                        |
|              | DC1L2| O43237          | Cytoplasmic dynein 1 light intermediate chain 2 |                        |
|              | DCXR | Q7Z4W1          | L-xylulose reductase | Pentosuria |
|              | ECHA | P40939          | Trifunctional enzyme subunit alpha, mitochondrial | Mitochondrial trifunctional protein deficiency |
|              | ENOB | P13929          | Beta-enzolase | Glycogen storage disease 13 |
|              | FLNA | P21333          | Filamin-A | Periventricular nodular heterotopia 1 |
|              | FLOT1| O75955          | Flotillin-1 |                        |
|              | FUBP2| Q92945          | Far upstream element-binding protein 2 |                        |
|              | GANAB| Q14697          | Neutral alpha-glucosidase AB | Polycystic kidney disease 3 with or without polycystic liver disease |
|              | GBB4 | Q9HAV0          | Guanine nucleotide-binding protein subunit beta-4 | Charcot-Marie-Tooth disease, dominant, intermediate type, F |
|              | GBG3 | P63215          | Guanine nucleotide-binding protein G |                        |
|              | GDE  | P35573          | Glycogen debranching enzyme | Glycogen storage disease 3 |
|              | GLU2B| P14314          | Glucosidase 2 subunit beta | Polycystic liver disease 1 with or without kidney cysts |
| Gene Symbol | Accession | Description                                                                                      | Disease/Condition                                                                 |
|-------------|-----------|--------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| GNAQ        | P50148    | Guanine nucleotide-binding protein G                                                              | Capillary malformations, congenital Brugada syndrome 2                             |
| GPD1L       | Q8N335    | Glycerol-3-phosphate dehydrogenase 1-like protein                                                  |                                                                                      |
| GPD1M       | P43304    | Glycerol-3-phosphate dehydrogenase, mitochondrial                                                 |                                                                                      |
| HINT1       | P49773    | Histidine triad nucleotide-binding protein 1                                                       | Neuromyotonia and axonal neuropathy, autosomal recessive                              |
| HS74L       | O95757    | Heat shock 70 kDa protein 4L                                                                     |                                                                                      |
| HSP76       | P17066    | Heat shock 70 kDa protein 6                                                                      |                                                                                      |
| ICAM5       | Q9UMF0    | Intercellular adhesion molecule 5                                                                 |                                                                                      |
| IDH3B       | O43837    | Isocitrate dehydrogenase [NAD] subunit beta, mitochondrial                                       | Retinitis pigmentosa 46                                                             |
| IF4A1       | P60842    | Eukaryotic initiation factor 4A-I                                                                |                                                                                      |
| IF4B        | P23588    | Eukaryotic translation initiation factor 4B                                                        |                                                                                      |
| IPYR        | Q15181    | Inorganic pyrophosphatase                                                                        |                                                                                      |
| KCC2A       | Q9UQM7    | Calcium/calmodulin-dependent protein kinase type II subunit alpha                                  | Mental retardation, autosomal dominant 53                                           |
| KCRM        | P06732    | Creatine kinase M-type                                                                           |                                                                                      |
| KT3K        | Q9HA64    | Ketosamine-3-kinase                                                                             |                                                                                      |
| L1CAM       | P32004    | Neural cell adhesion molecule L1                                                                  | Hydrocephalus due to stenosis of the aqueduct of Sylvius                           |
| LASP1       | Q14847    | LIM and SH3 domain protein 1                                                                     |                                                                                      |
| LIGO1       | Q96FE5    | Leucine-rich repeat and immunoglobulin-like domain-containing nogo receptor-interacting protein 1 | Mental retardation, autosomal recessive 64                                           |
| MAOM        | P23368    | NAD-dependent malic enzyme, mitochondrial                                                        |                                                                                      |
| MAP4        | P27816    | Microtubule-associated protein 4                                                                 |                                                                                      |
| MKO3        | P27361    | Mitogen-activated protein kinase 3                                                                |                                                                                      |
| MT1F        | P04733    | Metallothionein-1F                                                                               |                                                                                      |
| NCHL1       | O00533    | Neural cell adhesion molecule L1-like protein                                                      |                                                                                      |
| NCKP1       | Q9Y2A7    | Nck-associated protein 1                                                                         |                                                                                      |
| NCKX2       | Q9UI40    | Sodium/potassium/calcium exchanger 2                                                              |                                                                                      |
| NDRG1       | Q92597    | Protein NDRG1                                                                                     | Charcot-Marie- Tooth disease 4D                                                      |
| NEDD8       | Q15843    | NEDD8                                                                                              |                                                                                      |
| NEGR1       | Q7Z3B1    | Neuronal growth regulator 1                                                                       |                                                                                      |
| NP1L4       | Q99733    | Nucleosome assembly protein 1-like 4                                                               |                                                                                      |
| NTRI        | Q9P121    | Neurotrimin                                                                                        |                                                                                      |
| ODPA        | P08559    | Pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial                   | Pyruvate dehydrogenase E1-alpha deficiency                                           |
| OLA1        | Q9NTK5    | Obg-like ATPase 1                                                                                 |                                                                                      |
| OPA1        | O60313    | Dynamin-like 120 kDa protein, mitochondrial                                                        | Optic atrophy 1                                                                     |
| OPCM        | Q14982    | Opioid-binding protein/cell adhesion molecule                                                     | Ovarian cancer                                                                       |
| PAK1        | Q13153    | Serine/threonine-protein kinase PAK 1                                                              | Intellectual developmental disorder with macrocephaly, seizures, and speech delay    |
| Gene | Accession | Description |
|------|-----------|-------------|
| PAK3 | O75914 | Serine/threonine-protein kinase PAK 3 |
| PCSK1 | Q9UHG2 | ProSAAS |
| PCY2 | Q99447 | Ethanolamine-phosphate cytidylyltransferase |
| PFKAL | P17858 | ATP-dependent 6-phosphofructokinase, liver type |
| PFKAP | Q01813 | ATP-dependent 6-phosphofructokinase, platelet type |
| PHIPL | Q96FC7 | Phytanoyl-CoA hydroxylase-interacting protein-like |
| PLIN3 | O60664 | Perilipin-3 |
| PPT1 | P50897 | Palmitoyl-protein thioesterase 1 |
| PTN11 | Q06124 | Tyrosine-protein phosphatase non-receptor type 11 |
| QCR2 | P22695 | Cytochrome b-c1 complex subunit 2, mitochondrial |
| RAB8B | Q92930 | Ras-related protein Rab-8B |
| RALA | P11233 | Ras-related protein Ral-A |
| RD23B | P54727 | UV excision repair protein RAD23 homolog B |
| REEP5 | Q00765 | Receptor expression-enhancing protein 5 |
| RHOC | P08134 | Rho-related GTP-binding protein RhoC |
| SEMG1 | P04279 | Semenogelin-1 |
| Septin-3 | Q9UH03 | Neuronal-specific septin-3 |
| Septin-6 | Q14141 | Septin-6 |
| Septin-9 | Q9UHD8 | Septin-9 |
| SH3G1 | Q99961 | Endophilin-A2 |
| SHLB2 | Q9NR46 | Endophilin-B2 |
| SNAG | Q99747 | Gamma-soluble NSF attachment protein |
| SPTN2 | O15020 | Spectrin beta chain, non-erythrocytic 2 |
| SRC8 | Q14247 | Src substrate cortactin |
| SYNPO | Q8N3V7 | Synaptopodin |
| TCAL5 | Q5H9L2 | Transcription elongation factor A protein-like 5 |
| TCPB | P78371 | T-complex protein 1 subunit beta |
| TCPQ | P50990 | T-complex protein 1 subunit theta |
| TCTP | P13693 | Translationally-controlled tumor protein |
| rpAD | 4F2 | 4F2 cell-surface antigen heavy chain |
| 4F2 | P08195 | 4F2 cell-surface antigen heavy chain |
| ACTA | P62736 | Actin, aortic smooth muscle |
| ACY2 | P45381 | Aspartoacylase |
| ADDA | P35611 | Alpha-adducin |
| ADT2 | P05141 | ADP/ATP translocase 2 |
| AL7A1 | P49419 | Alpha-aminoadipic semialdehyde dehydrogenase |
| AMER2 | Q8N7J2 | APC membrane recruitment protein 2 |
| AMPL | P28838 | Cytosol aminopeptidase |
| ANK2 | Q01484 | Ankyrin-2 |
| AOF | P21937 | Amine oxidase [flavin-containing] A |
| AOFB | P27338 | Amine oxidase [flavin-containing] B |
| AP180 | O60641 | Clathrin coat assembly protein AP180 |
| ASAH1 | Q13510 | Acid ceramidase |

