High throughput method for identifying drug candidates for the treatment of neurodegenerative diseases

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Technology description

Summary

Some neurodegenerative diseases are linked to specific genetic mutations; however, the pathways that result in these mutations are not well understood. This technology uses paired systems of normal and mutated neural cells specific to neurodegenerative disorders such as Parkinson's disease, Huntington's disease, Friedreich's ataxia, and multiple sclerosis to test the efficacy of therapeutic candidates. The pair-wise testing of normal and mutant cell types allows for direct biological comparison of the negative and positive effects of a candidate drug. This model could be used as a high throughput screen for identifying therapeutic candidates for neurodegenerative diseases.
Autonomous cell models of neurodegenerative diseases improve screening of therapeutic candidates for treatment
The technology describes in vitro autonomous cell models of neurodegenerative diseases for screening therapies. Induced stem cells derived from patients are differentiated to cell types expressing a disease-specific mutation. Cell pairs are exposed to a stressor that accelerates the disease pathology and also a therapeutic candidate. The biofidelity of the cell model to portray disease can facilitate identification of therapeutic targets. Efficacy is quantified by evaluating the ability of the candidate to lower a normal cell to mutant survival ratio or to increase the survival of both the normal and mutant cell types.
This technology was used to identify a small SERCA inhibitor that increases motor neuron loss associated with amyotrophic lateral sclerosis (ALS) in stem cell-derived neurons.

Publications

* [Dimos JT, Rodolfa KT, Niakan KK, Weisenthal LM, Mitsumoto H, Chung W, Croft GF, Saphier G, Leibel

R, Goland R, Wichterle H, Henderson CE, Eggan K. Induced pluripotent stem cells generated from patients with ALS can be differentiated into motor neurons. Science, Vol. 321, Issue 5893, Jul 2008, pp. 1218-21.](http://goo.gl/2iEj1r)
* [Nagai M, Re DB, Nagata T, Chalazonitis A, Jessell TM, Wichterle H, Przedborski S. Astrocytes expressing ALS-linked mutated SOD1 release factors selectively toxic to motor neurons. Nat Neurosci, Vol. 10, Issue 5, Apr 2007, pp.615-22.]( )

Application area

* In vitro models for the study of ALS, Parkinson's disease, Huntington's disease, Friedreich's ataxia, or multiple sclerosis pathologies
* High throughput screening of therapeutic targets for neurodegenerative diseases
* Evaluation and selection of neurodegenerative disease therapeutics

Advantages

* Autonomous stem cell-derived neuron assay demonstrating biofidelity to neurodegenerative diseases

* In vitro model for improved understanding of the genetic development of different neurodegenerative diseases
* Rapid, high throughput screening for therapeutic targets
* Validation testing of potential therapeutics
Patent Information:
Patent Pending ([WO/2014/071042 A1](http://patentscope.wipo.int/search/en/WO2014071042))
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Institution

Columbia University

Inventors

Hynek Wichterle

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com