

SUPPLEMENTARY MATERIAL

Human-specific genomic variants associated with protein-coding genes suggest significant brain, immune and metabolic evolution.

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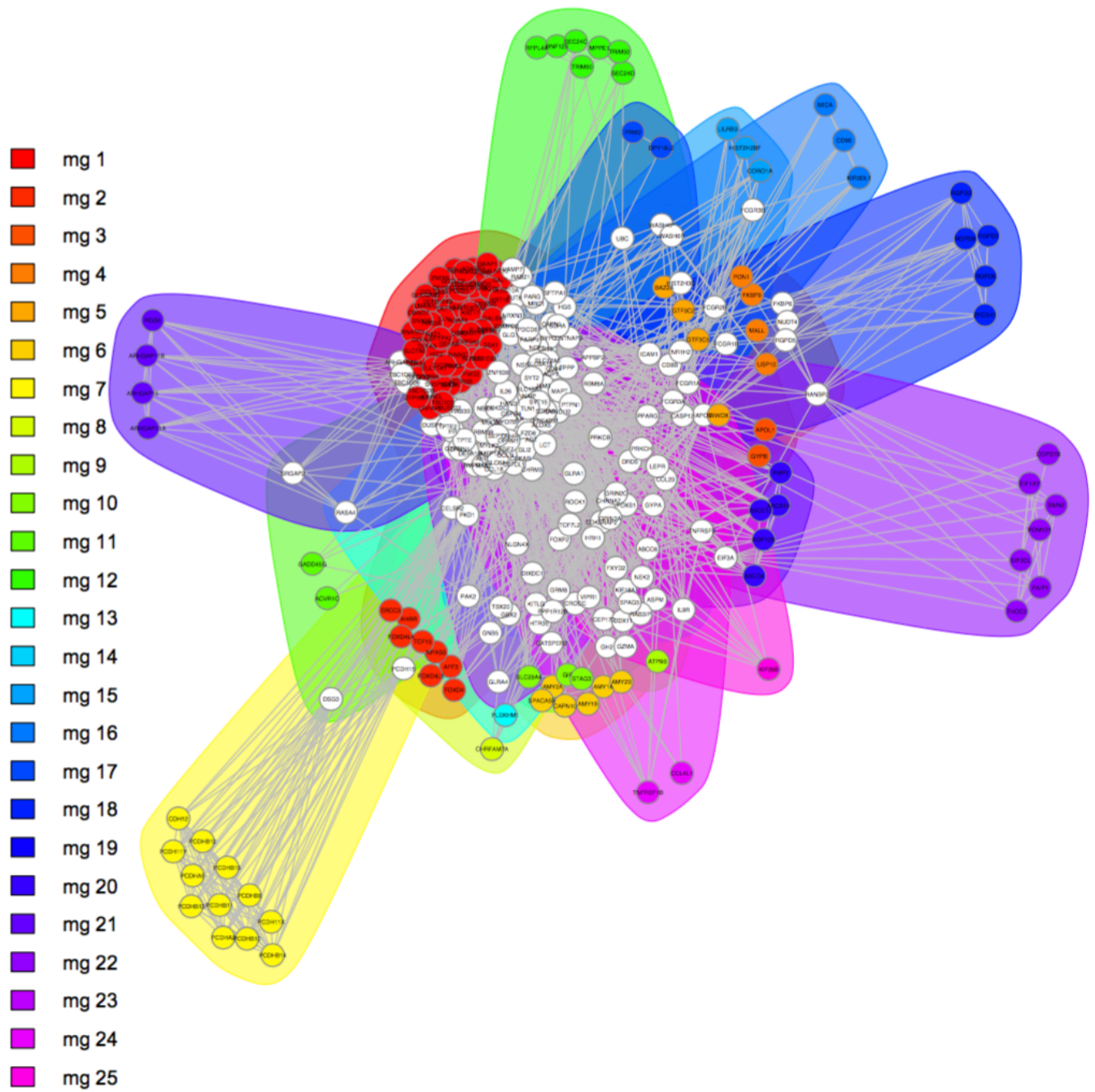
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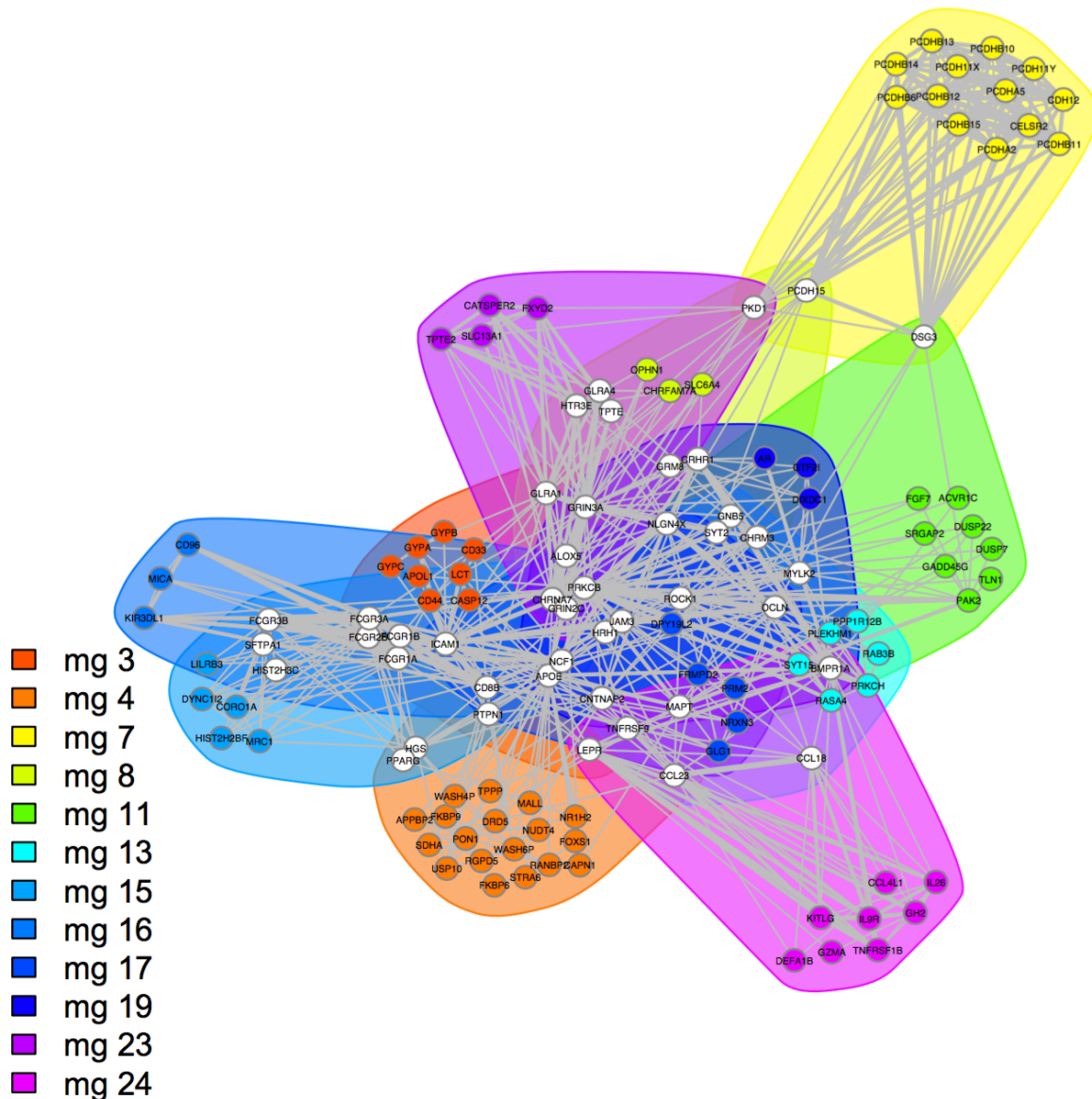
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Supplementary Figure 1 – Functional Networks of Genes with Human-Specific Features