Canavan disease:
- ADP/ATP translocase 2

Long QT syndrome 4:
- Ankyrin-2

Brunner syndrome:
- Amine oxidase [flavin-containing] A

Pyridoxine-dependent epilepsy:
- Alpha-aminoadipic semialdehyde dehydrogenase

Farber lipogranulomatosis:
- Acid ceramidase
| Protein | Entrez Gene ID | Description | Disease/Condition |
|---------|---------------|-------------|-------------------|
| AT2A2  | P16615        | Sarcoplasmic/endoplasmic reticulum calcium ATPase 2 | Acrokeratosis verruciformis |
| ATP5H  | O75947        | ATP synthase subunit d, mitochondrial | |
| ATP5J  | P18859        | ATP synthase-coupling factor 6, mitochondrial | |
| ATP5L  | O75964        | ATP synthase subunit g, mitochondrial | |
| CALX   | P27824        | Calnexin | |
| CD44   | P16070        | CD44 antigen | |
| CDS2   | O95674        | Phosphatidate cytidylyltransferase 2 | |
| CLD11  | O75508        | Claudin-11 | |
| CMC1   | O75746        | Calcium-binding mitochondrial carrier protein Aralar1 | Epileptic encephalopathy, early infantile, 39 |
| CO4A   | P0C0L4        | Complement C4-A | Complement component 4A deficiency |
| CO4B   | P0C0L5        | Complement C4-B | Systemic lupus erythematosus |
| COX41  | P13073        | Cytochrome c oxidase subunit 1 isoform 1, mitochondrial | |
| CPNS1  | P04632        | Calpain small subunit 1 | |
| CUTA   | O60888        | Protein CutA | |
| DC1I2  | Q13409        | Cytoplasmic dynein 1 intermediate chain 2 | |
| DDTL   | A6NHG4        | D-dopachrome decarboxylase-like protein | |
| EF2    | P13639        | Elongation factor 2 | Spinocerebellar ataxia 26 |
| ERMIN  | Q8TAM6        | Ermin | |
| FIS1   | Q9Y3D6        | Mitochondrial fission 1 protein | |
| GBG2   | P59768        | Guanine nucleotide-binding protein G | |
| GHC1   | Q9H936        | Mitochondrial glutamate carrier 1 | Epileptic encephalopathy, early infantile, 3 |
| GPM6B  | Q13491        | Neuronal membrane glycoprotein M6-b | |
| HEBP1  | Q9NRV9        | Heme-binding protein 1 | |
| HNRPD  | Q14103        | Heterogeneous nuclear ribonucleoprotein D0 | |
| HYEP   | P07099        | Epoxide hydrolase 1 | |
| IMB1   | Q14974        | Importin subunit beta-1 | |
| LAMP1  | P11279        | Lysosome-associated membrane glycoprotein 1 | |
| LANC2  | Q9NS86        | LanC-like protein 2 | |
| MAG    | P20916        | Myelin-associated glycoprotein | Spastic paraplegia 75, autosomal recessive |
| MRP    | P49006        | MARCKS-related protein | |
| MTP2   | P11137        | Microtubule-associated protein 2 | |
| MTPN   | P58546        | Myotrophin | |
| NDKA   | P15531        | Nucleoside diphosphate kinase A | |
| NDU4   | O00483        | Cytochrome c oxidase subunit NDUFA4 | Leigh syndrome |
| ODO2   | P36957        | Dihydrolipoamide-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex, mitochondrial | Platelet-activating factor acetylhydrolase IB subunit beta |
| PA1B2  | P68402        | | |
| PCBP2  | Q15366        | Poly(rC)-binding protein 2 | |
| PGAM2  | P15259        | Phosphoglycerate mutase 2 | Glycogen storage disease 10 |
| PHB    | P35232        | Prohibitin | |
| Gene | Accession | Description |
|------|-----------|-------------|
| PHB2 | Q99623 | Prohibitin-2 |
| PI42A | P48426 | Phosphatidylinositol 5-phosphate 4-kinase type-2 alpha |
| PRIO | P04156 | Major prion protein |
| QCR1 | P31930 | Cytochrome b-c1 complex subunit 1, mitochondrial |
| QCR6 | P07919 | Cytochrome b-c1 complex subunit 6, mitochondrial |
| RAP1A | P62834 | Ras-related protein Rap-1A |
| SCG1 | P05060 | Secretogranin-1 |
| SCG2 | P13521 | Secretogranin-2 |
| SDHA | P31040 | Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial |
| Septin-4 | O43236 | Septin-4 |
| SERA | O43175 | D-3-phosphoglycerate dehydrogenase |
| SIRB1 | O00241 | Signal-regulatory protein beta-1 |
| SNG3 | O43761 | Synaptogyrin-3 |
| SV2A | Q7L0J3 | Synaptic vesicle glycoprotein 2A |
| SV2B | Q7L112 | Synaptic vesicle glycoprotein 2B |
| SYNJ1 | O43426 | Synaptojanin-1 |
| TBA1B | P68363 | Tubulin alpha-1B chain |
| TCPE | P48643 | T-complex protein 1 subunit epsilon |
| TENA | P24821 | Tenascin |
| VA0D1 | P61421 | V-type proton ATPase subunit d 1 |
| VAT1 | Q99536 | Synaptic vesicle membrane protein VAT-1 homolog |
| | | Voltage-dependent anion-selective channel protein 1 |
| VDAC1 | P21796 | |
| VDAC2 | P45880 | |
| VDAC3 | Q9Y277 | |
| sCJD | A2MG | Alpha-2-macroglobulin |
| | AACT | Alpha-1-antichymotrypsin |
| | ACO13 | Acyl-coenzyme A thioesterase 13 |
| | ADHX | Alcohol dehydrogenase class-3 |
| | AL1A1 | Retinal dehydrogenase 1 |
| | ALDR | Aldo-keto reductase family 1 member B1 |
| | APEX1 | DNA-(apurinic or apyrimidinic site) lyase |
| | APOA1 | Apolipoprotein A-I |
| | ARP3 | Actin-related protein 3 |
| | ASGL1 | Isoaspartyl peptidase/L-asparaginase |
| | BIEA | Biliverdin reductase A |
| | CAB39 | Calcium-binding protein 39 |
| **CAT** | **P** | **Description** | **Disorder** |
|--------|------|-----------------|-------------|
| CATA  | P04040 | Catalase | Acatalasemia |
| CD59  | P13987 | CD59 glycoprotein | Hemolytic anemia, CD59-mediated, with or without polyneuropathy |
| CLIC4 | Q9Y696 | Chloride intracellular channel protein 4 | |
| CMBL  | Q96DG6 | Carboxymethylenebutenolidase homolog | |
| CPPED | Q98RF8 | Serine/threonine-protein phosphatase CPPED1 | |
| DOPD  | P30046 | D-dopachrome decarboxylase | |
| DYL2  | Q96FJ2 | Dynein light chain 2, cytoplasmic | |
| EFHD2 | Q96C19 | EF-hand domain-containing protein D2 | |
| FABP7 | O15540 | Fatty acid-binding protein, brain | |
| FAHD1 | Q6P587 | Acylpyruvase FAHD1, mitochondrial | |
| FBB   | P02675 | Fibrinogen beta chain | |
| FIBG  | P02679 | Fibrinogen gamma chain | Congenital afibrinogenemia, Congenital afibrinogenemia |
| FKBP4 | Q02790 | Peptidyl-prolyl cis-trans isomerase FKBP4 | |
| G6PD  | P11431 | Glucose-6-phosphate 1-dehydrogenase | Anemia, non-spherocytic hemolytic, due to G6PD deficiency |
| GBRL2 | P60520 | Gamma-aminobutyric acid receptor-associated protein-like 2 | |
| GGCT  | O75223 | Gamma-glutamylcyclotransferase | |
| GNAI2 | P04899 | Guanine nucleotide-binding protein G | |
| GNP1  | P46926 | Glucosamine-6-phosphate isomerase 1 | |
| GSHB  | P48637 | Glutathione synthetase | Glutathione synthetase deficiency |
| HMBG1 | P09429 | High mobility group protein B1 | |
| HNRPK | P61978 | Heterogeneous nuclear ribonucleoprotein K | Au-Kline syndrome |
| IDHC  | O75874 | Isocitrate dehydrogenase [NADP] cytoplasmic | Glioma |
| IDHP  | P48735 | Isocitrate dehydrogenase [NADP], mitochondrial | D-2-hydroxyglutaric aciduria 2 |
| IGLL5 | B9A064 | Immunoglobulin lambda-like polypeptide 5 | |
| ILF2  | Q12905 | Interleukin enhancer-binding factor 2 | |
| KAD3  | Q9UJ7  | GTP: AMP phosphotransferase AK3, mitochondrial | Phospholysine phosphohistidine inorganic pyrophosphate phosphatase |
| LHPP  | Q9H008 | | |
| LKHA4 | P09960 | Leukotriene A-4 hydrolase | |
| MPI   | P34949 | Mannose-6-phosphate isomerase | Congenital disorder of glycosylation 1B |
| MT2   | P02795 | Metallothionein-2 | |
| NNRE  | Q8NCW5 | NAD(P)H-hydrate epimerase | Encephalopathy, progressive, early-onset, with brain edema and/or leukoencephalopathy |
| NQO2  | P16083 | Ribosylhydrionicotinamide dehydrogenase | |
| NUDT5 | Q9UKK9 | ADP-sugar pyrophosphatase | |
| PDCD6 | O75340 | Programmed cell death protein 6 | |
| PITH1 | Q9GZP4 | PITH domain-containing protein 1 | |
| Gene Symbol | Protein Name | Description |
|-------------|--------------|-------------|
| PROF2       | Profilin-2   |             |
| PSA1        | Proteasome subunit alpha type-1 |             |
| PSA2        | Proteasome subunit alpha type-2 |             |
| PSA4        | Proteasome subunit alpha type-4 |             |
| PSA5        | Proteasome subunit alpha type-5 |             |
| PSA6        | Proteasome subunit alpha type-6 |             |
| PSA7        | Proteasome subunit alpha type-7 |             |
| PSA1        | Proteasome subunit beta type-1 |             |
| PSA2        | Proteasome subunit beta type-2 |             |
| PSA4        | Proteasome subunit beta type-4 |             |
| PSA5        | Proteasome subunit beta type-5 |             |
| PSA6        | Proteasome subunit beta type-6 |             |
| PSA7        | Proteasome subunit beta type-7 |             |
| PSA1        | Proteasome subunit beta type-1 |             |
| PSA2        | Proteasome subunit beta type-2 |             |
| PSA4        | Proteasome subunit beta type-4 |             |
| PSA5        | Proteasome subunit beta type-5 |             |
| PSA6        | Proteasome subunit beta type-6 |             |
| PSA7        | Proteasome subunit beta type-7 |             |
| PSA1        | Proteasome subunit beta type-1 |             |
| PSA2        | Proteasome subunit beta type-2 |             |
| PSA4        | Proteasome subunit beta type-4 |             |
| PSA5        | Proteasome subunit beta type-5 |             |
| PSA6        | Proteasome subunit beta type-6 |             |
| PSA7        | Proteasome subunit beta type-7 |             |
| PTGR1       | Prostaglandin reductase 1 |             |
| RAB21       | Ras-related protein Rab-21 |             |
| RAB5B       | Ras-related protein Rab-5B |             |
| RASK        | GTPase KRas | Leukemia, acute myelogenous leukemia |
| RB11B       | Ras-related protein Rab-11B | Neurodevelopmental disorder with ataxic gait, absent speech, and decreased cortic white matter |
| RHOA        | Transforming protein RhoA |             |
| SH3L2       | SH3 domain-binding glutamic acid-rich-like protein 2 |             |
| SKP1        | S-phase kinase-associated protein 1 |             |
| SPB6        | Serpin B6 | Deafness, autosomal recessive, 91 |
| SYWC        | Tryptophan–tRNA ligase, cytoplasmic | Neuronopathy, distal hereditary motor, 9 |
| TOLIP       | Toll-interacting protein |             |
| UBC12       | NEDD8-conjugating enzyme Ubc12 |             |

**Common between rpAD and SCJD**

| Gene Symbol | Protein Name | Description |
|-------------|--------------|-------------|
| A1AG1       | Alpha-1-acid glycoprotein 1 |             |
| A1AT        | Alpha-1-antitrypsin | Alpha-1-antitrypsin deficiency |
| ACTN1       | Alpha-actinin-1 | Bleeding disorder, platelet-type 15 |
| ACYP2       | Acylphosphatase-2 |             |
| AK1A1       | Aldo-keto reductase family 1 member A1 |             |
| CD81        | CD81 antigen | Immunodeficiency, common variable, 6 |
| CYTB        | Cystatin-B | Epilepsy, progressive myoclonic 1 |
| DNJC5       | DnaJ homolog subfamily C member 5 | Ceredoid lipofuscinosis, neuronal, 4B |
| FRIL        | Ferritin light chain | Hyperferritinemia with or without cataract |
| FSCN1       | Fascin |             |
| GLTP        | Glycolipid transfer protein |             |
| GSTM2       | Glutathione S-transferase Mu 2 |             |
| HPLN1       | Hyaluronan and proteoglycan link protein 1 |             |
| LIS1        | Platelet-activating factor acetylhydrolase IB subunit alpha | Lissencephaly 1 |
| OTUB1       | Ubiquitin thioesterase OTUB1 |             |
| PDIA3       | Protein disulfide-isomerase A3 |             |
| PEA15       | Astrocytic phosphoprotein PEA-15 |             |
| Gene Symbol | NCBI Taxonomy ID | Description |
|-------------|-----------------|-------------|
| PIPNA       | Q00169          | Phosphatidylinositol transfer protein alpha isoform |
| PPIA        | P62937          | Peptidyl-prolyl cis-trans isomerase A |
| PTGDS       | P41222          | Prostaglandin-H2 D-isomerase |
| QOR         | Q08257          | Quinone oxidoreductase |
| RAB5C       | P51148          | Ras-related protein Rab-5C |
| RIDA        | P52758          | 2-iminobutanoate/2-iminopropanoate deaminase |
| SCR1        | Q12765          | Secernin-1 |
| SERC        | Q9Y617          | Phosphoserine aminotransferase |
| SFPQ        | P23246          | Splicing factor, proline- and glutamine-rich |
| SH3L1       | O75368          | SH3 domain-binding glutamic acid-rich-like protein |
| SNAI        | P54920          | Alpha-soluble NSF attachment protein |
| SNAB        | Q9H115          | Beta-soluble NSF attachment protein |
| SODM        | P04179          | Superoxide dismutase [Mn], mitochondrial |
| TKT         | P29401          | Transketolase |
| TRFE        | P02787          | Serotransferrin |
| UGPA        | Q16851          | UTP:glucose-1-phosphate uridylyltransferase |
| VATH        | Q9UI12          | V-type proton ATPase subunit H |
| VCP         | P55072          | Valosin containing protein |

