

Additional file S6. Biological processes (BPs) obtained in AD and FTD comparisons applying GO database.

| sEOAD vs. CTRL | | | | | |
|-------------------------------|----------------|---------------------------------|---|----------------|----------------------------------|
| BRAIN | | | LCLs | | |
| Biological process | Enrichment FDR | Root node | Biological process | Enrichment FDR | Root node |
| Extracellular matrix assembly | 0.026 | Cellular component organization | Activation of protein kinase activity | 0.021 | Metabolic process |
| Cell adhesion | 0.026 | // | Positive regulation of extrinsic apoptotic signaling pathway via death domain receptors | 0.030 | Regulation of biological process |
| Biological adhesion | 0.026 | // | Locomotory behavior | 0.030 | Behavior |
| | | | Positive regulation of signal transduction | 0.030 | Regulation of biological process |
| | | | Astral microtubule organization | 0.030 | Cellular process |
| | | | Ion transmembrane transport | 0.030 | Transport |
| | | | Regulation of protein kinase activity | 0.030 | Regulation of biological process |
| | | | Genetic imprinting | 0.030 | Regulation of biological process |
| | | | Intracellular signal transduction | 0.032 | // |
| | | | Response to endogenous stimulus | 0.041 | Response to stimulus |
| | | | Regulation of transferase activity | 0.041 | Biological regulation |
| | | | Calcium ion transmembrane transport | 0.041 | Transport |
| | | | Inorganic ion transmembrane transport | 0.050 | Transport |
| PSEN1 vs. CTRL | | | | | |
| BRAIN | | | LCLs | | |
| Biological process | Enrichment FDR | Root node | Biological process | Enrichment FDR | Root node |
| Phospholipid transport | 0.002 | Macromolecule localization | Homophilic cell adhesion via plasma membrane adhesion molecules | 0.000 | Cell adhesion |

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|---|-------|---------------------------------|---|-------|-----------------------|
| Sterol metabolic process | 0.002 | Metabolism | Cell-cell adhesion via plasma-membrane adhesion molecules | 0.000 | Cell adhesion |
| Phospholipid translocation | 0.005 | Macromolecule localization | Cell-cell adhesion | 0.011 | Cell adhesion |
| Lipid translocation | 0.005 | Macromolecule localization | Cell adhesion | 0.031 | // |
| Steroid metabolic process | 0.005 | Metabolism | Plasma membrane repair | 0.031 | Cellular process |
| Organophosphate ester transport | 0.008 | Macromolecule localization | Biological adhesion | 0.031 | Cell adhesion |
| Organic hydroxy compound metabolic process | 0.009 | Metabolism | Negative regulation of dendritic spine development | 0.031 | Developmental process |
| Cholesterol metabolic process | 0.022 | Metabolism | Cholesterol metabolic process | 0.038 | Metabolic process |
| Regulation of membrane lipid distribution | 0.024 | Cellular component organization | Secondary alcohol metabolic process | 0.040 | Metabolic process |
| Secondary alcohol metabolic process | 0.024 | Metabolism | Plasma membrane organization | 0.040 | Cellular process |
| Axonogenesis | 0.029 | Cell development | Import into cell | 0.049 | Transport |
| Anterior commissure morphogenesis | 0.031 | Cell development | | | |
| Regulation of ATP metabolic process | 0.034 | Metabolism | | | |
| Central nervous system projection neuron axonogenesis | 0.034 | Cell development | | | |
| Regulation of modification of postsynaptic actin cytoskeleton | 0.037 | Cellular component organization | | | |
| Lipid metabolic process | 0.037 | Metabolism | | | |
| Axon development | 0.037 | Cell development | | | |
| Neuron projection guidance | 0.043 | Cell development | | | |
| Regulation of modification of postsynaptic structure | 0.043 | Cellular component organization | | | |
| Regulation of purine nucleotide metabolic process | 0.043 | Metabolism | | | |
| Alcohol metabolic process | 0.043 | Metabolism | | | |
| Organic hydroxy compound biosynthetic process | 0.043 | Metabolism | | | |