A



B



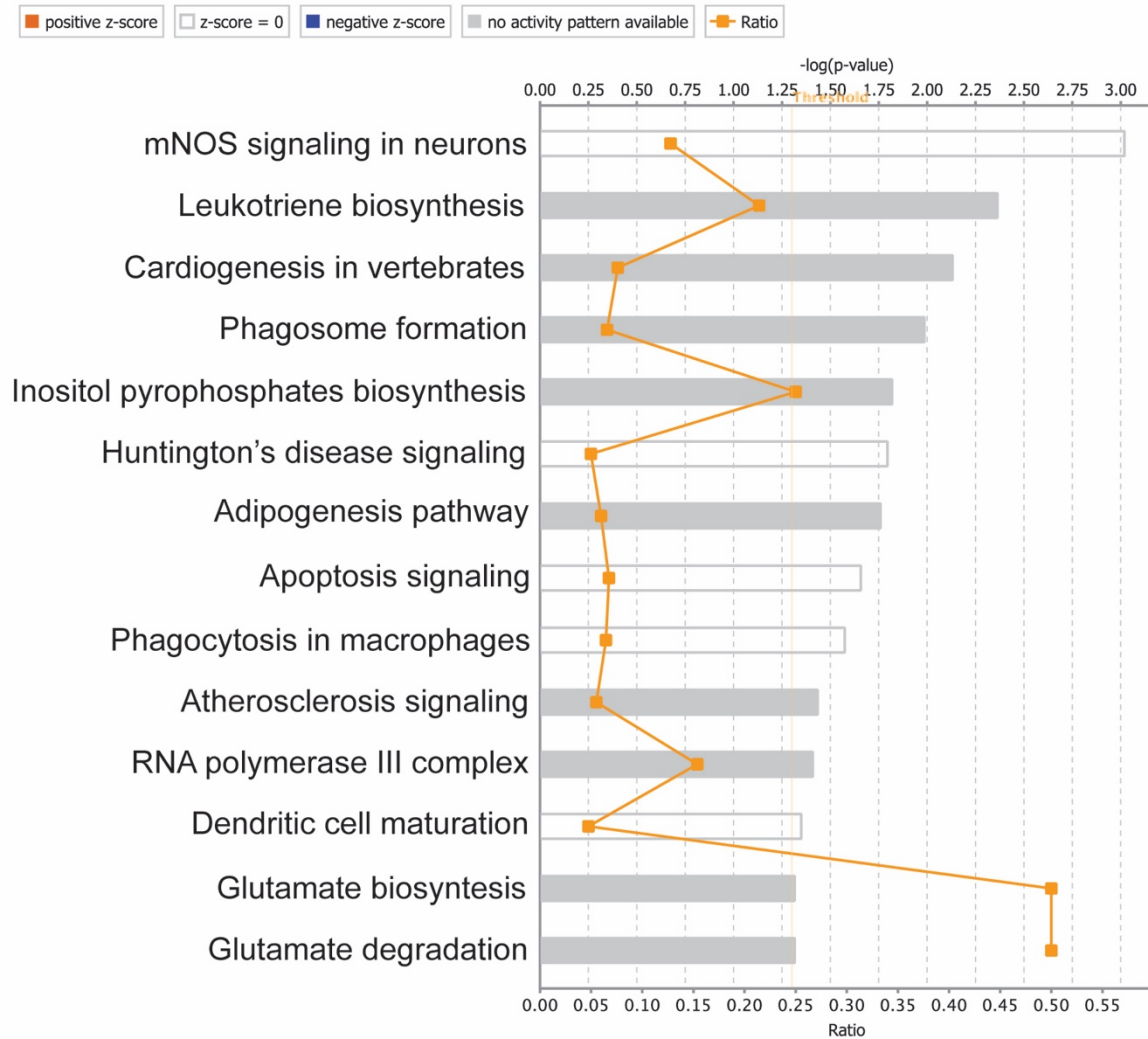
Supplementary Figure 1:

These functional networks describe the set of genes with human-specific features. The network outputs were generated with FGNet to represent the metagroups defined with GeneTerm Linker. Individual files are provided to allow assessment of gene names and network topology. **A)** From a total of 25 metagroups (clusters of associated genes with coherent biological significance), 2 were filtered out for not meeting the parameters for measuring relevance, in terms of significance and coherence. The remaining 23 metagroups represent 225 genes and many different functions, including neuronal, metabolic and immunological. Metagroups are color-coded and their full description is given in the Supplementary Table 3. Gene names and network topology can be better visualized when magnified. White circles denote genes shared by multiple metagroups.