**spAD and sCJD**

| Gene Symbol | NCBI Taxonomy ID | Description |
|-------------|-----------------|-------------|
| spAD and sCJD |                 | Microvascular complications of diabetes 6, Short stature, developmental delay, and congenital heart defects |
| CYBP        | Q9HB71          | Calcyclin-binding protein |
| DDAH2       | O95865          | N(G), N(G)-dimethylarginine dimethylaminohydrolase 2 |
| ECH1        | Q13011          | Delta(3.5)-Delta (2.4)-dienoyl-CoA isomerases, mitochondrial |
| ENOPH       | Q9UHY7          | Enolase-phosphatase E1 |
| FPFS        | P14324          | Farnesyl pyrophosphate synthase |
| O43488      |                | Affatoxin B1 aldehyde reductase member 2 |
| GLO2        | Q16775          | Hydroxyacylglutathione hydrolase, mitochondrial |
| GLOD4       | Q9HC38          | Glyoxalase domain-containing protein 4 |
| GMBF        | P60983          | Glia maturation factor beta |
| GMFB        | P14324          | Farnesyl pyrophosphate synthase |
| GSTM1       | P09488          | Glutathione S-transferase Mu 1 |
| GSTM3       | P21266          | Glutathione S-transferase Mu 3 |
| GUL         | Q04760          | Lactoylglutathione lyase |
| LSAMP       | Q13449          | Limbic system-associated membrane protein |
| MK01        | P28482          | Mitogen-activated protein kinase 1 |
| NCDN        | Q9UBB6          | Neurochondrin |
| PGM2L       | Q6PCE3          | Glucose 1,6-bisphosphate synthase |
| Protein ID | Gene Symbol | Description |
|------------|-------------|-------------|
| PP2BB      |             | Serine/threonine-protein phosphatase 2B catalytic subunit beta isoform |
| RAB2A      |             | Ras-related protein Rab-2A |
| RAB5A      |             | Ras-related protein Rab-5A |
| TAGL       |             | Transgelin |

**spAD and rpAD**

| Protein ID | Gene Symbol | Description |
|------------|-------------|-------------|
| AKA12      | Q02952      | A-kinase anchor protein 12 |
| ANX7       | P20073      | Annexin A7 |
| APOE       | P02649      | Apolipoprotein E |
| AQ4        | P55087      | Aquaporin-4 |
| AT2B1      | P20020      | Plasma membrane calcium-transporting ATPase 1 |
| AT2B2      | Q01814      | Plasma membrane calcium-transporting ATPase 2 |
| AT2B3      | Q16720      | Plasma membrane calcium-transporting ATPase 3 |
| AT2B4      | P23634      | Plasma membrane calcium-transporting ATPase 4 |
| AT5F1      | P24539      | ATP synthase F |
| ATPG       | P36542      | ATP synthase subunit gamma, mitochondrial |
| BCA1       | O75363      | Breast carcinoma-amplified sequence 1 |
| BSN        | Q9UPA5      | Protein bassoon |
| CADM2      | Q8N3J6      | Cell adhesion molecule 2 |
| CXA1       | P17302      | Gap junction alpha-1 protein |
| EAA1       | P43003      | Excitatory amino acid transporter 1 |
| EAA2       | P43004      | Excitatory amino acid transporter 2 |
| F10A1      | P50502      | Hsc70-interacting protein |
| FIBA       | P02671      | Fibrinogen alpha chain |
| HECAM      | Q14CZ8      | Hepatocyte cell adhesion molecule |
| MAON       | Q16798      | NADP-dependent malic enzyme, mitochondrial |
| MOG        | Q16653      | Myelin-oligodendrocyte glycoprotein |
| MT1G       | P13640      | Metallothionein-1G |
| MT3        | P25713      | Metallothionein-3 |
| NCAM2      | O15394      | Neural cell adhesion molecule 2 |
| NCAN       | O14594      | Neurocan core protein |
| NHRF1      | O14745      | Na (+)/H (+) exchange regulatory cofactor NHE-RF1 |
| NPTN       | Q9Y639      | Neuroplastin |
| NRCAM      | Q92823      | Neuronal cell adhesion molecule |
| OXR1       | Q8N573      | Oxidation resistance protein 1 |
| PADI2      | Q9Y2J8      | Protein-arginine deiminase type-2 |
| PALM       | O75781      | Paralemmin-1 |
| PDLA6      | Q15084      | Protein disulfide-isomerase A6 |
| PFKAM      | P08237      | ATP-dependent 6-phosphofructokinase, muscle type |

- **Hyperlipoproteinemia 3**
- **Spinocerebellar ataxia, X-linked 1**
- **Episodic ataxia 6**
- **Epileptic encephalopathy, early infantile, 41**
- **Myelination-deficient ataxia, X-linked, 1**
- **Oculudentodigital dysplasia**
- **Congenital afibrinogenemia**
- **Leukoencephalopathy, megalencephalic, with subcortical cysts, 2A**
- **Nephrolithiasis/osteoporosis, hypophosphatemic, 2A**
- **Glycogen storage disease 7**
| No. | UniProt ID | UniProt Accession | Protein names | (WT vs Cont.) (p-values) | (P301L vs Cont.) (p-values) |
|-----|------------|-------------------|---------------|--------------------------|-----------------------------|
| 1   | IST1       | P53990            | IST1 homolog  | 2.80404                  |                             |
| 2   | XCT        | Q9UPY5            | Cystine/glutamate transporter | 2.70942 |                             |
| 3   | ITPR3      | Q14573            | Inositol 1,4,5-trisphosphate receptor type 3 | 3.74147 |                             |
| 4   | CAD13      | P55290            | Cadherin-13  | 3.29636                  |                             |
| 5   | TMEDA      | P49755            | Transmembrane emp24 domain-containing protein 10 | 2.79315 |                             |
| 6   | APC7       | Q9UJX3            | Anaphase-promoting complex subunit 7 | 2.64649 |                             |
| 7   | PXDC2      | Q6UX71            | Plexin domain-containing protein 2 | 2.60679 |                             |
| 8   | PLCA       | Q99943            | 1-acyl-sn-glycerol-3-phosphate acyltransferase alpha | 2.77202 |                             |
| 9   | NUDC1      | Q96RS6-2          | NudC domain-containing protein 1 | 2.58966 |                             |
| 10  | SYUG       | O76070            | Gamma-synuclein | 3.30288 |                             |
| 11  | A0A1W2PS43 | A0A1W2PS 43      | Lysosome membrane protein 2 | 3.00432 |                             |
| 12  | F8VX04     | F8VX04            | Sodium-coupled neutral amino acid transporter 1 | 3.15582 |                             |
| 13  | RAB18      | Q9NP72            | Ras-related protein Rab-18 | 2.60603 |                             |
| 14  | Q5VZR0     | Q5VZR0            | Golgi-associated plant pathogenesis-related protein 1 | 2.6549 |                             |
| 15  | CD44       | P16070            | CD44 antigen | 2.89138 |                             |
|   |   |   |   |   |
|---|---|---|---|---|
|16| COX2 | P00403 | Cytochrome c oxidase subunit 2 | 2.89006 |
|17| PYRG1 | P17812 | CTP synthase 1 | 2.64826 |
|18| C9JYN0 | C9JYN0 | Synaptophsin-like protein 1 | 3.73999 |
|19| E7ER44 | E7ER44 | Lactotransferrin | 5.61449 |
|20| K7NL2 | K7NL2 | WW domain-binding protein 2 | 3.25965 |
|21| IF16 | Q16666 | Gamma-interferon-inducible protein 16 | 2.54071 |
|22| A0A1B0GW0 | A0A1B0GW0 | Carnitine O-palmitoyltransferase 2, mitochondrial | 3.83877 |
|23| A0A087WX97 | A0A087WX97 | Bcl-2-like protein 13 | 3.19665 |
|24| RND3 | P61587 | Rho-related GTP-binding protein RhoE | 3.65369 |
|25| PODXL | O00592 | Podocalyxin | 5.52997 |
|26| MOT1 | P53985 | Monocarboxylate transporter 1 | 4.65667 |
|27| CLIC4 | Q9Y696 | Chloride intracellular channel protein 4 | 4.5989 |
|28| A0A075B730 | A0A075B730 | Epilakin | 2.80249 |
|29| S38A2 | Q96QD8 | Sodium-coupled neutral amino acid transporter 2 | 3.7117 |
|30| TPBG | Q13641 | Trophoblast glycoprotein | 3.97711 |
|31| LAT1 | Q01650 | Large neutral amino acids transporter small subunit 1 | 6.21328 |
|32| SQOR | Q9Y696 | Sulfide: quinone oxidoreductase, mitochondrial | 3.5484 |
|33| E9PEB5 | E9PEB5 | Far upstream element-binding protein 1 | 3.65134 |
|34| AAAT | Q15758 | Neutral amino acid transporter B | 4.73081 |
|35| AHNK2 | Q81VF2 | Protein AHNAK2 | 2.93411 |
|36| RTN4 | Q9NQC3-2 | Reticulin-4 | 2.78976 |
|37| AT1A1 | P05023-4 | Sodium/potassium-transporting ATPase subunit alpha-1 | 2.80245 |
|38| A0A087X054 | A0A087X054 | Hypoxia up-regulated protein 1 | 2.67896 |
|39| J3KPF3 | J3KPF3 | 4F2 cell-surface antigen heavy chain | 3.40599 |
|40| VINC | P18206 | Vinculin | 2.67223 |
|41| SYWC | P23381-2 | Tryptophan--tRNA ligase, cytoplasmic | 2.87585 |
|42| UAP1 | Q16222 | UDP-N-acetylhexosamine pyrophosphorylase | 2.53642 |
### Table 8: Tau down-regulated proteins: list of unique and common proteins (with their -log_{10}p-values), that were down-regulated after expression of either WT-tau or P301L-tau