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| Regulation of glycolytic process | 0.043 | Metabolism | | | |
| Regulation of nucleotide metabolic process | 0.043 | Metabolism | | | |
| Cell morphogenesis involved in differentiation | 0.043 | Developmental process | | | |
| Axon guidance | 0.043 | Cell development | | | |
| Response to external stimulus | 0.043 | Response to stimulus | | | |
| Organic acid biosynthetic process | 0.043 | Metabolism | | | |
| Central nervous system neuron axonogenesis | 0.043 | Cell development | | | |
| Regulation of nucleotide catabolic process | 0.043 | Metabolism | | | |
| PSEN1 vs. sEOAD | | | | | |
| BRAIN | | | LCLs | | |
| Biological process | Enrichment FDR | Root node | Biological process | Enrichment FDR | Root node |
| Endothelial cell morphogenesis | 0.005 | Developmental process | Phosphorus metabolic process | 0.001 | Metabolic process |
| Cellular component morphogenesis | 0.022 | Developmental process | Phosphate-containing compound metabolic process | 0.001 | Metabolic process |
| Epithelial cell morphogenesis | 0.028 | Developmental process | Negative regulation of phosphorus metabolic process | 0.001 | Regulation of biological process |
| Positive regulation of lipid kinase activity | 0.029 | Regulation of metabolic process | Dephosphorylation | 0.001 | Metabolic process |
| Anatomical structure formation involved in morphogenesis | 0.038 | Developmental process | Negative regulation of protein phosphorylation | 0.001 | Regulation of biological process |
| Positive regulation of phospholipid metabolic process | 0.044 | Regulation of metabolic process | Regulation of signaling | 0.001 | Regulation of biological process |
| Negative regulation of dendritic cell differentiation | 0.050 | Cell differentiation | Negative regulation of protein modification process | 0.001 | Regulation of biological process |
| Cell morphogenesis | 0.050 | Developmental process | Negative regulation of phosphate metabolic process | 0.001 | Regulation of biological process |
| Anatomical structure morphogenesis | 0.050 | Developmental process | Regulation of cell communication | 0.001 | Regulation of biological process |
| Positive regulation of cell morphogenesis involved in differentiation | 0.050 | Developmental process | Negative regulation of cellular metabolic process | 0.001 | Regulation of biological process |
| Endothelial cell development | 0.050 | Developmental process | Negative regulation of cellular protein metabolic process | 0.001 | Regulation of biological process |

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| Tube development | 0.050 | Developmental process | Negative regulation of protein serine/threonine kinase activity | 0.001 | Regulation of biological process |
| Regulation of lipid kinase activity | 0.050 | Regulation of metabolic process | Negative regulation of nitrogen compound metabolic process | 0.001 | Regulation of biological process |
| | | | Negative regulation of intracellular signal transduction | 0.001 | Regulation of biological process |
| | | | Negative regulation of protein metabolic process | 0.001 | Regulation of biological process |
| | | | Negative regulation of phosphorylation | 0.002 | Regulation of biological process |
| | | | Regulation of signal transduction | 0.002 | Regulation of biological process |
| | | | Anatomical structure morphogenesis | 0.003 | Developmental process |
| | | | Negative regulation of protein kinase activity | 0.004 | Regulation of biological process |
| | | | Regulation of catalytic activity | 0.004 | Regulation of biological process |
| | | | Protein dephosphorylation | 0.004 | Metabolic process |
| | | | Negative regulation of macromolecule metabolic process | 0.004 | Regulation of biological process |
| | | | Negative regulation of MAP kinase activity | 0.004 | Regulation of biological process |
| | | | Negative regulation of MAPK cascade | 0.004 | Regulation of biological process |
| | | | Nervous system development | 0.005 | Developmental process |
| | | | Negative regulation of metabolic process | 0.005 | Regulation of biological process |
| | | | Negative regulation of cell communication | 0.006 | Regulation of biological process |
| | | | Negative regulation of signaling | 0.006 | Regulation of biological process |
| | | | Osteoclast development | 0.006 | Developmental process |
| | | | Negative regulation of kinase activity | 0.006 | Regulation of biological process |

