A Novel Method and Protocol to Induce Pluripotent Stem Cells Toward Astrocyte Differentiation

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Technology description

Researchers at UC San Diego have developed a novel and highly efficient method for generating astrocytes from induced pluripotent stem cells (iPSCs). Using a well-characterized rare male Rett Syndrome (RTT) patient-derived and genome-edited isogenic lines, enriched populations of cortical neurons and astrocytes were generated. RTT derived astrocytes showed significant gene expression and physiological differences compared to control cells. Co-culture experiments revealed that RTT-derived astrocyte impaired neuronal dendritic arborization and spinogenesis in control cells. In contrast, control-derived astrocytes rescued morphological RTT neuronal phenotypes. Astrocytes used in these studies were characterized by immune-staining methods, followed by plating and neuronal enrichment.

Rett syndrome (RTT) is a devastating disease that affects 1 in every 10,000 children born in the United States, primarily females. RTT patients undergo apparently normal development until 6-18 months of age, followed by impaired motor function, stagnation and then regression of developmental skills, hypotonia, seizures and a spectrum of autistic behaviors. Rett syndrome is a rare disease that shares certain pathways with major developmental disorders such as autism and schizophrenia, increasing the potential impact. There is no cure for Rett syndrome and the animal model does not entirely recapitulate the human disease. Thus, having the possibility to screen drugs directly in human neurons is a major milestone.

Related Materials

Thomas CA, Tejwani L, Trujillo CA, Negraes PD, Herai RH, Mesci P, Macia A, Crow YJ, Muotri AR. Cell Stem Cell. 2017 Sep 7;21(3):319-331.e8. doi: 10.1016/j.stem.2017.07.009. Epub 2017 Aug 10. Modeling of TREX1-Dependent Autoimmune Disease using Human Stem Cells Highlights L1 Accumulation as a Source of Neuroinflammation.

Russo FB, Freitas BC, Pignatari GC, Fernandes IR, Sebat J, Muotri AR, Beltrão-Braga PCB. Modeling the Interplay Between Neurons and Astrocytes in Autism Using Human Induced Pluripotent Stem Cells. Biol Psychiatry. 2018 Apr 1;83(7):569-578. doi: 10.1016/j.biopsych.2017.09.021. Epub 2017 Oct 3.

Application area

The study of autism spectrum disorder (ASD) risk variants is critical for the understanding of autism pathophysiology and related diseases. Induced pluripotent stem cells (iPSCs) provide a valuable strategy to study the effects of these variants in living patient cells. These cells are known to play a role in Parkinson’ s, Alzheirmer, autism, as well as other neurological disorders and would be a useful platform for drug screening directly in human neurons.

Advantages

While models have been developed for monogenic forms of ASD, no models of idiopathic ASD using iPSCs have heretofore been reported. Thus, these new iPSCs derived astrocytes provides an advancement of the current state of the art. This concept also accelerates the differentiation process reducing the time from 180 to 300 days as proposed in the literature in 30 days.

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