| No. | UniProt ID | UniProt Accession | Protein names                                      | WT vs Cont. (p-values) | P301L vs Cont. (p-values) |
|-----|------------|-------------------|---------------------------------------------------|------------------------|--------------------------|
| 1   | CAPZB      | P47756-2          | F-actin-capping protein subunit beta               | 2.90632                |                          |
| 2   | CLIC1      | O00299            | Chloride intracellular channel protein 1          | 2.74343                |                          |
| 3   | 1433E      | P62258            | 14-3-3 protein epsilon                            | 2.97992                |                          |
| 4   | PDLI7      | Q9NR12            | PDZ and LIM domain protein 7                      | 2.87187                |                          |
| 5   | DHPR       | P09417            | Dihydropoteridine reductase                       | 3.29976                |                          |
| 6   | TBB4B      | P68371            | Tubulin beta-4B chain                             | 2.61161                |                          |
|   | Protein | Accession | Description                                      | Score  |
|---|---------|-----------|--------------------------------------------------|--------|
| 7 | CYBP    | Q9HB71    | Calcyclin-binding protein                        | 4.20659|
| 8 | GSH0    | P48507    | Glutamate–cysteine ligase regulatory subunit     | 3.64493|
| 9 | IDHC    | O75874    | Isocitrate dehydrogenase [NADP] cytoplasmic     | 3.18656|
| 10| CRK     | P46108    | Adapter molecule crk                             | 2.66295|
| 11| LKHA4   | P09960    | Leukotriene A-4 hydrolase                        | 3.07686|
| 12| LDHA    | P00338    | L-lactate dehydrogenase A chain                  | 2.60496|
| 13| COF1    | P23528    | Cofilin-1                                        | 2.86394|
| 14| PSME3   | P61289    | Proteasome activator complex subunit 3           | 2.59093|
| 15| XPO6    | Q96Q8     | Exportin-6                                       | 2.63751|
| 16| PFKAM   | P08237    | ATP-dependent 6-phosphofructokinase, muscle type | 2.77411|
| 17| METK2   | P31153    | S-adenosylmethionine synthase isofrom type-2     | 2.59551|
| 18| I3L0H8  | I3L0H8    | ATP-dependent RNA helicase DDX19A                | 3.00712|
| 19| A0A087WYT3| A0A087WYT3| Prostaglandin E synthase 3                        | 6.25017|
| 20| MBB1A   | Q98BQ0    | Myb-binding protein 1A                           | 3.31109|
| 21| GANAB   | Q14697-2  | Neutral alpha-glucosidase AB                     | 3.99331|
| 22| RPAC1   | O15160    | DNA-directed RNA polymerases I and III subunit RPAC1 | 2.95675|
| 23| 6PGD    | P52209    | 6-phosphogluconate dehydrogenase, decarboxylating | 3.15286|
| 24| F22Y4   | F22Y4     | Pyridoxal kinase                                 | 3.349  |
| 25| KTHY    | P23919    | Thymidylate kinase                               | 4.05072|
| 26| ACADM   | P11310-2  | Medium-chain specific acyl-CoA dehydrogenase, mitochondrial | 3.37726|
| 27| RT27    | Q92552    | DNA replication licensing factor MCM6            | 2.65651|
| 28| A0A1B0GW77| A0A1B0GW77| Alpha-aminoadipic semialdehyde dehydrogenase     | 2.57993|
| 29| IPYR    | Q15181    | Inorganic pyrophosphatase                        | 2.56092|
| 30| KPYM    | P14618    | Pyruvate kinase PKM                              | 3.3471 |
| 31| TWF1    | Q12792    | Twinfilin-1                                      | 3.16219|
| 32| MCM6    | Q14566    | DNA replication licensing factor MCM6            | 2.98343|
| 33| I3L2B0  | I3L2B0    | Clustered mitochondria protein homolog           | 3.14353|
| 34| KPRA    | Q14558    | Phosphoribosyl pyrophosphate synthase-associated protein 1 | 2.88641|
| 35| ERO1A   | Q96HE7    | ERO1-like protein alpha                          | 3.48398|
| 36| AP3D1   | O14617    | AP-3 complex subunit delta-1                     | 2.64148|
| 37| QSO7M7  | Q5QPM7    | Proteasome inhibitor PI31 subunit                | 2.779  |
| 38| TNPO3   | Q9Y5L0    | Transportin-3                                    | 3.19029|
| 39| NAT10   | Q9H0A0    | RNA cytidine acetyltransferase                   | 2.60558|
| 40| F6WQW2  | F6WQW2    | Ran-specific GTPase-activating protein            | 2.6097 |
| 41| HAT1    | O14929    | Histone acetyltransferase type B catalytic subunit | 2.61858|
| 42| E7ESZ7  | E7ESZ7    | NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 10, mitochondrial | 3.34015|
| 43| A0A1B0GWE8| A0A1B0GWE8| Cathepsin D                                      | 3.59333|
| 44| APEX1   | P27695    | DNA-(apurinic or apyrimidinic site) lyase         | 2.573  |
| Gene  | Accession | Description                                                                 | Log2 Fold Change |
|-------|-----------|-------------------------------------------------------------------------------|------------------|
| LNP   | Q9C0E8    | Endoplasmic reticulum junction formation protein lunapark                      | 3.024            |
| PARK7 | Q99497    | Protein/nucleic acid deglycase DJ-1                                            | 3.53845          |
| PP2AA | P67775    | Serine/threonine-protein phosphatase 2A catalytic subunit alpha isoform         | 2.85783          |
| DUS23 | Q9BVJ7    | Dual specificity protein phosphatase 23                                        | 2.6001           |
| NUP43 | Q8NFH3    | Nucleoporin Nup43                                                              | 2.92109          |
| TF3C4 | Q9UKN8    | General transcription factor 3C polypeptide 4                                  | 2.85149          |
| UBA3  | Q8TBC4    | NEDD8-activating enzyme E1 catalytic subunit                                   | 2.85788          |
| B1AH49| B1AH49    | 3-mercaptopropionate sulfurtransferase                                          | 4.16312          |
| ABCD3 | P28288    | ATP-binding cassette sub-family D member 3                                     | 2.89151          |
| Q5QPR3| Q5QPR3    | Cyclin-dependent kinase 11A                                                   | 3.07425          |
| D6RG13| D6RG13    | 40S ribosomal protein S3a                                                      | 3.40351          |
| B7Z4B8| B7Z4B8    | Heterogeneous nuclear ribonucleoprotein U-like protein 1                       | 3.80247          |
| AN32E | Q9BTT0    | Acidic leucine-rich nuclear phosphoprotein 32 family member E                  | 3.0431           |
| HPBP1 | Q9NZL4    | Hsp70-binding protein 1                                                        | 3.14118          |
| PAIRB | Q8NC51    | Plasminogen activator inhibitor 1 RNA-binding protein                           | 2.72168          |
| CDK1  | P06493    | Cyclin-dependent kinase 1                                                      | 6.03772          |
| X6RLT1| X6RLT1    | Negative elongation factor C/D                                                  | 2.93622          |
| TNAP2 | Q03169    | Tumor necrosis factor alpha-induced protein 2                                  | 2.62938          |
| MLKL  | Q8NB16    | Mixed lineage kinase domain-like protein                                        | 3.39344          |
| E7ETK0| E7ETK0    | 40S ribosomal protein S24                                                       | 3.59647          |
| DHX36 | Q9H2U1    | ATP-dependent DNA/RNA helicase DHX36                                           | 3.02912          |
| TBCC  | Q15814    | Tubulin-specific chaperone C                                                    | 2.65875          |
| RL6   | Q02878    | 60S ribosomal protein L6                                                        | 3.71789          |
| TOM34 | Q15785    | Mitochondrial import receptor subunit TOM34                                    | 3.64649          |
| HP1B3 | Q5SSJ5    | Heterochromatin protein 1-binding protein 3                                    | 3.88668          |
| C19L1 | Q69YN2    | CWF19-like protein 1                                                           | 2.65963          |
| RS17  | P08708    | 40S ribosomal protein S17                                                       | 3.74528          |
| E7ESA6| E7ESA6    | Focal adhesion kinase 1                                                         | 2.64713          |
| AP3M1 | Q9Y2T2    | AP-3 complex subunit mu-1                                                      | 2.75333          |
| M0QXD6| M0QXD6    | General transcription factor IIIF subunit 1                                    | 2.56235          |
| WNT5A | P41221    | Protein Wnt-5a                                                                 | 2.59575          |
| GMDS  | O60547    | GDP-mannose 4,6 dehydratase                                                    | 3.08654          |
| I3LOX5| I3LOX5    | Sperm-associated antigen 7                                                      | 3.3113           |
| E9PH64| E9PH64    | NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 9                   | 2.95705          |
| MIPEP | Q99797    | Mitochondrial intermediate peptidase                                           | 2.7807           |
| A0A087WZR9 | A0A087WZR9 | Pyrroline-5-carboxylate reductase                                              | 5.26058          |
| CHIP  | Q9UNE7    | E3 ubiquitin-protein ligase CHIP                                               | 2.93915          |
|   |     | Description                                      |   |
|---|-----|------------------------------------------------|---|
| 82 | TBCE | Q15813 Tubulin-specific chaperone E              | 2.57258 |
| 83 | SAAL1 | Q96ER3 Protein SAAL1                           | 2.84296 |
| 84 | SYRC | P54136 Arginine--tRNA ligase, cytoplasmic      | 3.68764 |
| 85 | HTAI2 | Q9BUP3 Oxidoreductase HTATIP2                  | 2.52883 |
| 86 | GRP75 | P38646 Stress-70 protein, mitochondrial        | 3.35915 |
| 87 | PSB3 | P49720 Proteasome subunit beta type-3          | 2.82347 |
| 88 | GSTP1 | P09211 Glutathione S-transferase P             | 3.25767 |
| 89 | RAB7A | P51149 Ras-related protein Rab-7a              | 2.95429 |
| 90 | TCPG | P49368 T-complex protein 1 subunit gamma       | 3.5822  |
| 91 | RAB9A | P51151 Ras-related protein Rab-9A              | 2.60002 |
| 92 | PHB  | P35232 Prohibitin                               | 2.76765 |
| 93 | RS27A | P62979 Ubiquitin-40S ribosomal protein S27a    | 3.44529 |
| 94 | E7EQR4 | E7EQR4 Ezrin                                   | 2.70739 |
| 95 | RIR1 | P23921 Ribonucleoside-diphosphate reductase large subunit | 2.55098 |
| 96 | J3QQT2 | J3QQT2 60S ribosomal protein L17               | 2.99247 |
| 97 | SRP68 | Q9UHB9 Signal recognition particle subunit SRP68 | 3.01785 |
| 98 | SMD3 | P62318 Small nuclear ribonucleoprotein Sm D3   | 3.12363 |
| 99 | SYQ  | P47897 Glutamine--tRNA ligase                  | 2.65577 |
| 100| H3BQI1 | H3BQI1 Dynein light chain roadblock-type 2     | 2.72107 |
| 101| MCM5 | P33992 DNA replication licensing factor MCM5   | 2.94611 |
| 102| Q8WVC2 | Q8WVC2 40S ribosomal protein S21               | 2.76124 |
| 103| NDUS3 | O75489 NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial | 3.63337 |
| 104| RL7  | P18124 60S ribosomal protein L7                | 2.73981 |
| 105| C9JA28 | C9JA28 Translocon-associated protein subunit gamma | 3.0665 |
| 106| S4R3E9 | S4R3E9 NEDD8-MDP1 readthrough                 | 3.09505 |
| 107| VIME | P08670 Vimentin                                 | 3.24861 |
| 108| I3L504 | I3L504 Eukaryotic translation initiation factor 5A-1 | 2.65408 |
| 109| TM109 | Q9BVC6 Transmembrane protein 109              | 3.52926 |
| 110| DRG1 | Q9Y295 Developmentally-regulated GTP-binding protein 1 | 3.14037 |
| 111| SMD1 | P62314 Small nuclear ribonucleoprotein Sm D1   | 3.54617 |
| 112| H0YEN5 | H0YEN5 40S ribosomal protein S2               | 3.76272 |
| 113| MCM3 | P25205-2 DNA replication licensing factor MCM3 | 3.01339 |
| 114| ARF6 | P62330 ADP-ribosylation factor 6               | 3.18205 |
| 115| RL7A | P62424 60S ribosomal protein L7a               | 3.56152 |
| 116| BZW2 | Q9Y6E2 Basic leucine zipper and W2 domain-containing protein 2 | 4.20893 |
| 117| A0A0A0MTN0 | A0A0A0MTN0 Cullin-2                      | 2.85465 |
| 118| THOP1 | P52888 Thimet oligopeptidase                  | 3.49956 |
| 119| J3QRI7 | J3QRI7 60S ribosomal protein L26             | 5.03306 |
| 120| ATP0 | P48047 ATP synthase subunit O, mitochondrial     | 2.73623 |
| 121| LSM3 | P62310 U6 snRNA-associated Sm-like protein LSm3 | 3.12073 |
| ID   | Accession   | Description                                                                 |
|------|-------------|----------------------------------------------------------------------------|
| 122  | SRP14       | Signal recognition particle 14 kDa protein                                  |
| 123  | NCBP2       | Nuclear cap-binding protein subunit 2                                      |
| 124  | RAN         | GTP-binding nuclear protein Ran                                             |
| 125  | J3KQ48      | Peptidyl-tRNA hydrolase Ran, mitochondrial                                  |
| 126  | TXD17       | Thioredoxin domain-containing protein 17                                    |
| 127  | MGST1       | Microsomal glutathione S-transferase 1                                     |
| 128  | SNX1        | Sorting nexin-1                                                            |
| 129  | HNRPF       | Heterogeneous nuclear ribonucleoprotein F                                  |
| 130  | RL13        | 60S ribosomal protein L13                                                  |
| 131  | A0A087WUD3  | Oligosaccharyltransferase complex subunit OSTC                             |
| 132  | RS28        | 40S ribosomal protein S28                                                  |
| 133  | J3KTA4      | Probable ATP-dependent RNA helicase DDX5                                  |
| 134  | DDX6        | Probable ATP-dependent RNA helicase DDX6                                  |
| 135  | ZC3HF       | Zinc finger CCCH domain-containing protein 15                               |
| 136  | RM21        | 39S ribosomal protein L21, mitochondrial                                   |
| 137  | ULA1        | NEDD8-activating enzyme E1 regulatory subunit                              |
| 138  | RL11        | 60S ribosomal protein L11                                                  |
| 139  | RS11        | 40S ribosomal protein S11                                                  |
| 140  | RS8         | 40S ribosomal protein S8                                                   |
| 141  | RL21        | 60S ribosomal protein L21                                                  |
| 142  | A0A087X0X3  | Heterogeneous nuclear ribonucleoprotein M                                  |
| 143  | RS23        | 40S ribosomal protein S23                                                  |
| 144  | ATD3A       | ATPase family AAA domain-containing protein 3A                              |
| 145  | RL23        | 60S ribosomal protein L23                                                  |
| 146  | 2A5D        | Serine/threonine-protein phosphatase 2A 56 kDa regulatory subunit delta isoform |
| 147  | RS13        | 40S ribosomal protein S13                                                  |
| 148  | G5E9Q6      | Profilin                                                                   |
| 149  | RL12        | 60S ribosomal protein L12                                                  |
| 150  | XPO5        | Exportin-5                                                                 |
| 151  | DDX23       | Probable ATP-dependent RNA helicase DDX2                                   |
| 152  | RL27        | 60S ribosomal protein L27                                                  |
| 153  | E5RI99      | 60S ribosomal protein L30                                                  |
| 154  | SHIP2       | Phosphatidylinositol 3,4,5-trisphosphate 5-phosphatase 2                    |
| 155  | PRP6        | Pre-mRNA-processing factor 6                                                |
| 156  | SYDM        | Aspartate-tRNA ligase, mitochondrial                                        |
| 157  | KIF2A       | Kinesin-like protein KIF2A                                                  |
| 158  | J3QR09      | Ribosomal protein L19                                                      |
| 159  | OCAD2       | OCIA domain-containing protein 2                                            |
| 160  | J3QSV6      | Ribosomal L1 domain-containing protein 1                                   |
| 161  | RL38        | 60S ribosomal protein L38                                                  |
| Gene ID | Gene Name | Description | Log2 Fold Change in WT | Log2 Fold Change in P301L-tau expressing cells |
|---------|-----------|-------------|------------------------|-----------------------------------------------|
| A0A087X2D0 | A0A087X2D0 | Serine/arginine-rich-splicing factor 3 | 4.36894 | |
| GPI8 | Q92643 | GPI-anchor transamidase | 2.86273 | |
| NU160 | Q12769 | Nuclear pore complex protein Nup160 | 2.76185 | |
| SMYD3 | Q9H7B4 | Histone-lysine N-methyltransferase SMYD3 | 3.2229 | |
| YME1L1 | Q96TA2 | ATP-dependent zinc metalloprotease YME1L1 | 2.84011 | |
| PDCD4 | Q53EL6 | Programmed cell death protein 4 | 3.59557 | |
| TMED1 | Q13445 | Transmembrane emp24 domain-containing protein 1 | 2.72926 | |
| RCN2 | Q14257 | Reticulocalbin-2 | 3.22922 | |
| R39L5 | Q13445 | Histone-lysine N-methyltransferase SMYD3 | 3.32229 | |
| YME1L1 | Q96TA2 | ATP-dependent zinc metalloprotease YME1L1 | 2.84011 | |
| PDCD4 | Q53EL6 | Programmed cell death protein 4 | 3.59557 | |
| TMED1 | Q13445 | Transmembrane emp24 domain-containing protein 1 | 2.72926 | |
| RCN2 | Q14257 | Reticulocalbin-2 | 3.22922 | |
| R39L5 | Q13445 | Histone-lysine N-methyltransferase SMYD3 | 3.32229 | |
| YME1L1 | Q96TA2 | ATP-dependent zinc metalloprotease YME1L1 | 2.84011 | |
| PDCD4 | Q53EL6 | Programmed cell death protein 4 | 3.59557 | |
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| RCN2 | Q14257 | Reticulocalbin-2 | 3.22922 | |
| R39L5 | Q13445 | Histone-lysine N-methyltransferase SMYD3 | 3.32229 | |
| YME1L1 | Q96TA2 | ATP-dependent zinc metalloprotease YME1L1 | 2.84011 | |
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| RCN2 | Q14257 | Reticulocalbin-2 | 3.22922 | |
| R39L5 | Q13445 | Histone-lysine N-methyltransferase SMYD3 | 3.32229 | |
| YME1L1 | Q96TA2 | ATP-dependent zinc metalloprotease YME1L1 | 2.84011 | |
| PDCD4 | Q53EL6 | Programmed cell death protein 4 | 3.59557 | |
| TMED1 | Q13445 | Transmembrane emp24 domain-containing protein 1 | 2.72926 | |
| RCN2 | Q14257 | Reticulocalbin-2 | 3.22922 | |
| R39L5 | Q13445 | Histone-lysine N-methyltransferase SMYD3 | 3.32229 | |
| YME1L1 | Q96TA2 | ATP-dependent zinc metalloprotease YME1L1 | 2.84011 | |
| PDCD4 | Q53EL6 | Programmed cell death protein 4 | 3.59557 | |
| TMED1 | Q13445 | Transmembrane emp24 domain-containing protein 1 | 2.72926 | |
| RCN2 | Q14257 | Reticulocalbin-2 | 3.22922 | |
| R39L5 | Q13445 | Histone-lysine N-methyltransferase SMYD3 | 3.32229 | |