| sFTD-Tau vs. CTRL | | | sFTD-TDP43 vs. CTRL | | |
|---|----------------|-----------------------|---|----------------|-----------------------|
| Biological process | Enrichment FDR | Root node | Biological process | Enrichment FDR | Root node |
| Neuron projection guidance | 0.003 | Developmental process | Cell adhesion | 0.000 | Biological adhesion |
| Nervous system development | 0.003 | Developmental process | Biological adhesion | 0.000 | // |
| Axon guidance | 0.003 | Developmental process | Homophilic cell adhesion via plasma membrane adhesion molecules | 0.000 | Biological adhesion |
| Cell morphogenesis involved in differentiation | 0.004 | Developmental process | Cell-cell adhesion via plasma-membrane adhesion molecules | 0.000 | Biological adhesion |
| Cell development | 0.004 | Developmental process | Cell-cell adhesion | 0.000 | Biological adhesion |
| Cell morphogenesis involved in neuron differentiation | 0.004 | Developmental process | Cell morphogenesis involved in neuron differentiation | 0.000 | Developmental process |
| Axonogenesis | 0.004 | Developmental process | Cell morphogenesis involved in differentiation | 0.000 | Developmental process |
| Central nervous system development | 0.005 | Developmental process | Neuron projection development | 0.000 | Developmental process |
| Neuron differentiation | 0.005 | Developmental process | Cell morphogenesis | 0.000 | Developmental process |
| Neuron projection morphogenesis | 0.008 | Developmental process | Neuron development | 0.000 | Developmental process |
| Axon development | 0.008 | Developmental process | Dendrite development | 0.000 | Developmental process |
| Plasma membrane bounded cell projection morphogenesis | 0.009 | Developmental process | Cellular component morphogenesis | 0.000 | Developmental process |
| Cell projection morphogenesis | 0.009 | Developmental process | Neuron projection morphogenesis | 0.000 | Developmental process |
| Cell part morphogenesis | 0.012 | Developmental process | Anatomical structure morphogenesis | 0.000 | Developmental process |
| Neuron development | 0.012 | Developmental process | Plasma membrane bounded cell projection morphogenesis | 0.000 | Developmental process |
| Generation of neurons | 0.012 | Developmental process | Cell projection morphogenesis | 0.000 | Developmental process |
| Head development | 0.014 | Developmental process | Axonogenesis | 0.000 | Developmental process |
| Neuron migration | 0.014 | Developmental process | Cell part morphogenesis | 0.000 | Developmental process |
| Brain development | 0.015 | Developmental process | Cell development | 0.000 | Developmental process |

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| Movement of cell or subcellular component | 0.015 | Cellular process | Movement of cell or subcellular component | 0.000 | Cellular process |
| Neurogenesis | 0.015 | Developmental process | Generation of neurons | 0.000 | Developmental process |
| Cell differentiation | 0.015 | Developmental process | Neurogenesis | 0.000 | Developmental process |
| Response to transforming growth factor beta | 0.016 | Response to stimulus | Neuron differentiation | 0.000 | Developmental process |
| Anatomical structure morphogenesis | 0.020 | Developmental process | Axon development | 0.000 | Developmental process |
| Cell morphogenesis | 0.028 | Developmental process | Cell projection organization | 0.000 | Cellular process |
| Neuron projection development | 0.028 | Developmental process | Synapse organization | 0.000 | Cellular process |
| Forebrain development | 0.029 | Developmental process | Nervous system development | 0.000 | Developmental process |
| Positive regulation of caveolin-mediated endocytosis | 0.030 | Regulation of biological process | Plasma membrane bounded cell projection organization | 0.000 | Cellular process |
| Telencephalon development | 0.032 | Developmental process | Cell differentiation | 0.000 | Developmental process |
| Cellular localization | 0.034 | Localization | Regulation of cell differentiation | 0.000 | Developmental process |
| sFTD-TDP43 vs. sFTD-Tau | | | | | |
| Biological process | Enrichment FDR | Root node | | | |
| Response to phorbol 13-acetate 12-myristate | 0.031 | Response to stimulus | | | |
| Cellular response to phorbol 13-acetate 12-myristate | 0.031 | Response to stimulus | | | |
| Response to biotic stimulus | 0.031 | Response to stimulus | | | |