B) The full network described in Figure 1A was filtered to allow for a figure within the main manuscript. This is the higher-resolution version of the manuscript Figure 1B. The color-code and numbering of metagroups was maintained to allow comparison between figures. Metagroups are color-coded and their full description is given in the Supplementary Table 3. Gene names and network topology can be better visualized when magnified.

Supplementary Figure 2 – Pathway Analysis of Genes with Human-Specific Features

A



B

Physiological System Development and Function

| Name | p-value range | Molecules |
|---|----------------------|-----------|
| Nervous System Development and Function | 7.36E-03 - 9.30E-07 | 71 |
| Digestive System Development and Function | 7.84E-03 - 4.340E-06 | 33 |
| Hepatic System Development and Function | 7.74E-03 - 4.34E-06 | 20 |
| Organ Development | 7.74E-03 - 4.34E-06 | 31 |
| Tissue Morphology | 8.40E-03 - 2.30E-05 | 58 |

Supplementary Figure 2:

The Ingenuity Pathway Analysis (IPA) is an additional tool for functional analysis of high-throughput sequencing data. In this figure we present results generated using IPA for the set of genes with human-specific features. This result includes >85% of the 845 genes in the dataset and describes these in terms of the pathways in which they function.

A) The plot presents category scores. The "threshold" line (vertical line in light orange, set

here to 1.25) indicates the minimum significance level in terms of inverse logarithmic p-values [-log(p-value)] derived from performing a Fisher's exact test. The proportion of genes in the dataset that map to each pathway in the IPA knowledgebase is represented as the "ratio" (line in darker orange). The z-score is color-coded and refers to the difference between observed and predicted up/down regulation states of pathways.

B) The table shows higher-order functional classes with their respective significance (p-values) and the number of genes (molecules) by which they are composed.

Supplementary Table 1 – Genes with Human-Specific Features

| A | B | C | D | E | F | G | H |
|-------------|--------------|------------|-----------------------------|-------------------|---|---|--------------|
| Gene Name | Ensembl ID | Chromosome | Gene Type | General Gene Type | Mechanism of Origin | General Mechanism of Origin | Reference(s) |
| AATBC | ENSG0000021 | | antisense | long non-coding | hominoid-specific de novo originated protein-coding gene | de novo origin | 1 |
| ABC10 | ENSG0000011 | | protein_coding | protein-coding | human-specific gene amplification | gene amplification | 2,3 |
| ABCC12 | ENSG00000116 | | protein_coding | protein-coding | modern human-specific coding change | gene sequence alteration | 4 |
| ABCC6 | ENSG00000016 | | protein_coding | protein-coding | human-specific gene duplication or expansion | gene amplification | 5 |
| ABCD1P2 | ENSG00000210 | | unprocessed_pseudogene | pseudogene | human-specific gene | human-specific gene (undefined feature) | 6 |
| ABCD1P5 | ENSG0000022 | | unprocessed_pseudogene | pseudogene | human-specific gene | human-specific gene (undefined feature) | 6 |
| ABCD4 | ENSG00000114 | | protein_coding | protein-coding | modern human-specific stop loss generating NMD transcript | gene structure alteration | 4 |
| ABHD17A | ENSG00000119 | | protein_coding | protein-coding | human-specific gene duplication | gene amplification | 7 |
| ABHD17AP1 | ENSG0000011 | | unprocessed_pseudogene | pseudogene | human-specific gene | human-specific gene (undefined feature) | 6 |
| AC005042.4 | ENSG0000022 | | antisense | long non-coding | human-specific de novo originated protein-coding gene | de novo origin | 8 |
| AC005488.1 | ENSG0000027 | | unprocessed_pseudogene | pseudogene | human-specific gene | human-specific gene (undefined feature) | 6 |
| AC008132.1 | ENSG00000122 | | transcribed_unprocessed_pse | pseudogene | human-specific gene | human-specific gene (undefined feature) | 6 |
| AC008132.1 | ENSG00000122 | | lincRNA | long non-coding | human-specific gene | human-specific gene (undefined feature) | 6 |
| AC026271.5 | ENSG00000117 | | processed_pseudogene | pseudogene | human-specific gene | human-specific gene (undefined feature) | 6 |
| AC027612.6 | ENSG0000012 | | transcribed_unprocessed_pse | pseudogene | human-specific gene | human-specific gene (undefined feature) | 6 |
| AC062028.1 | ENSG0000012 | | lincRNA | long non-coding | hominoid-specific de novo originated protein-coding gene | de novo origin | 1 |
| AC083899.3 | ENSG0000022 | | unprocessed_pseudogene | pseudogene | human-specific gene | human-specific gene (undefined feature) | 6 |
| AC096670.3 | ENSG0000022 | | antisense | long non-coding | human-specific de novo originated protein-coding gene | de novo origin | 8 |
| AC111200.7 | ENSG0000022 | | processed_pseudogene | pseudogene | human-specific gene duplication | gene amplification | 7 |
| AC129778.2 | ENSG0000019 | | lincRNA | long non-coding | human-specific gene | human-specific gene (undefined feature) | 6 |
| AC138969.4 | ENSG00000116 | | protein_coding | protein-coding | human-specific gene | human-specific gene (undefined feature) | 6 |
| ACTR3B | ENSG0000017 | | protein_coding | protein-coding | human-specific gene duplication | gene amplification | 9 |
| ACVR1C | ENSG0000012 | | protein_coding | protein-coding | human-specific inactivation by retrotransposon insertion | gene loss | 10 |
| ADARB1 | ENSG00000121 | | protein_coding | protein-coding | human-specific exon gain | gene structure alteration | 11,12 |
| ADORA2A-AS1 | ENSG00000122 | | antisense | long non-coding | hominoid-specific de novo originated protein-coding gene | de novo origin | 13,1 |
| AFF3 | ENSG0000012 | | protein_coding | protein-coding | human-specific gene duplication | gene amplification | 9 |
| AGR3 | ENSG0000017 | | protein_coding | protein-coding | human-specific gene amplification | gene amplification | 47 |
| AGAP1 | ENSG0000012 | | protein_coding | protein-coding | flanking human accelerated region | regulatory region alteration | 14 |
| AGT | ENSG0000011 | | protein_coding | protein-coding | human-specific derived allele | human-specific gene (undefined feature) | 15 |
| AH9 | ENSG0000016 | | protein_coding | protein-coding | human-specific accelerated evolution | gene sequence alteration | 16,17 |
| AHRR | ENSG0000005 | | protein_coding | protein-coding | human-specific gene duplication | gene amplification | 9 |
| AL592528.1 | ENSG0000021 | | antisense | long non-coding | human-specific de novo originated protein-coding gene | de novo origin | 8 |
| AL772307.1 | ENSG0000019 | | processed_pseudogene | pseudogene | human-specific gene | human-specific gene (undefined feature) | 6 |