**Common in both WT- and P301L-tau expressing cells**

| Gene ID | Gene Name | Description | Log2 Fold Change in WT | Log2 Fold Change in P301L-tau expressing cells |
|---------|-----------|-------------|------------------------|-----------------------------------------------|
| F8WCF6 | F8WCF6 | Actin-related protein 2/3 complex subunit 4 | 3.33715 | 4.14691 |
| RACK1 | P63244 | Receptor of activated protein C kinase 1 | 3.39824 | 4.51018 |
| SYDC | P14868 | Aspartate--tRNA ligase, cytoplasmic | 2.74959 | 2.57307 |
| EIF3K | Q9UBQ5 | Eukaryotic translation initiation factor 3 subunit K | 2.81828 | 4.58194 |
| H9KV45 | H9KV45 | Ubiquitin-conjugating enzyme E2 D3 | 2.67823 | 5.42209 |
| Q5JR08 | Q5JR08 | Rho-related GTP-binding protein RhoC | 3.44748 | 3.81268 |
| PROF1 | P07737 | Profilin-1 | 3.07127 | 4.69295 |
| FPPS | P14324 | Farnesyl pyrophosphate synthase | 3.80014 | 3.24431 |
| Q5VV89 | Q5VV89 | Microsomal glutathione S-transferase 3 | 3.6279 | 4.42465 |
| SYK | Q15046 | Lysine--tRNA ligase | 3.9661 | 3.1659 |
| PUR2 | P22102 | Trifunctional purine biosynthetic protein adenosine-3' [Includes: Phosphoribosylamine--glycine ligase] | 2.81901 | 2.93211 |
| SND1 | Q7KZF4 | Staphylococcal nuclease domain-containing protein 1 | 3.019 | 3.608 |
| C9JZR2 | C9JZR2 | Catenin delta-1 | 2.6207 | 2.99525 |
| CAN2 | P17655 | Calpain-2 catalytic subunit | 3.42537 | 3.11891 |
| AAAS | Q9NRG9 | Aladin | 4.28764 | 4.41039 |
| SYLC | Q9P2J5 | Leucine--tRNA ligase, cytoplasmic | 3.39758 | 3.6911 |
| RNZ2 | Q9BQ52 | Zinc phosphodiesterase ELAC protein 2 | 3.34161 | 3.22 |
| TIF1B | Q13263 | Transcription intermediary factor 1-beta | 3.23108 | 3.44094 |
| EIF3B | P55884 | Eukaryotic translation initiation factor 3 subunit B | 4.32237 | 4.51386 |
| PPIA | P62937 | Peptidyl-prolyl cis-trans isomerase A | 3.8054 | 4.17 |
| H0YAK1 | H0YAK1 | G-rich sequence factor 1 | 3.46677 | 2.53854 |
| ID   | Accession | Description                                                                 | Score1 | Score2 |
|------|-----------|------------------------------------------------------------------------------|--------|--------|
| 197  | EIF3G     | Eukaryotic translation initiation factor 3 subunit G                        | 2.72457| 3.04545|
| 198  | Q32Q12    | Nucleoside diphosphate kinase                                                | 3.00854| 3.04007|
| 199  | EFTU      | Elongation factor Tu, mitochondrial                                          | 3.64175| 3.42478|
| 200  | RS3       | 40S ribosomal protein S3                                                    | 2.61813| 3.38603|
| 201  | MTREX     | Exosome RNA helicase MTR4                                                    | 2.57741| 2.61761|
| 202  | RS26      | 40S ribosomal protein S26                                                    | 2.66498| 3.15958|
| 203  | RS16      | 40S ribosomal protein S16                                                    | 2.87042| 5.66172|
| 204  | A0A087WZT3| BoLa-like protein 2                                                          | 2.62918| 3.9663 |
| 205  | LANC1     | Glutathione S-transferase                                                    | 4.28469| 3.09074|
| 206  | CND3      | Condensin complex subunit 3                                                 | 2.9969 | 2.66232|
| 207  | AIMP2     | Aminoacyl tRNA synthase complex-interacting multifunctional protein 2       | 3.83739| 3.0309 |
| 208  | G3V325    | ATP5MF-PTCD1 readthrough                                                    | 4.35305| 4.77429|
| 209  | TGM2      | Protein-glutamine gamma-glutamyltransferase 2                               | 3.47902| 3.32233|
| 210  | RS18      | 40S ribosomal protein S18                                                    | 3.20805| 4.17992|
| 211  | RS14      | 40S ribosomal protein S14                                                    | 2.67833| 4.25944|
| 212  | C9JXB8    | 60S ribosomal protein L24                                                    | 2.98512| 4.69503|
| 213  | MGST2     | Microsomal glutathione S-transferase 2                                      | 2.68604| 3.32233|
| 214  | RL13A     | 60S ribosomal protein L13a                                                   | 2.87139| 4.09016|
| 215  | SNR40     | USp small nuclear ribonucleoprotein 40 kDa protein                          | 2.83902| 2.94416|
| 216  | SRP54     | Signal recognition particle 54 kDa protein                                  | 3.37647| 3.10435|
| 217  | CUL4A     | U2 small nuclear ribonucleoprotein 40 kDa protein                            | 5.00644| 2.58406|
| 218  | UCK2      | Uridine-cytidine kinase 2                                                   | 2.99612| 2.78459|
| 219  | K7EP65    | 60S ribosomal protein L22                                                    | 3.68703| 6.73393|
| 220  | RS19      | 40S ribosomal protein S19                                                    | 3.54415| 7.35693|
| 221  | TSYL1     | Testis-specific Y-encoded-like protein 1                                    | 2.66813| 3.09096|
| 222  | E9PJD9    | 60S ribosomal protein L27a                                                   | 3.04224| 5.20122|
| 223  | VPS45     | Vacular protein sorting-associated protein 45                               | 2.73297| 4.2448 |
| 224  | M0R3D6    | 60S ribosomal protein L18a                                                   | 3.29172| 4.15871|
| 225  | RS6       | 40S ribosomal protein S6                                                     | 2.85538| 3.91982|
| 226  | H7C2W9    | 60S ribosomal protein L31                                                    | 2.97225| 6.33005|
| 227  | NUCL      | Nucleolin                                                                    | 3.49248| 4.59942|
| 228  | A0A0D9SG12| ATP-dependent RNA helicase DDX3X                                             | 2.69323| 4.56215|
| 229  | CDC73     | Parafibromin                                                                 | 3.60285| 2.99202|
| 230  | APT       | Adenine phosphoribosyltransferase Ribosomal protein L15                     | 3.34193| 2.61598|
| 231  | E7ENU7    | Ribosomal protein L15                                                        | 3.97322| 2.8185 |
| 232  | G3BP1     | Ras GTPase-activating protein-binding protein 1                              | 3.04396| 3.61278|
| 233  | K7ERT8    | 60S ribosomal protein L23a                                                   | 4.22784| 5.36401|
| 234  | J3Q067    | 60S ribosomal protein L18                                                    | 2.66443| 2.95231|
| 235  | XRCC6     | X-ray repair cross-complementing protein 6                                   | 3.48879| 3.75823|
| 236  | M0R0R2    | 40S ribosomal protein S5                                                     | 4.26617| 5.14718|
| 237  | RFC5      | Replication factor C subunit 5                                               | 4.36703| 3.35394|
Table 9: Top 5 networks identified from IPA analysis in WT-tau expressing cells