| MAPT vs. CTRL | | | | | |
|---|----------------|-----------------------|---|----------------|----------------------------------|
| BRAIN | | | LCLs | | |
| Biological process | Enrichment FDR | Root node | Biological process | Enrichment FDR | Root node |
| Cell morphogenesis involved in differentiation | 0.001 | Developmental process | Nervous system development | 0.000 | Developmental process |
| Movement of cell or subcellular component | 0.001 | Cellular process | Cell development | 0.000 | Developmental process |
| Axonogenesis | 0.001 | Developmental process | Anatomical structure morphogenesis | 0.000 | Developmental process |
| Cell development | 0.001 | Developmental process | Neurogenesis | 0.000 | Developmental process |
| Axon development | 0.001 | Developmental process | Generation of neurons | 0.000 | Developmental process |
| Plasma membrane bounded cell projection morphogenesis | 0.002 | Developmental process | Neuron differentiation | 0.000 | Developmental process |
| Negative regulation of cellular protein localization | 0.002 | Biological regulation | Cellular component morphogenesis | 0.000 | Developmental process |
| Cell morphogenesis | 0.002 | Developmental process | Movement of cell or subcellular component | 0.000 | Cellular process |
| Neuron differentiation | 0.002 | Developmental process | Locomotion | 0.000 | Locomotion |
| Cellular component morphogenesis | 0.002 | Developmental process | Cellular developmental process | 0.000 | Developmental process |
| Neuron development | 0.002 | Developmental process | Neuron development | 0.000 | Developmental process |
| Cell morphogenesis involved in neuron differentiation | 0.002 | Developmental process | Regulation of localization | 0.000 | Regulation of biological process |
| Neuron projection morphogenesis | 0.002 | Developmental process | Neuron projection development | 0.000 | Developmental process |
| Cell projection morphogenesis | 0.002 | Developmental process | Cell differentiation | 0.000 | Developmental process |
| Anatomical structure morphogenesis | 0.002 | Developmental process | Cell morphogenesis | 0.000 | Developmental process |
| Neuron projection development | 0.002 | Developmental process | Plasma membrane bounded cell projection organization | 0.000 | Cellular process |
| Chondrocyte differentiation | 0.002 | Developmental process | Cell morphogenesis involved in neuron differentiation | 0.000 | Developmental process |

