**Supplementary Table 1.** Selected recent studies which have used iPSC-derived neurons to probe the pathogenesis of other neurodegenerative diseases.

| **Disease & Ref** | **Gene** | **Mutation** | **Reprogramming strategy** | **Target cell type** | **Key findings** |
| --- | --- | --- | --- | --- | --- |
| AD [[1](#_ENREF_1)] | PS1 PS2 | A246E (PS1), and N141I (PS2) | Retroviral delivery of OSK + LIN28 + NANOG (for PS1 and PS2 mutants, C-MYC was used instead of LIN28 and NANOG for controls) | Neurons | Increased ratio of secreted Aβ42/Aβ40 in AD neurons compared to normal and sporadic PD controls. This phenotype is rescued by γ-secretase inhibition. |
| AD [[2](#_ENREF_2)] | APP | APP duplication and idiopathic | Retroviral delivery of OSKM | Neurons | Increased Aβ40, tau phosphorylation, and GSK3β activity in neurons from familial AD patients and one of the sporadic AD patients. Inhibitors of β secretase (but not γ secretase) restore normal tau and GSK3β phenotypes. Enhanced early endosome accumulation in familial and sporadic AD neurons. |
| AD [[3](#_ENREF_3)] | APP | Trisomy 21 (Down's Syndrome) | Retroviral delivery of OSKM | Cortical Neurons | Increased γ-secretase-dependent Aβ peptide secretion from day 20 in culture, Aβ plaque formation, increased Aβ42/Aβ40 ratio, and abnormal tau phosphorylation and localisation in Down's Syndrome patient-derived cortical neurons. |
| HD [[4](#_ENREF_4)] | Htt | Heterozygous (72 CAG repeats) | Retroviral delivery of OSKM | NSCs | HD patient-derived NSCs show increased apoptosis and capsase 3/7 activity, decreased BDNF mRNA levels, decreased maximum mitochondrial respiration, and changes in gene expression compared to control NSCs. Correction of the triplet expansion in HD iPSCs rescues all of these phenotypes. Corrected NSCs can differentiate into functional striatal neurons *in vitro* and *in vivo*. |
| HD [[5](#_ENREF_5)] | Htt | Two heterozygous subjects (60 and 180 CAG repeats) | Lentiviral delivery of OSKM + LIN28 + NANOG | NPCs, neurons, striatal neurons | Increased cell death under normal conditions and following BDNF withdrawal, increased glutamate excitotoxicity, and increased sensitivity to oxidative stress and autophagy inhibition in HD-derived neurons. Some evidence of a dose-dependence of severity of phenotype on number of CAG repeats. |
| HD [[6](#_ENREF_6)] | Htt | Heterozygous (72 CAG repeats) | Retroviral delivery of OSKM | NSCs | Increased caspase 3/7 activity following 24 hour growth factor withdrawal in HD-NSCs but not in control NSCs. |
| HD [[7](#_ENREF_7)] | Htt | Heterozygous (72 CAG repeats) | Retroviral delivery of OSKM | NPCs, neurons, striatal neurons | No detectable Htt aggregation in cultures of HD-derived or control neurons. Transplantation of HD and control-derived NPCs into a rat model of HD alleviates behavioural defects to a similar extent by 12 weeks post-graft. Huntingtin aggregation is observed *in vivo* at >30 weeks following transplantation of HD (but not control) NPCs into normal P2 mouse brains. |
| HD [[8](#_ENREF_8)] | Htt | Two homozygous subjects (42/44 and 39/42 repeats) and one heterozygous subject (45 repeats) | Retroviral or lentiviral delivery of OSK (and C-MYC for 4 of 8 lines) | Neurons | Increased size of the lysosomal and autophagosomal compartments in HD-derived neurons compared to control. |
| HD [[9](#_ENREF_9)] | Htt | Two heterozygous subjects (50 and 109 CAG repeats) | Retroviral delivery of OSKM | Astrocytes | HD patient-derived astrocytes accumulate electron-clear vesicles whereas control astrocytes show very few. The number of vacuoles depends in a dose-dependent manner on the number of CAG repeats. |
| MJD [[10](#_ENREF_10)] | ATXN3 | Four heterozygous subjects (with 73 or 74 repeats in the mutant gene) | Retroviral delivery of OSKM | Neurons | Excitation-dependent calpain-mediated cleavage of ATNX3 leads to formation of insoluble aggregates of N-terminal fragments in MJD neurons (but not control neurons or other cell types). This process is dependent on membrane depolarisation, functional AMPA and NMDA receptors, and the presence of extracellular Calcium. |
| ALS [[11](#_ENREF_11)] | TDP-43 | Heterozygous M337V | Retroviral delivery of OSKM | Neurons, motor neurons | Increased soluble and detergent-resistant TDP-43 protein levels in ALS-derived neurons compared to controls despite similar levels of mRNA. Increased risk of cell death under basal conditions and following PI3K blockade in ALS-derived neurons compared to controls. |
| ALS [[12](#_ENREF_12)] | TDP-43 | Three heterozygous subjects (with the Q343R, M337V, and G298S mutations) | Retroviral delivery of OSKM or episomal plasmid delivery of OSK + L-MYC, anti-p53 shRNA, and LIN28 | Neurons, motor neurons | Shorter neurites, increased expression of RNA metabolism genes, and decreased expression of intermediate filament genes in ALS motor neurons. Increased insoluble full-length TDP-43, insoluble TDP-43 fragments, and cytosolic TDP-43 aggregation in ALS neurons. Increased arsenite-induced cell death in ALS motor neurons. Many aspects of ALS phenotype are reversed by anacardic acid. |
| ALS8 [[13](#_ENREF_13)] | VAPB | P56S | Retroviral delivery of OSKM | Neurons, motor neurons | Decreased expression of VAPB protein in ALS8 neurons compared to control, despite similar mRNA levels. |
| FTD [[14](#_ENREF_14)] | Progranulin | One heterozygous subject with the S116X mutation and one sporadic subject | Retroviral delivery of OCT4, SOX2, KLF4, and C-MYC | Neurons, microglia | Decreased expression and secretion of progranulin, increased sentivity to kinase inhibitors, downregulation of the kinase S6K2 in S116X mutant neurons. Phenotypes rescued by expression of WT progranulin. |

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