Supplementary Table 1:

The screenshot above represents the first lines of the table. The full version is given as an independent Supplementary Table in xls format. This file contains all 845 genes with human-specific features retrieved in this study (**Sheet 1** - "HumanSpecific genes") and describes for each gene its: (A) Gene name (updated to the current Ensembl description, when necessary); (B) Ensembl ID; (C) Chromosome number; (D) Gene type (the specific type, as described by Ensembl); (E) General gene type (a general classification which may group multiple gene types - e.g. pseudogenes includes processed, unprocessed and transcribed pseudogenes); (F) Mechanism of origin (specifically as described by the author of the correspondent reference); (G) General mechanism of origin (a manually assigned general classification which may group multiple subclasses from column (F) - data from this column was used to generate the pie chart presented in Figure 1A in the main manuscript) and (H) At least one reference in which the gene is reported (the full list of references, numbered accordingly, is given as **Sheet 2** - "References"). The file also contains information on 19 large gene families (**Sheet 3** - "HumanSpecific GeneFamilies"), described as undergoing significant expansion or accelerated evolution across all (or many of) its members. These were not included in the main table, mainly to prevent their high gene numbers to introduce a functional bias in the dataset.

Supplementary Table 2 – Genomic Distribution of Genes with Human-Specific Features per Chromosome

| Chromosome | % of protein-coding genes with human-specific features | % of protein-coding genes | P-value |
|------------|--|---------------------------|----------|
| X | 11.41 | 4.15 | 4.50E-06 |
| 7 | 7.72 | 4.86 | 2.40E-03 |
| 5 | 2.85 | 4.36 | 0.012 |
| 15 | 2.52 | 2.99 | 0.013 |
| 10 | 6.38 | 3.6 | 0.016 |
| 8 | 2.68 | 3.31 | 0.041 |
| 2 | 7.55 | 6.38 | 0.1 |
| 16 | 4.70 | 4.27 | 0.11 |
| Y | 4.19 | 0.22 | 0.15 |
| 1 | 5.37 | 10.1 | 0.16 |
| 9 | 5.37 | 3.83 | 0.35 |
| 22 | 2.85 | 2.41 | 0.58 |
| 17 | 1.01 | 5.85 | 0.59 |
| 18 | 2.68 | 1.32 | 0.8 |
| 11 | 4.70 | 6.42 | 0.88 |
| 13 | 5.37 | 1.6 | 0.92 |
| 4 | 5.70 | 3.68 | 0.96 |
| 14 | 1.01 | 4.05 | 0.97 |
| 20 | 3.19 | 2.67 | 0.99 |
| 21 | 1.34 | 1.16 | 0.99 |
| 3 | 0.34 | 5.3 | 1 |
| 6 | 2.35 | 5.13 | 1 |
| 12 | 8.22 | 5.1 | 1 |
| 19 | 0.50 | 7.25 | 1 |

Supplementary Table 2:

This table presents the percentage of protein-coding genes in each chromosome (A), both for the set of genes with human-specific features (B) and the entire set of human proteins retrieved from the Ensembl database (C). A p-value is given (D), generated with a Fisher's exact test to represent the significance of the difference between (B) and (C) per chromosome. Chromosomes X and 7 are clearly enriched in genes with human-specific features and another four (in green) have significantly more of such genes than expected.

Supplementary Table 3 – Description of GeneTerm Linker Metagroups Comprising the Functional Networks on Supplementary Figure 1

| MG | Silhouette | P-value | Genes | Terms / Exclusion criteria |
|----|------------|---------|-------|---|
| 1 | -0.07 | 1.2e-52 | 145 | Filtered out due to a silhouette size <0 |
| 2 | 0.15 | 6.6e-15 | 31 | Blood vessel development (BP) GO Camera-type eye development (BP) GO Cerebellum development (BP) GO DNA bending activity (MF) GO Double-stranded DNA binding (MF) GO Embryonic development (BP) GO Embryonic heart tube development (BP) GO Heart looping (BP) GO Helix-loop-helix DNA-binding domain IPR Negative regulation of transcription factor activity (BP) GO Neural crest cell migration (BP) GO Pattern specification process (BP) GO Patterning of blood vessels (BP) GO Regulation of transcription factor activity (BP) GO Righting reflex (BP) GO RNA polymerase II transcription factor activity, enhancer binding (MF) GO Somitogenesis (BP) GO Transcription factor binding (MF) * GO Transcription factor complex (CC) GO Transcription factor, fork head IPR |
| 3` | 0.00 | 2.6e-12 | 25 | African trypanosomiasis KEGG Cell adhesion molecules (CAMs) * KEGG Cytokine-mediated signaling pathway (BP) GO External side of plasma membrane (CC) * GO Interferon-gamma-mediated signaling pathway (BP) GO Leukocyte migration (BP) GO Leukocyte transendothelial migration * KEGG Malaria KEGG Positive regulation of vasoconstriction (BP) GO Regulation of immune response (BP) * GO Response to ethanol (BP) GO Staphylococcus aureus infection * KEGG Transmembrane receptor activity (MF) GO |
| 4` | 0.13 | 3.1e-12 | 29 | Alzheimer's disease KEGG Artery morphogenesis (BP) GO Cellular calcium ion homeostasis (BP) GO Cholesterol homeostasis (BP) GO Cholesterol metabolic process (BP) GO Early endosome (CC) * GO Intracellular transport (BP) * GO Isomerase activity (MF) GO Lipid homeostasis (BP) GO Microtubule (CC) * GO Peptidyl-prolyl cis-trans isomerase activity (MF) GO Positive regulation of cholesterol efflux (BP) GO Protein folding (BP) GO |
| 5 | 0.20 | 1.7e-11 | 30 | Basal cell carcinoma KEGG Chromatin binding (MF) GO DNA regulatory region binding (MF) GO Drug binding (MF) GO Enzyme binding (MF) GO Nuclear hormone receptor, ligand-binding, core IPR Positive regulation of NF-kappaB transcription factor activity (BP) GO PPAR signaling pathway KEGG Protein dimerization activity (MF) GO Response to cold (BP) GO Steroid hormone receptor IPR Transcription factor binding (MF) * GO Transcription, DNA-dependent (BP) GO Zinc finger, nuclear hormone receptor-type IPR |
| 6 | -0.05 | 8.4e-11 | 31 | Filtered out due to a silhouette size <0 |
| 7` | 0.62 | 2.3e-10 | 16 | Cadherin IPR Calcium-dependent cell-cell adhesion (BP) GO Homophilic cell adhesion (BP) GO Synapse assembly (BP) GO |
| 8` | 0.12 | 3.6e-10 | 19 | Calcium ion transport (BP) GO Calcium signaling pathway * KEGG Extracellular ligand-gated ion channel activity (MF) GO Glutamatergic synapse KEGG Glycine binding (MF) GO |