| ID | Associated network functions                                                                 | Score |
|----|-----------------------------------------------------------------------------------------------|-------|
| 1  | RNA damage and repair, protein synthesis, cancer                                              | 61    |
| 2  | DNA replication, recombination, and repair, cellular assembly and organization, cell morphology| 41    |
| 3  | Cell cycle, cellular function and maintenance, molecular transport                           | 28    |
| 4  | Cellular movement, haematological system development and function, immune cell trafficking   | 21    |
| 5  | Organismal injury and abnormalities, cellular movement, skeletal and muscular system development and function | 17    |

Table 10: Top 5 networks identified from IPA analysis in P301L-tau expressing cells

| ID | Associated network functions                                                                 | Score |
|----|-----------------------------------------------------------------------------------------------|-------|
| 1  | RNA damage and repair, protein synthesis, cancer                                              | 55    |
| 2  | Cellular assembly and organization, cellular compromise, cellular function and maintenance   | 52    |
| 3  | Nucleic acid metabolism, small molecule biochemistry, digestive system development and function | 27    |
| 4  | Cellular compromise, developmental disorder, endocrine system disorders                       | 22    |
| 5  | Developmental disorder, endocrine system disorders, organ morphology                          | 11    |
Table 11: Significantly enriched proteins in all comparisons (rpAD vs Cont, spAD vs Cont, sCJD vs Cont, rpAD vs spAD, spAD vs sCJD, rpAD vs sCJD) are listed

