HDL2 iPSCs

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Technology description

Invention Novelty

Generation of three lines of induced pluripotent stem cells derived from fibroblast cell lines developed from patients with Huntington's disease-like 2.

Value Proposition

HDL2, discovered and genetically defined by the Margolis group, is a rare, autosomal dominant neurodegenerative disorder, clinically and neuropathologically very similar from Huntington’ s disease. Like HD, the neuropathology of HDL2 is characterized by cortical and striatal neurodegeneration and the presence of neuronal protein aggregates. HDL2 is caused by a CTG/CAG expansion on chromosome 16q24. Normal alleles contain 6-28 triplets, while pathogenic repeats range from 40-59 triplets, again remarkably similar to HD. In the CTG orientation, the repeat falls in the gene junctophilin-3 (JPH3). We have hypothesized that the HDL2 mutation leads to neurodegeneration via a combination of loss of JPH3 expression, toxicity of the sense strand transcript containing an expanded CUG repeat, and expression of polyglutamine from a cryptic gene on the antisense strand. The relative contribution and interactions of these mechanisms remains unknown, and modeling HDL2 has proven challenging. The JHU researchers generated induced pluripotent cells from fibroblasts of individuals with HDL2.

Technical Details

Johns Hopkins researchers collected skin biopsies from patients with Huntington's disease-like 2 under IRB protocol NA_00018358. The biopsies were used to generate fibroblast lines at the Johns Hopkins Genetics Resources Core Facility. Three different fibroblast lines were sent to Cedars Sinai to be made into iPSCs. Three lines were generated and partially returned to us: 85iHDL2, 14iHDL2, 81iHDL2.

Publication(s)/Associated Cases:

Am J Med Genet B Neuropsychiatr Genet. 2015 Oct;168(7):573-85

Advantages

improved understanding of HDL2 itself,

new insights into fundamental pathogenic processes relevant to other repeat expansion diseases, and the opportunity to find pathogenic points of convergence between HD and HDL2 that will lead to a focus on therapeutic targets of most promise for both diseases.

Institution

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