| | | | | |
|----|------|---------|----|---|
| | | | | <p>Ion channel activity (MF) * GO Memory (BP) GO Neuroactive ligand-receptor interaction * KEGG Neurotransmitter-gated ion-channel IPR Postsynaptic density (CC) GO Postsynaptic membrane (CC) * GO Synapse (CC) GO Transporter activity (MF) * GO</p> |
| 9 | 0.01 | 7.6e-10 | 27 | <p>Activation of phospholipase C activity by G-protein coupled receptor protein signaling pathway coupled to IP3 second messenger (BP) GO External side of plasma membrane (CC) * GO GPCR, family 2-like IPR GPCR, family 2, extracellular hormone receptor domain IPR GPCR, family 2, secretin-like IPR Ion transmembrane transport (BP) * GO Muscle contraction (BP) GO Neuroactive ligand-receptor interaction * KEGG Neuropeptide signaling pathway (BP) GO Postsynaptic membrane (CC) * GO Protein localization (BP) GO Trans-Golgi network (CC) GO</p> |
| 10 | 0.02 | 2.4e-09 | 34 | <p>Actin cytoskeleton (CC) GO Apical plasma membrane (CC) GO Axon terminus (CC) GO Centriole (CC) GO Centrosome (CC) * GO Chromosome (CC) GO Cilium (CC) GO Condensed chromosome kinetochore (CC) GO Hindbrain development (BP) GO Microtubule cytoskeleton (CC) GO Midbody (CC) GO Mitosis (BP) * GO Structural molecule activity (MF) GO</p> |
| 11 | 0.22 | 9.6e-09 | 16 | <p>Axon guidance KEGG Cell structure disassembly during apoptosis (BP) GO Focal adhesion * KEGG MAPK signaling pathway KEGG Regulation of actin cytoskeleton KEGG TGF-beta signaling pathway KEGG</p> |
| 12 | 0.16 | 2.4e-08 | 20 | <p>Antigen processing and presentation of peptide antigen via MHC class I (BP) GO B302/SPRY domain IPR Butyrophilin-like IPR Cellular membrane organization (BP) GO Cellular protein metabolic process (BP) GO Early endosome (CC) * GO Early endosome membrane (CC) GO Endosome transport (BP) GO ER to Golgi vesicle-mediated transport (BP) GO Intracellular membrane-bounded organelle (CC) GO Post-translational protein modification (BP) GO Protein amino acid N-linked glycosylation via asparagine (BP) GO SPla/Ryanodine receptor subgroup IPR SPRY-associated IPR Zinc finger, RING-type IPR</p> |
| 13 | 0.29 | 2.8e-08 | 18 | <p>AGC-kinase, C-terminal IPR C2 calcium-dependent membrane targeting IPR C2 membrane targeting protein IPR C2 region IPR Calcium signaling pathway * KEGG Chemokine signaling pathway KEGG Focal adhesion * KEGG Gastric acid secretion KEGG Leukocyte transendothelial migration * KEGG Protein kinase C-like, phorbol ester/diacylglycerol binding IPR Tight junction * KEGG Vascular smooth muscle contraction KEGG</p> |
| 14 | 0.06 | 1.4e-07 | 15 | <p>External side of plasma membrane (CC) * GO Growth factor activity (MF) GO Hematopoietic cell lineage KEGG Melanogenesis KEGG Ovarian follicle development (BP) GO Positive regulation of peptidyl-tyrosine phosphorylation (BP)</p> |