| No. | Proteins                                                                 | Accession No. | rpAD/cont | spAD/cont | sCJD/cont | rpAD/s pAD | spAD/s CJD | rpAD/s CJD |
|-----|--------------------------------------------------------------------------|----------------|-----------|-----------|-----------|------------|------------|------------|
| 1   | Clathrin coat assembly protein AP180                                     | AP180          | +         | +         | +         |            |            |            |
| 2   | 60 kDa heat shock protein, mitochondrial                                 | CH60           | +         | +         |           |            |            |            |
| 3   | N(G),N(G)-dimethylarginine dimethylaminohydrolase 1                      | DDAH1          | +         |           | +         | +          | +          |            |
| 4   | Filaggrin-2                                                              | Fila2          | +         | +         | +         |            |            |            |
| 5   | Fascin                                                                   | FSCN1          | +         | +         | +         |            |            |            |
| 6   | Guanine nucleotide-binding protein G(o) subunit alpha                    | GNAO           | +         |           |           |            |            |            |
| 7   | Lysozyme C                                                               | LYSC           | +         |           |           |            |            |            |
| 8   | Microtubule-associated protein 1A                                         | MAP1A          | +         |           |           |            |            |            |
| 9   | Protein kinase C and casein kinase substrate in neurons protein 1        | PACN1          | +         |           |           |            |            |            |
| 10  | Ras-related protein Rab-1A                                               | RAB1A          | +         |           |           | +          | +          | +          |
| 11  | Rho-related GTP-binding protein RhoB                                     | RHOB           | +         |           |           |            |            |            |
| 12  | Ribonuclease inhibitor                                                   | RNI            | +         | +         | +         | +          |            |            |
| 13  | Prosaposin                                                              | SAP            | +         | +         | +         |            |            |            |
| 14  | Secernin-1                                                               | SCRN1          | +         |           |           |            |            |            |
| 15  | Septin-7                                                                 | Septin-7       | +         | +         | +         |            |            |            |
| 16  | Protein-glutamine gamma-glutamyltransferase E                             | TGM3           | +         | +         |           |            |            |            |
| 17  | 14-3-3 protein sigma                                                     | 1433S         |           |           |           |            |            |            |
| 18  | 3-hydroxyisobutyrate dehydrogenase, mitochondrial                       | 3HIDH          | +         |           |           |            |            |            |
| 19  | 6-phosphogluconate dehydrogenase                                         | 6PGD           | +         |           |           |            |            |            |
| 20  | Alpha-1-acid glycoprotein 1                                              | A1AG1          | +         |           |           |            |            |            |
| 21  | Alpha-1-antitrypsin                                                     | A1AT           | +         |           |           |            |            |            |
| 22  | Alpha-2-macroglobulin                                                   | A2MG           | +         |           |           |            |            |            |
| 23  | Alpha-1-antichymotrypsin                                                 | AACT           | +         |           |           |            |            |            |
| 24  | Aspartate aminotransferase, cytoplasmic                                  | AATC           | +         |           |           |            |            |            |
| 25  | Aconitate hydratase, mitochondrial                                       | ACON           | +         |           |           |            |            |            |
| 26  | Alpha-actinin-1                                                          | ACTN1          | +         |           |           |            |            |            |
| 27  | Acylphosphatase-2                                                        | ACYP2          | +         |           |           |            |            |            |
| 28  | Beta-adducin                                                             | ADDB           | +         |           |           |            |            |            |
| 29  | Alcohol dehydrogenase class-3                                            | ADHX           | +         |           |           |            |            |            |
| 30  | Retinal dehydrogenase 1                                                  | AL1A1          | +         |           |           |            |            |            |
| 31  | Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial             | AL4A1          | +         |           |           |            |            |            |
| 32  | Alpha-aminoacidic semialdehyde dehydrogenase                            | AL7A1          | +         |           |           |            |            |            |
|   | Protein Name                                                                 | Gene Symbol |   |   |   |
|---|------------------------------------------------------------------------------|-------------|---|---|---|
|33| 4-trimethylaminobutyraldehyde dehydrogenase                                | AL9A1       | + |   | + |
|34| Aldehyde dehydrogenase, mitochondrial                                       | ALDH2       | + |   | + |
|35| Fructose-bisphosphate aldolase A                                            | ALDOA       |   | + |   |
|36| Fructose-bisphosphate aldolase C                                            | ALDOC       |   | + |   |
|37| Aldose reductase                                                              | ALDR        |   | + |   |
|38| Cytosol aminopeptidase                                                        | AMPL        |   | + |   |
|39| Annexin A2                                                                   | ANXA2       |   | + |   |
|40| Annexin A5                                                                   | ANXA5       | + | + |   |
|41| Annexin A6                                                                   | ANXA6       | + | + |   |
|42| Annexin A7                                                                   | ANXA7       |   | + |   |
|43| AP-2 complex subunit beta                                                    | AP2B1       | + | + |   |
|44| Apolipoprotein E                                                             | APOE        |   | + |   |
|45| ADP-ribosylation factor 1                                                     | ARF1        |   | + |   |
|46| Aflatoxin B1 aldehyde reductase member 2                                     | ARK72       |   | + |   |
|47| Actin-related protein 2                                                       | ARP2        | + | + |   |
|48| Sodium/potassium-transporting ATPase subunit beta-1                          | AT1B1       | + | + |   |
|49| ATP synthase subunit beta, mitochondrial                                     | ATPB        | + | + |   |
|50| Cytosolic acyl coenzyme A thioester hydrolase                                | BACH        |   | + | + |
|51| Myc box-dependent-interacting protein 1                                       | BIN1        | + |   | + |
|52| Carbonic anhydrase 1                                                          | CAH1        | + |   | + |
|53| Carbonic anhydrase 2                                                          | CAH2        | + | + |   |
|54| Cullin-associated NEDD8-dissociated protein 1                                 | CAND1       | + |   | + |
|55| Adenylyl cyclase-associated protein 1                                         | CAP1        | + |   | + |
|56| Cathepsin D                                                                  | CATD        | + | + |   |
|57| F-actin-capping protein subunit alpha-2                                       | CA2A2       | + |   | + |
|58| Carbonyl reductase [NADPH] 1                                                 | CBR1        | + |   | + |
|59| Cell division control protein 42 homolog                                     | CDC42       | + |   |   |
|60| 10 kDa heat shock protein, mitochondrial                                     | CH10        | + |   | + |
|61| Citrate synthase, mitochondrial                                              | CISY        | + | + |   |
|62| Cytosolic non-specific dipeptidase                                             | CNDP2       | + |   | + |
|63| CB1 cannabinoid receptor-interacting protein 1                               | CNRP1       | + |   | + |
|64| Contactin-1                                                                  | CNTN1       | + |   |   |
|65| Cofilin-1                                                                    | COF1        | + | + |   |
|66| Copine-5                                                                     | CPNE5       | + | + |   |
|67| Cytochrome c                                                                 | CYC         | + | + |   |
|68| 2,4-dienoyl-CoA reductase, mitochondrial                                     | DECR        | + | + |   |
| 69 | Glutamate dehydrogenase 1, mitochondrial | DHE3 | + | + | + | + |
| 70 | Dihydropteridine reductase | DHPR | + |
| 71 | Dihydrolipoyl dehydrogenase, mitochondrial | DLDH | + | + | + |
| 72 | D-3-dopachrome decarboxylase | DOPD | + | + |
| 73 | Dihydropterymidinase-related protein 1 | DPYL1 | + |
| 74 | Dihydropterymidinase-related protein 3 | DPYL3 | + | + |
| 75 | Dihydropterymidinase-related protein 5 | DPYL5 | + | + |
| 76 | Dynactin light chain 2, cytoplasmic | DYL2 | + | + |
| 77 | Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial | ECH1 | + |
| 78 | Enoyl-CoA hydratase, mitochondrial | ECHM | + | + | + | + |
| 79 | Enoyl-CoA delta isomerase 1, mitochondrial | ECT1 | + | + |
| 80 | Elongation factor 1-gamma | EFG1 | + | + |
| 81 | Alpha-enolase | ENOA | + | + |
| 82 | Enolase-phosphatase E1 | ENOPH | + | + |
| 83 | S-formylglutathione hydrolase | ESTD | + | + |
| 84 | Electron transfer flavoprotein subunit alpha, mitochondrial | ETFA | + | + |
| 85 | Ezrin | EZRI | + | + | + |
| 86 | Hsc70-interacting protein | F10A1 | + | + | + |
| 87 | Protein FAM49B | FA49B | + | + | + |
| 88 | Fatty acid-binding protein, heart | FABPH | + | + |
| 89 | Acylpyruvase FAHD1, mitochondrial | FAHD1 | + | + |
| 90 | Fibrinogen beta chain | FIBB | + | + |
| 91 | Fibrinogen gamma chain | FIBG | + | + |
| 92 | Filaggrin | FILA | + |
| 93 | Ferritin heavy chain | FRH | + | + | + |
| 94 | Ferritin light chain | FRIL | + | + |
| 95 | Fumarate hydratase, mitochondrial | FUMH | + | + |
| 96 | Glucose-6-phosphate isomerase | G6PI | + | + |
| 97 | 4-aminobutyrate aminotransferase, mitochondrial | GABT | + | + | + |
| 98 | Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-1 | GBB1 | + | + |
| 99 | Rab GDP dissociation inhibitor alpha | GDIA | + | + | + |
| 100 | Rab GDP dissociation inhibitor beta | GDIB | + | + | + | + |
| 101 | Rho GDP-dissociation inhibitor 1 | GDIR1 | + | + |
| 102 | Gelsolin | GELS | + | + |
|   | Protein Name                                    | Initials |   |   |   |
|---|------------------------------------------------|----------|---|---|---|
|103| Gamma-glutamylcyclotransferase                  | GGCT     |   |   |   |
|104| Glutamine synthetase                            | GLNA     | + | + | + |
|105| Glyoxalase domain-containing protein 4          | GLOD4    | + | + | + |
|106| Neuronal membrane glycoprotein M6-a             | GPM6A    | + | + | + |
|107| Stress-70 protein, mitochondrial                | GRP75    | + | + | + |
|108| Glutathione S-transferase Mu 1                  | GSTM1    | + | + | + |
|109| Glutathione S-transferase Mu 2                  | GSTM2    | + | + | + |
|110| Glutathione S-transferase Mu 3                  | GSTM3    | + | + | + |
|111| Glutathione S-transferase omega-1               | GSTO1    | + | + | + |
|112| Glutathione S-transferase P                     | GSTP1    | + | + | + |
|113| Guanine deaminase                               | GUAD     | + | + | + |
|114| Haloacid dehalogenase-like hydrolase domain-containing protein 2 | HDHD2 | + | + | + |
|115| Heterogeneous nuclear ribonucleoprotein D0      | HNRPD    |   |   |   |
|116| Heterogeneous nuclear ribonucleoprotein K       | HNRPK    | + | + | + |
|117| Hyaluronan and proteoglycan link protein 1      | HPLN1    | + | + | + |
|118| Hypoxanthine-guanine phosphoribosyltransferase  | HPRT     | + | + | + | + |
|119| Haptoglobin                                    | HPT      | + | + | + |
|120| Heat shock protein 105 kDa                     | HS105    | + | + | + |
|121| Heat shock protein HSP 90-alpha                 | HS90A    | + | + | + |
|122| Heat shock protein HSP 90-beta                  | HS90B    | + | + | + |
|123| Heat shock 70 kDa protein 4                     | HSP74    | + | + | + |
|124| Hexokinase-1                                    | HXK1     | + | + | + |
|125| Immunoglobulin gamma-1 heavy chain              | IGG1     | + | + | + | + |
|126| Immunoglobulin heavy constant alpha 1           | IGHA1    | + | + | + |
|127| Immunoglobulin heavy constant gamma 2           | IGHG2    | + | + | + |
|128| Immunoglobulin heavy constant gamma 3           | IGHG3    | + | + | + | + |
|129| Immunoglobulin heavy constant gamma 4           | IGHG4    | + | + | + | + |
|130| Immunoglobulin kappa constant                   | IGKC     | + | + | + | + |
|131| Inositol monophosphatase 1                      | IMPA1    | + | + | + |
|132| GTP:AMP phosphotransferase AK3, mitochondrial   | KAD3     | + | + | + |
|133| Pyruvate kinase PKM                             | KPYM     | + | + | + |
|134| LanC-like protein 1                             | LANC1    | + | + | + | + |
|135| Galectin-1                                      | LEG1     | + | + | + |
|136| Malate dehydrogenase, cytoplasmic               | MDHC     | + | + | + |
|   | Protein/Enzyme Name                      | Gene Symbol |   |   |   |
|---|----------------------------------------|-------------|---|---|---|
| 137 | Malate dehydrogenase, mitochondrial     | MDHM        |   |   | + |
| 138 | Mitogen-activated protein kinase 1      | MK01        | + |   |   |
| 139 | Methylmalonate-semialdehyde dehydrogenase [acylating], mitochondrial | MMSA        | + |   | + |
| 140 | Moesin                                  | MOES        | + | + |   |
| 141 | NAD kinase 2, mitochondrial             | NAKD2       | + |   | + |
| 142 | Neural cell adhesion molecule 1         | NCAM1       |   |   | + |
| 143 | Neurocan core protein                   | NCAN        | + | + | + |
| 144 | Neurochondrin                           | NCDN        | + | + | + |
| 145 | Neurofascin                             | NFASC       |   |   | + |
| 146 | NAD(P)H-hydrate epimerase               | NNRE        | + |   | + |
| 147 | Neuronal cell adhesion molecule         | NRCAM       | + |   | + |
| 148 | Protein/nucleic acid deglycase DJ-1     | PARK7       | + | + | + |
| 149 | Poly(rC)-binding protein 2              | PCBP2       | + |   | + |
| 150 | Protein disulfide-isomerase             | PDIa1       | + | + | + |
| 151 | Protein disulfide-isomerase A6          | PDIa6       | + | + |   |
| 152 | ATP-dependent 6-phosphofructokinase, muscle type | PFKAM       | + | + | + |
| 153 | Phosphoglycerate mutase 1               | PGAM1       |   |   | + |
| 154 | Brevican core protein                   | PGCB        | + | + | + |
| 155 | Phosphoglycerate kinase 1               | PGK1        | + |   | + |
| 156 | Phosphoglucomutase-1                    | PGM1        | + | + | + |
| 157 | Protein-L-isooaspartate(D-aspartate) O-methyltransferase | PIMT       | + | + | + |
| 158 | Junction plakoglobin                    | PLAK        |   |   | + |
| 159 | Pyridoxal phosphate phosphatase          | PLPP        |   |   | + |
| 160 | Protein phosphatase 1 regulatory subunit 7 | PP1R7       | + |   | + |
| 161 | Serine/threonine-protein phosphatase 2A catalytic subunit alpha isoform | PP2AA | + |   | + |
| 162 | Serine/threonine-protein phosphatase 2B catalytic subunit alpha isoform | PP2BA | + | + | + |
| 163 | Serine/threonine-protein phosphatase 5  | PPP5        | + | + | + |
| 164 | Palmitoyl-protein thioesterase 1        | PPT1        | + |   |   |
| 165 | Peroxiredoxin-1                         | PRDX1       | + |   | + |
| 166 | Peroxiredoxin-2                         | PRDX2       | + |   | + |
| 167 | Peroxiredoxin-5, mitochondrial          | PRDX5       | + |   | + |
| 168 | Peroxiredoxin-6                         | PRDX6       | + | + | + |
| 169 | Profilin-1                              | PROF1       | + | + | + |
| 170 | Profilin-2                              | PROF2       | + | + | + |
|   | Description                                                                 | Symbol |   |   |   |
|---|----------------------------------------------------------------------------|--------|---|---|---|
|171| Puromycin-sensitive aminopeptidase                                           | PSA    | + | + | + |
|172| Proteasome subunit alpha type-4                                              | PSA4   | + | + | + |
|173| Proteasome subunit alpha type-6                                              | PSA6   | + |   |   |
|174| Proteasome subunit alpha type-7                                              | PSA7   | + | + | + |
|175| Proteasome subunit beta type-4                                               | PSB4   | + |   |   |
|176| Proteasome subunit beta type-6                                               | PSB6   | + |   |   |
|177| Prostaglandin-H2 D-isomerase                                                 | PTGDS  | + | + | + |
|178| Receptor-type tyrosine-protein phosphatase zeta                              | PTPRZ  | + | + | + |
|179| Multifunctional protein ADE2                                                 | PUR6   | + | + | + |
|180| Quinone oxidoreductase                                                       | QOR    | + |   |   |
|181| Ras-related protein Rab-2A                                                   | RAB2A  | + |   |   |
|182| Ras-related protein Rab-5A                                                   | RAB5A  | + | + | + |
|183| Ras-related protein Rab-5B                                                   | RAB5B  | + |   |   |
|184| Ras-related protein Rab-5C                                                   | RAB5C  | + |   |   |
|185| Ras-related protein Rab-7a                                                   | RAB7A  | + | + | + |
|186| Ras-related C3 botulinum toxin substrate 1                                  | RAC1   | + | + | + |
|187| Radixin                                                                    | RAD1   | + | + | + |
|188| GTP-binding nuclear protein Ran                                              | RAN    | + |   |   |
|189| Transforming protein RhoA                                                    | RHOA   | + |   |   |
|190| 2-iminobutanooate/2-iminopropanoate deaminase                               | RIDA   | + | + | + |
|191| 40S ribosomal protein S16                                                    | RS16   | + |   |   |
|192| Reticulon-1                                                                 | RTN1   | + |   |   |
|193| U2 small nuclear ribonucleoprotein B"                                      | RU2B   | + |   |   |
|194| Adenosylhomocysteinase                                                       | SAHH   | + | + | + |
|195| S-adenosylhomocysteine hydrolase-like protein 1                             | SAHH2  | + | + | + |
|196| Selenium-binding protein 1                                                   | SBP1   | + | + | + |
|197| Septin-11                                                                   | Septin-11 | + | + | + |
|198| Septin-2                                                                    | Septin-2 | + | + | + |
|199| Phosphoserine aminotransferase                                              | SERC   | + |   |   |
|200| Endophilin-A1                                                               | SH3G2  | + | + | + |
|201| Superoxide dismutase [Cu-Zn]                                                 | SODC   | + |   |   |
|202| Superoxide dismutase [Mn], mitochondrial                                    | SODM   | + | + | + |
|203| Serpin B3                                                                   | SPB3   | + |   |   |
|204| Spectrin beta chain, non-erythrocytic 1                                     | SPTB2  | + | + | + |
|205| Spectrin alpha chain, non-erythrocytic 1                                    | SPTN1  | + |   |   |
|206| Single-stranded DNA-binding protein, mitochondrial                          | SSBP   | + |   |   |
| Row | Gene Name | Protein Name | Description | Symbol |
|-----|-----------|--------------|-------------|--------|
| 207 | Succinate-semialdehyde dehydrogenase, mitochondrial | SSDH | + | + | + |
| 208 | Stress-induced-phosphoprotein 1 | STIP1 | + |  |
| 209 | Syntaxin-1B | STX1B | + |  |
| 210 | Synapsin-2 | SYN2 | + |  |
| 211 | Transgelin-3 | TAGL3 | + | + | + |
| 212 | Transaldolase | TALDO | + |  |
| 213 | T-complex protein 1 subunit theta | TCPQ | + |  |
| 214 | Tenascin-R | TENR |  |  |
| 215 | Transitional endoplasmic reticulum ATPase | TERA | + |  |
| 216 | Acetyl-CoA acetyltransferase, mitochondrial | THIL | + |  |
| 217 | Thy-1 membrane glycoprotein | THY1 | + | + | + |
| 218 | Transketolase | TKT | + | + | + |
| 219 | Triosephosphate isomerase | TPIS | + | + |  |
| 220 | Serotransferrin | TRFE | + |  |
| 221 | Ubiquitin-conjugating enzyme E2 variant 2 | UB2V2 | + |  |
| 222 | Polyubiquitin-B | UBB | + | + | + |
| 223 | UTP--glucose-1-phosphate uridylyltransferase | UGPA | + |  |
| 224 | V-type proton ATPase catalytic subunit A | VATA | + | + | + |
| 225 | V-type proton ATPase subunit B, brain isoform | VATB2 | + |  |
| 226 | V-type proton ATPase subunit E 1 | VATE1 | + | + | + |
| 227 | V-type proton ATPase subunit H | VATH |  | + |
| 228 | Visinin-like protein 1 | VISL1 |  | + | + |
| 229 | 14-3-3 protein epsilon | 1433E | + | + | + |
| 230 | 14-3-3 protein eta | 1433F | + |  |
| 231 | Serum albumin | ALBU | + |  |
| 232 | Plasma membrane calcium-transporting ATPase 2 | AT2B2 | + | + | + |
| 233 | Cell adhesion molecule 2 | CADM2 | + | + | + |
| 234 | Cell adhesion molecule 3 | CADM3 | + |  |
| 235 | Cell cycle exit and neuronal differentiation protein 1 | CEND | + | + | + |
| 236 | Hydroxycarboxyl glutathione hydrolase, mitochondrial | GLO2 | + |  |
| 237 | Microtubule-associated protein 1B | MAP1B |  | + |
| 238 | MARCKS-related protein | MRP | + | + | + |
| 239 | Metallothionein-2 | MT2 | + | + | + |
| 240 | Metallothionein-3 | MT3 | + | + | + |
| 241 | Neurogranin | NEUG | + |  |
| 242 | Neuroplastin | NPTN | + | + | + |
| 243 | Oxidation resistance protein 1 | OXR1 | + |  |
| 244 | ProSAAS | PCSK1 |  | + |  |
|   |   |   |   |
|---|---|---|---|
| 245 | Synaptotagin-1 | SYNJ1 | + |
| 246 | Alpha-synuclein | SYUA | + |
| 247 | Ubiquitin-like modifier-activating enzyme 1 | UBA1 | + |
| 248 | Aspartate aminotransferase, mitochondrial | AATM | + + |
| 249 | L-aminoacipate-semialdehyde dehydrogenase-phosphopantetheinyl transferase | ADPPT | + |
| 250 | ADP/ATP translocate 1 | ADT1 | + |
| 251 | Amine oxidase [flavin-containing] A | AOFA | + |
| 252 | Amine oxidase [flavin-containing] B | AOFB | + + + |
| 253 | Actin-related protein 2/3 complex subunit 1A | ARC1A | + |
| 254 | Acid ceramidase | ASAH1 | + |
| 255 | Sodium/potassium-transporting ATPase subunit alpha-3 | AT1A3 | + |
| 256 | Sodium/potassium-transporting ATPase subunit beta-2 | AT1B2 | + |
| 257 | ATP synthase F(0) complex subunit B1, mitochondrial | AT5F1 | + |
| 258 | ATP synthase subunit d, mitochondrial | ATP5H | + + + |
| 259 | ATP synthase-coupling factor 6, mitochondrial | ATP5J | + + + |
| 260 | ATP synthase subunit g, mitochondrial | ATP5L | + + + |
| 261 | ATP synthase subunit O, mitochondrial | ATPO | + + |
| 262 | Biliverdin reductase A | BIEA | + |
| 263 | Calmodulin-1 | CALM1 | + + |
| 264 | Catalase | CATA | + |
| 265 | CD81 antigen | CD81 | + + + |
| 266 | CDGSH iron-sulfur domain-containing protein 1 | CISD1 | + + + |
| 267 | Clusterin | CLUS | + |
| 268 | Cofilin-2 | COF2 | + + |
| 269 | Lambda-crystallin homolog | CRYL1 | + |
| 270 | Ketimine reductase mu-crystallin | CRYM | + |
| 271 | Versican core protein | CSPG2 | + |
| 272 | Cysteine and glycine-rich protein 1 | CSR1P1 | + |
| 273 | Excitatory amino acid transporter 1 | EAA1 | + + + |
| 274 | Excitatory amino acid transporter 2 | EAA2 | + |
| 275 | Electron transfer flavoprotein subunit beta | ETFB | + |
| 276 | Fatty acid-binding protein, epidermal | FABP5 | + |
| 277 | Growth arrest-specific protein 7 | GAS7 | + |
|    |                  |                  |    |
|----|-----------------|-----------------|----|
| 278 | Glial fibrillary acidic protein | GFAP            | +  |
| 279 | 78 kDa glucose-regulated protein | GRP78           | +  |
| 280 | Very-long-chain (3R)-3-hydroxyacyl-CoA dehydratase 3 | HACD3           | +  |
| 281 | Hepatocyte cell adhesion molecule | HECAM           | +  |
| 282 | Delta-aminolevulinic acid dehydratase 1A | HEM2            |    |
| 283 | Heat shock 70 kDa protein 1A | HS71A           | +  |
| 284 | Heat shock-related 70 kDa protein 2 | HSP72           | +  |
| 285 | Heat shock cognate 71 kDa protein | HSP7C           | +  |
| 286 | Isocitrate dehydrogenase [NADP] cytoplasmic | IDHC            | +  |
| 287 | Immunoglobulin lambda constant 2 | IGLC2           | +  |
| 288 | Immunoglobulin superfamily member 8 | IGSF8           | +  |
| 289 | LIM and SH3 domain protein 1 | LASP1           | +  |
| 290 | Myelin-associated glycoprotein | MAG             | +  |
| 291 | Microtubule-associated protein 6 | MAP6            | +  |
| 292 | Myristoylated alanine-rich C-kinase substrate | MARCS           | +  |
| 293 | Myelin basic protein | MBP             | +  |
| 294 | Macrophage migration inhibitory factor | MIF             | +  |
| 295 | Myelin-oligodendrocyte glycoprotein | MOG             | +  |
| 296 | Metallothionein-1F | MT1F            | +  |
| 297 | Myotrophin | MTPN            | +  |
| 298 | Myelin proteolipid protein | MYPR            | +  |
| 299 | Protein NDRG1 | NDRG1           |    |
| 300 | Protein NDRG2 | NDRG2           |    |
| 301 | Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex, mitochondrial | ODO2            | +  |
| 302 | Platelet-activating factor acetylhydrolase IB subunit beta | PA1B2           | +  |
| 303 | Programmed cell death 6-interacting protein | PDC6I           | +  |
| 304 | Phosphatidylethanolamine-binding protein 1 | PEBP1           | +  |
| 305 | Phosphatidylinositol-binding clathrin assembly protein | PICAL           | +  |
| 306 | Phosphatidylinositol transfer protein alpha isoform | PIPNA           | +  |
| 307 | Plectin | PLEC            | +  |
| 308 | Serine/threonine-protein ph | PP1G            | +  |
| No. | Gene Name                                      | Protein Function                                    | Symbol  | +
|-----|-----------------------------------------------|-----------------------------------------------------|---------|---
| 309 | Peptidyl-prolyl cis-trans isomerase A          |                                                     | PPIA    | +  
| 310 | Peptidyl-prolyl cis-trans isomerase B          |                                                     | PPIB    | +  
| 311 | PRA1 family protein 3                         |                                                     | PRAF3   | +  
| 312 | Proline-rich transmembrane protein 2           |                                                     | PRRT2   | +  
| 313 | Proteasome subunit alpha type-3                |                                                     | PSA3    | +  
| 314 | Prothymosin alpha                              |                                                     | PTMA    | +  
| 315 | Glycogen phosphorylase, brain form             |                                                     | PYGB    | +  
| 316 | Cytochrome b-c1 complex subunit 1, mitochondrial|                                                     | QCR1    | +  
| 317 | UV excision repair protein RAD23 homolog B     |                                                     | RD23B   | +  
| 318 | Protein S100-B                                 |                                                     | S100B   | +  
| 319 | Protein S100-A1                                |                                                     | S10A1   | +  
| 320 | Neutral amino acid transporter A               |                                                     | SATT    | +  
| 321 | Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial | | SDHA    | +  
| 322 | SH3 domain-binding glutamic acid-rich-like protein |                                                     | SH3L1   | +  
| 323 | Tyrosine-protein phosphatase non-receptor type substrate 1 | | SHPS1   | +  
| 324 | Beta-soluble NSF attachment protein            |                                                     | SNAB    | +  
| 325 | Synaptogyrin-3                                 |                                                     | SNG3    | +  
| 326 | Serpin B6                                     |                                                     | SPB6    | +  
| 327 | Syntaxin-12                                    |                                                     | STX12   | +  
| 328 | Synaptotagmin-1                                |                                                     | SYT1    | +  
| 329 | Transcription elongation factor A protein-like 3 |                                                     | TCAL3   | +  
| 330 | Toll-interacting protein                       |                                                     | TOLIP   | +  
| 331 | Thioredoxin-like protein 1                     |                                                     | TXNL1   | +  
| 332 | Thymosin beta-10                               |                                                     | TYB10   | +  
| 333 | Thymosin beta-4                                |                                                     | TYB4    | +  
| 334 | Ubiquitin-conjugating enzyme E2 L3             |                                                     | UB2L3   | +  
| 335 | Ubiquitin-conjugating enzyme E2 N              |                                                     | UBE2N   | +  
| 336 | Up-regulated during skeletal muscle growth protein 5 | | USMG5   | +  
| 337 | Vesicle-associated membrane protein 2          |                                                     | VAMP2   | +  
| 338 | Voltage-dependent anion-selective channel protein 2 | | VDAC2   | +  