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| Cell part morphogenesis | 0.002 | Developmental process | Cell motility | 0.000 | Locomotion |
| Plasma membrane bounded cell projection organization | 0.006 | Cellular process | Localization of cell | 0.000 | Localization |
| Nervous system development | 0.008 | Developmental process | Cell-cell signaling | 0.000 | Signaling |
| Negative regulation of protein localization to membrane | 0.009 | Localization | Cell projection organization | 0.000 | Cellular process |
| Cell projection organization | 0.009 | Cellular process | Actin filament-based process | 0.000 | Cellular process |
| Regulation of GTPase activity | 0.010 | Biological regulation | Plasma membrane bounded cell projection morphogenesis | 0.000 | Developmental process |
| Regulation of hydrolase activity | 0.010 | Biological regulation | Cell part morphogenesis | 0.000 | Developmental process |
| Generation of neurons | 0.013 | Developmental process | Cell projection morphogenesis | 0.000 | Developmental process |
| Cell adhesion | 0.014 | Biological adhesion | Cell migration | 0.000 | Locomotion |
| Central nervous system neuron axonogenesis | 0.014 | Developmental process | Cytoskeleton organization | 0.000 | Cellular process |
| Cell differentiation | 0.014 | Developmental process | Cell-cell adhesion via plasma-membrane adhesion molecules | 0.000 | Cell adhesion |
| Regulation of catalytic activity | 0.014 | Biological regulation | Regulation of biological quality | 0.000 | Regulation of biological process |
| Regulation of membrane repolarization | 0.014 | Biological regulation | Cell morphogenesis involved in differentiation | 0.000 | Developmental process |
| GRN vs. CTRL | | | | | |
| BRAIN | | | LCLs | | |
| Biological process | Enrichment FDR | Root node | Biological process | Enrichment FDR | Root node |
| Response to organic substance | 0.000 | Response to stimulus | Negative regulation of multicellular organism growth | 0.005 | Regulation of biological process |
| Cell morphogenesis | 0.000 | Developmental process | Negative regulation of growth | 0.005 | Regulation of biological process |
| Movement of cell or subcellular component | 0.000 | Cellular process | Response to hydroperoxide | 0.014 | Response to stimulus |
| Cell adhesion | 0.000 | Biological adhesion | Negative regulation of developmental growth | 0.014 | Regulation of biological process |
| Biological adhesion | 0.000 | // | | | |

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| Cellular component morphogenesis | 0.000 | Response to stimulus |
| Locomotion | 0.000 | // |
| Cell motility | 0.000 | Locomotion |
| Localization of cell | 0.000 | Localization |
| Cell migration | 0.000 | Locomotion |
| Cellular response to organic substance | 0.000 | Response to stimulus |
| Blood vessel development | 0.000 | Developmental process |
| Cell proliferation | 0.000 | Developmental process |
| Vasculature development | 0.000 | Developmental process |
| Extracellular matrix organization | 0.000 | Cellular process |
| Cell-substrate adhesion | 0.000 | Biological adhesion |
| Cardiovascular system development | 0.000 | Developmental process |
| Nervous system development | 0.000 | Developmental process |
| Homophilic cell adhesion via plasma membrane adhesion molecules | 0.001 | Biological adhesion |
| Circulatory system development | 0.001 | Developmental process |
| Extracellular structure organization | 0.001 | Cellular process |
| Regulation of cell proliferation | 0.001 | Biological regulation |
| Anatomical structure morphogenesis | 0.001 | Developmental process |
| Response to oxygen-containing compound | 0.001 | Response to stimulus |
| Anatomical structure formation involved in morphogenesis | 0.001 | Developmental process |
| Cellular response to chemical stimulus | 0.001 | Response to stimulus |
| Cell morphogenesis involved in differentiation | 0.001 | Developmental process |
| Regulation of biological quality | 0.002 | Biological regulation |
| Angiogenesis | 0.002 | Developmental |

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| | | process |
| Enzyme linked receptor protein signaling pathway | 0.002 | Signaling |

For each BPs, the FDR and the root node in which the BPs belongs is shown. LCLs samples of C9orf72 group and sporadic FTD were not available. C9orf72 did not retrieve any BPs. Filters applied: adjusted-p value <0.05. Abbreviations: CTRL, healthy controls; sEOAD, sporadic early-onset Alzheimer's disease; PSEN1, autosomal dominant Alzheimer's disease caused by mutation in *PSEN1*; MAPT, GRN, C9orf72, familial frontotemporal dementia caused by mutation in *MAPT*, *GRN* or *C9orf72*; sFTD-Tau, sporadic frontotemporal dementia with tau deposits; sFTD-TDP43, sporadic frontotemporal dementia with TDP43 deposits; LCLs, lymphoblastoid cell lines.