| | | | | GO |
|---|------|---------|----|--|
| 15` | 0.33 | 1.6e-06 | 17 | Fc gamma R-mediated phagocytosis KEGG IgG binding (MF) GO Leishmaniasis KEGG Natural killer cell mediated cytotoxicity * KEGG Osteoclast differentiation KEGG Phagosome * KEGG Staphylococcus aureus infection * KEGG Systemic lupus erythematosus * KEGG Tuberculosis KEGG |
| 16` | 0.21 | 1.1e-05 | 11 | Natural killer cell mediated cytotoxicity * KEGG Phagosome * KEGG Regulation of immune response (BP) * GO Staphylococcus aureus infection * KEGG Systemic lupus erythematosus * KEGG |
| 17` | 0.29 | 1.2e-05 | 14 | Cell adhesion molecules (CAMs) * KEGG Leukocyte transendothelial migration * KEGG Spermatid development (BP) GO Tight junction * KEGG Tight junction (CC) GO |
| 18 | 0.73 | 2.4e-05 | 11 | GRIP IPR Intracellular transport (BP) * GO Protein targeting to Golgi (BP) GO Ran binding protein 1 IPR Tetratricopeptide repeat IPR Tetratricopeptide repeat-containing IPR |
| 19` | 0.16 | 5e-05 | 13 | Dendrite (CC) GO Neuroactive ligand-receptor interaction * KEGG Neuronal cell body (CC) GO |
| 20 | 0.33 | 0.00018 | 17 | ABC transporter-like IPR ABC transporter, integral membrane type 1 IPR ABC transporters KEGG ATPase activity (MF) GO ATPase activity, coupled to transmembrane movement of substances (MF) GO ATPase, AAA+ type, core IPR Sodium ion transport (BP) GO Transporter activity (MF) * GO |
| 21 | 0.69 | 0.00024 | 11 | GTPase activator activity (MF) GO Rho GTPase-activating protein domain IPR |
| 22 | 0.41 | 0.00037 | 10 | Proteasome component (PCI) domain IPR RNA transport KEGG Translation initiation factor activity (MF) GO |
| 23` | 0.24 | 0.00043 | 12 | Ion channel activity (MF) * GO Ion transmembrane transport (BP) * GO Transporter activity (MF) * GO |
| 24` | 0.30 | 0.00054 | 13 | Chemokine activity (MF) GO Chemokine interleukin-8-like domain IPR Chemotaxis (BP) GO Cytokine-cytokine receptor interaction KEGG Inflammatory response (BP) GO Jak-STAT signaling pathway KEGG Neuroactive ligand-receptor interaction * KEGG |
| 25 | 0.33 | 0.00059 | 14 | Cell division (BP) GO Centrosome (CC) * GO G2/M transition of mitotic cell cycle (BP) GO Microtubule (CC) * GO Microtubule binding (MF) GO Mitosis (BP) * GO Mitotic cell cycle (BP) GO Spindle pole (CC) GO |
| * Terms marked with an asterisk are in several Metagroups. | | | | |
| ` Metagroups marked with an accent are depicted in Figure 1B in the main manuscript | | | | |

Supplementary Table 3:

This table describes the metagroups generated by GeneTerm Linker using FGNet. The metagroup number corresponds to numbers in Supplementary Figures 1A and 1B (and information can be transferred to Figure 1B in the manuscript). For each metagroup this file presents its silhouette size (a clustering coefficient), significance (p-value), number of constituent genes and constituent functional terms (or, for metagroups 1 and 6, which do not meet inclusion cutoffs, their exclusion criteria). The last column on the right describes functional terms in each metagroup and their annotation space, which can be a gene ontology assignment (GO for biological process, molecular function or cellular component), a KEGG pathway or a function inferred from the description of InterPro motifs or domains (IPR).

Supplementary Table 4 – Expression levels of transcripts produced by human-specific genes in subpopulations of glial cells

(See Below)

Supplementary Table 4:

This table presents gene expression levels (in FPKM) for transcripts related to 61 human-specific genes which were characterized as highly expressed in at least one subpopulation of glial cell (sequencing data retrieved from SRA). Highly expressed transcripts were defined as the top ~10% of the expressed transcripts (i.e. the 2,000 transcripts) with highest average FPKM values for each set of samples under investigation. On average ~1580 genes were characterized as highly expressed in each cell type and compared with the set of 856 genes with human-specific features. We retrieved 23 highly expressed human-specific genes from the radial glial cell samples, 17 from the outer radial glial cell samples, 26 from the progenitor cells samples and 24 from the neuron cell samples, resulting in a set of 61 non-redundant genes and 91 transcripts.