Annexure

Uncropped blots

**Fig. 5a uncropped blots**: Additional bands for SFPQ: We are unsure as to the identity of these extra bands. For reference abcam image has been displayed showing additional bands.

**Fig. 7f uncropped blots**: For TIA-1, two banding patterns have been reported, in 12 % gels, a double band pattern and in gradient gels (4-12 %), a single band pattern. We have run TIA-1 in both gradient (**Gel 1**, representative blot in the Manuscript) and in 12% gel (**Gel 2**) for confirmation. Abcam images for the antibody are also displayed on the right side. **Gel 3**: Tau-5 antibody, Tau-5 detects total tau both phosphorylated and unphosphorylated form of tau protein. Different isoforms of tau are reported between 75-50 kDa and tau cleavage products below 50 kDa. Star * represents high molecular weight phosphorylated oligomeric species of tau as Tau-5 also detects phosphorylated tau.
Fig. 8d uncropped blots: Additional bands for SFPQ: We are unsure as to the identity of these extra bands. For reference abcam image has been attached.

Fig. 9 uncropped blots: Representative immunoblot images for tau, p-tau, SFPQ and TIA-1 after transient transfection of WT-tau or P301L-tau (0N4R) in HeLa cells. All bands for tau and its phosphorylated form were cut and identified by Mass spectrometry to confirm the identification of Tau after Transfection.
**Fig. 11a uncropped blots:** Representative full blots and reference blots of corresponding antibodies are displayed. For TIA-1 (N-terminal), 3 different gels have been displayed. We are unsure of these additional bands which are appearing with TIA-1 (N-terminal).

**Supplementary Fig. 2a uncropped blot:** Representative full blots, For TIA-1 a typical double band pattern was observed. For SFPQ, **Gel_1**: As the expression of SFPQ was very low in particularly MM1 and VV2, and bands were visible only in controls (refer to arrows in Gel-1). Another gel is displayed (Gel-2), where concentration of secondary antibody was increased to enhance detection of SFPQ, which has resulted in high background bands. A third gel (Gel-3) is displayed as well for reference, where upper part of the membrane was probed with SFPQ to increase specificity, showing a good expression of SFPQ.