| Gene ID | Gene Name | Gene Type | Transcript ID | Expression in FPKM | | | |
|-----------------|-----------|----------------|-----------------|--------------------|---------|---------|-----------|
| | | | | RG | oRG | IPC | Neuron |
| ENSG00000128185 | DGCR6L | protein_coding | ENST00000248879 | 35.0375 | 35.1325 | 65.785 | 2.6 |
| ENSG00000131051 | RBM39 | protein_coding | ENST00000253363 | 97.235 | 27.1025 | 150.645 | 58.045 |
| ENSG00000154016 | GRAP | protein_coding | ENST00000284154 | 96.785 | 0.0775 | 0 | 0 |
| ENSG00000163956 | LRPAP1 | protein_coding | ENST00000296325 | 203.52 | 361.44 | 64.3225 | 0.196667 |
| ENSG00000166803 | KIAA0101 | protein_coding | ENST00000300035 | 98.1675 | 107.323 | 0.0975 | 0.0666667 |
| ENSG00000167977 | KCTD5 | protein_coding | ENST00000301738 | 19.77 | 0.295 | 88.51 | 33.735 |
| ENSG00000143742 | SRP9 | protein_coding | ENST00000304786 | 172.805 | 105.73 | 184.972 | 327.2 |
| ENSG00000172239 | PAIP1 | protein_coding | ENST00000306846 | 0.035 | 0 | 0.0875 | 91.66 |
| ENSG00000125462 | C1orf61 | protein_coding | ENST00000310027 | 34.495 | 267.295 | 0 | 14.1767 |
| ENSG00000176476 | CCDC101 | protein_coding | ENST00000317058 | 139.74 | 74.38 | 0.2475 | 0 |
| ENSG00000144218 | AFF3 | protein_coding | ENST00000317233 | 0.0325 | 0 | 6.7575 | 71.8017 |
| ENSG00000076382 | SPAG5 | protein_coding | ENST00000321765 | 0.79 | 0 | 142.222 | 0.0516667 |
| ENSG00000186868 | MAPT | protein_coding | ENST00000334239 | 0 | 0 | 0 | 66.3583 |
| ENSG00000176809 | LRR37A3 | protein_coding | ENST00000339474 | 100.13 | 0 | 22.0275 | 0.0816667 |
| ENSG00000150991 | UBC | protein_coding | ENST00000339647 | 89.79 | 316.275 | 207.647 | 287.858 |
| ENSG00000146872 | TLK2 | protein_coding | ENST00000343388 | 0.1325 | 47.11 | 31.04 | 70.755 |
| ENSG00000142330 | CAPN10 | protein_coding | ENST00000352879 | 67.1225 | 14.75 | 76.2625 | 38.5017 |
| ENSG00000196937 | FAM3C | protein_coding | ENST00000359943 | 74.605 | 0 | 27.4625 | 54.2933 |
| ENSG00000198826 | ARHGAP11A | protein_coding | ENST00000361627 | 10.14 | 0.5525 | 179.1 | 0.0633333 |
| ENSG00000117650 | NEK2 | protein_coding | ENST00000366999 | 0.0975 | 0 | 394.72 | 0.451667 |
| ENSG00000066279 | ASPM | protein_coding | ENST00000367408 | 0.03 | 0.035 | 199.335 | 0.153333 |
| ENSG00000066279 | ASPM | protein_coding | ENST00000367409 | 0 | 0 | 67.8525 | 0.105 |
| ENSG00000125462 | C1orf61 | protein_coding | ENST00000368243 | 4.225 | 76.55 | 0 | 0 |
| ENSG00000265241 | RBM8A | protein_coding | ENST00000369307 | 0 | 19.01 | 135.275 | 35.845 |
| ENSG00000188610 | FAM72B | protein_coding | ENST00000369390 | 0 | 0 | 77.6275 | 0 |
| ENSG00000148308 | GTF3C5 | protein_coding | ENST00000372099 | 86.97 | 0 | 0 | 6.485 |
| ENSG00000175170 | FAM182B | protein_coding | ENST00000376404 | 73.255 | 0 | 0 | 0 |
| ENSG00000132406 | TMEM128 | protein_coding | ENST00000382753 | 0.1725 | 119.58 | 8.795 | 108.818 |
| ENSG00000141562 | NARF | protein_coding | ENST00000390006 | 0 | 0 | 104.927 | 24.7217 |
| ENSG00000241973 | PI4KA | protein_coding | ENST00000399213 | 41.2725 | 10.115 | 8.32 | 56.325 |
| ENSG00000125462 | C1orf61 | protein_coding | ENST00000400991 | 71.11 | 482.913 | 35.7175 | 112.928 |
| ENSG00000077380 | DYNC112 | protein_coding | ENST00000409197 | 0.19 | 98.2775 | 177.692 | 0.808333 |
| ENSG00000152076 | CCDC74B | protein_coding | ENST00000409943 | 96.2325 | 0 | 0 | 0 |
| ENSG00000077380 | DYNC112 | protein_coding | ENST00000410079 | 0.18 | 24.2225 | 73.7925 | 23.39 |
| ENSG00000197620 | CXorf40A | protein_coding | ENST00000423421 | 0 | 84.1375 | 0 | 79.2817 |
| ENSG00000197620 | CXorf40A | protein_coding | ENST00000423540 | 0 | 0 | 0 | 67.1217 |
| ENSG00000219481 | NBPF1 | protein_coding | ENST00000430580 | 29.7625 | 30.6825 | 71.01 | 50.1583 |
| ENSG00000122545 | SEPT7 | protein_coding | ENST00000432293 | 67.1525 | 140.39 | 135.148 | 95.235 |
| ENSG00000136861 | CDK5RAP2 | protein_coding | ENST00000433194 | 0.27 | 45.0875 | 11.215 | 148.2 |
| ENSG00000122545 | SEPT7 | protein_coding | ENST00000435235 | 29.61 | 232.685 | 292.915 | 72.6783 |
| ENSG00000130305 | NSUN5 | protein_coding | ENST00000438747 | 30.235 | 2.99 | 27.45 | 72.735 |
| ENSG00000166086 | JAM3 | protein_coding | ENST00000441717 | 101.55 | 26.575 | 0.7575 | 1.1 |
| ENSG00000131051 | RBM39 | protein_coding | ENST00000444878 | 100.245 | 0 | 16.005 | 0 |
| ENSG00000186868 | MAPT | protein_coding | ENST00000446361 | 36.7275 | 0 | 0 | 58.3133 |
| ENSG00000235597 | LINC01102 | lincRNA | ENST00000447380 | 31.0375 | 0 | 35.275 | 124.353 |
| ENSG00000219481 | NBPF1 | protein_coding | ENST00000449853 | 0.035 | 0 | 11.3125 | 83.3 |
| ENSG00000143702 | CEP170 | protein_coding | ENST00000451408 | 0 | 0 | 18.0875 | 86.1533 |

| | | | | | | | |
|-----------------|-----------|--------------------|-----------------|---------|---------|---------|-----------|
| ENSG00000082684 | SEMA5B | protein_coding | ENST00000451541 | 63.57 | 98.5325 | 0.07 | 0.151667 |
| ENSG00000130305 | NSUN5 | protein_coding | ENST00000455763 | 0 | 0 | 1.62 | 69.125 |
| ENSG00000131051 | RBM39 | protein_coding | ENST00000461283 | 11.445 | 76.815 | 143.235 | 55.2917 |
| ENSG00000197021 | CXorf40B | protein_coding | ENST00000462691 | 73.3975 | 0 | 0 | 36.1167 |
| ENSG00000257267 | ZNF271P | unitary_pseudogene | ENST00000465539 | 0.1 | 29.9775 | 4.18 | 70.0783 |
| ENSG00000143702 | CEP170 | protein_coding | ENST00000468254 | 0.0325 | 68.28 | 234.855 | 266.102 |
| ENSG00000134899 | ERCC5 | protein_coding | ENST00000472247 | 0 | 0 | 77.26 | 15.0317 |
| ENSG00000077380 | DYNC112 | protein_coding | ENST00000479806 | 63.9 | 34.56 | 69.395 | 144.263 |
| ENSG00000125462 | C1orf61 | protein_coding | ENST00000484428 | 120.882 | 0 | 24.2025 | 0 |
| ENSG00000075292 | ZNF638 | protein_coding | ENST00000487638 | 58.5775 | 0 | 29.5575 | 60.615 |
| ENSG00000131051 | RBM39 | protein_coding | ENST00000496183 | 7.6625 | 45.0975 | 2.32 | 56.66 |
| ENSG00000125462 | C1orf61 | protein_coding | ENST00000497824 | 332.195 | 271.06 | 52.5625 | 140.453 |
| ENSG00000143126 | CELSR2 | protein_coding | ENST00000498157 | 70.0225 | 1.71 | 0.6875 | 38.5617 |
| ENSG00000125462 | C1orf61 | protein_coding | ENST00000498346 | 152.225 | 50.37 | 19.505 | 57.55 |
| ENSG00000249915 | PDCD6 | protein_coding | ENST00000507528 | 0 | 0 | 106.448 | 0 |
| ENSG00000073578 | SDHA | protein_coding | ENST00000509564 | 3.3525 | 0.495 | 64.405 | 7.16667 |
| ENSG00000145725 | PIIP5K2 | protein_coding | ENST00000509597 | 5.25 | 45.845 | 6.66 | 124.932 |
| ENSG00000135541 | AHI1 | protein_coding | ENST00000524469 | 87.865 | 47.3275 | 0 | 0.41 |
| ENSG00000137812 | CASC5 | protein_coding | ENST00000526913 | 0 | 16.2575 | 92.8 | 0.0416667 |
| ENSG00000137812 | CASC5 | protein_coding | ENST00000531626 | 0 | 16.35 | 238.06 | 1.03 |
| ENSG00000148737 | TCF7L2 | protein_coding | ENST00000534894 | 0 | 78.7 | 0 | 0 |
| ENSG00000172915 | NBEA | protein_coding | ENST00000537702 | 0 | 0 | 0 | 74.32 |
| ENSG00000139372 | TDG | protein_coding | ENST00000544060 | 94.4075 | 27.16 | 0 | 18.77 |
| ENSG00000150991 | UBC | protein_coding | ENST00000544481 | 19.88 | 113.353 | 41.98 | 28.5333 |
| ENSG00000150991 | UBC | protein_coding | ENST00000546120 | 45.935 | 82.28 | 62.375 | 122.56 |
| ENSG00000123064 | DDX54 | protein_coding | ENST00000549271 | 71.25 | 0 | 43.1075 | 0.15 |
| ENSG00000123064 | DDX54 | protein_coding | ENST00000550016 | 105.697 | 0 | 0 | 0 |
| ENSG00000165525 | NEMF | protein_coding | ENST00000555970 | 0 | 0 | 67.0975 | 19.1383 |
| ENSG00000185650 | ZFP36L1 | protein_coding | ENST00000555997 | 32.1725 | 130.873 | 0 | 0 |
| ENSG00000166803 | KIAA0101 | protein_coding | ENST00000558043 | 85.665 | 159.188 | 0 | 0.13 |
| ENSG00000166803 | KIAA0101 | protein_coding | ENST00000559519 | 99.265 | 188.282 | 0 | 0 |
| ENSG00000198826 | ARHGAP11A | protein_coding | ENST00000562481 | 0 | 0.3375 | 246.488 | 0 |
| ENSG00000205336 | GPR56 | protein_coding | ENST00000564907 | 131.873 | 74.7225 | 11.4225 | 0.0616667 |
| ENSG00000198826 | ARHGAP11A | protein_coding | ENST00000565905 | 0 | 0 | 256.26 | 0 |
| ENSG00000140365 | COMMD4 | protein_coding | ENST00000566843 | 80.5675 | 0.345 | 0.67 | 0.635 |
| ENSG00000140365 | COMMD4 | protein_coding | ENST00000567195 | 0 | 0 | 108.877 | 0 |
| ENSG00000120071 | KANSL1 | protein_coding | ENST00000576870 | 4.3125 | 5.84 | 17.5525 | 79.6517 |
| ENSG00000076382 | SPAG5 | protein_coding | ENST00000582076 | 21.925 | 0 | 162.292 | 0.19 |
| ENSG00000187951 | ARHGAP11B | protein_coding | ENST00000602616 | 36.78 | 0 | 99.8325 | 0 |
| ENSG00000272398 | CD24 | protein_coding | ENST00000606017 | 27.57 | 146.417 | 1584.35 | 2219.95 |
| ENSG00000066279 | ASPM | protein_coding | ENST00000612785 | 0.02 | 0.1275 | 115.62 | 0.261667 |
| ENSG00000128408 | RIBC2 | protein_coding | ENST00000614167 | 155.197 | 0.1 | 0 | 0.0933333 |
| ENSG00000249915 | PDCD6 | protein_coding | ENST00000614778 | 161.93 | 0 | 8.055 | 46.865 |
| ENSG00000125462 | C1orf61 | protein_coding | ENST00000615748 | 217.755 | 139.843 | 30.4325 | 0 |

Supplementary Table 5 – Primers Used for RT-qPCR

| Gene Name | Forward Primer (5' - 3') | Reverse Primer (5' - 3') | Accession # |
|------------------|---------------------------------|---------------------------------|--------------------|
| TENM1 | GAACCCACCTACACACCCTG | CCATTGCTGCTGGTAATCGC | NM_001163279.1 |
| CAPN1 | GGCCAGGATTATGAGCAGCT | GGTCCTTGTAACCCAGGCTC | NR_040008.1 |
| FAM21A | GCAGGAGAAGACACGAGAGC | TTGCTCAAAGGCACTGTCCA | NM_001330102.1 |
| SLC7A6 | GCGCTCATTGCCATCATTGT | GTTTCCCATGTCCCAGGAGG | NM_001076785.2 |
| SEPT7 | GGACTCTGAAGCTGAGCTCC | CATCCTCGAACTGACGACGT | NM_001788.5 |
| RBM39 | ATCTCTTCCCGAACACGAGC | GGAGCCTCAAGCATTGCTTC | NR_136587.1 |
| KIAA0319L | AGAGAAGGGCAAACCTCCTGC | ACCAGGTGGCTACAGGATCT | NM_024874.4 |
| AFF3 | CTCCGGGAATGATCAGAGGC | GATGTCACCTGGTGGTCTGG | NM_002285.2 |
| PPIP5K2 | ATGAAGAGAGCCCCCTGAGT | GTTCCCCTGATCTGCGTCTT | NM_015216.4 |
| TLK2 | TGGAGCTGAAATGGGAGACG | CGACCACATGTTTCAGGCTCT | NM_001330418.1 |
| NLGN4X | GCAATGGGCTGCCAAGAAAA | GGCTTTCCAGGGAGCAGTAG | NM_001282146.1 |
| ZNF286A | TCGATCGTCCGATTCTCCA | GCCCGGAACTACAATTCCA | NM_001288645.1 |

Supplementary Table 5:

Primers designed for each of the 12 genes described in the Figure 4 of the main manuscript. Gene names and accession numbers are also provided.