Neuron and astrocyte co-culture method for development of molecular ALS therapies

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Technology description

Summary

Amyotrophic lateral sclerosis (ALS) is a debilitating progressive neurological disease with very few medical options, most of which are only palliative. This imbalance in treatment options is due in part to a paucity of model systems that recapitulate the complex progression of ALS, therefore allowing the screening and evaluation of potential therapeutic agents against this disease. This technology is a method for co-culturing stem cell derived motor neurons with astrocytes. Further, this technology is able to model the neuronal death seen in ALS caused by a mutation in the SOD1 enzyme. As such this technology provides a robust platform for the evaluation of molecules with therapeutic potential for treating ALS.

Robust cellular growth and monitoring allows for rapid drug development

This technology overcomes much of the difficulty associated with neuronal cell culture by generating the neurons from stem cells. Thus, these cells can be readily expanded and seeded. Furthermore, neuronal viability can be monitored via fluorescence of GFP stably integrated into the stem cell's genome. To model the neural environment of ALS, stem cell derived neurons are grown on a monolayer of astrocytes expressing a mutant SOD1 protein which is specifically lethal to motor neurons. As such this technology is a robust cellular model of ALS. Implementation of this technology may result in a rigorous and robust system for the discovery of therapeutic molecules that prevent the death of motor neurons, potentially aiding in the development of curative therapies for ALS.

A working prototype of this technology has been developed and validated by comparison to primary neuron morphology and behavior.

Tech Ventures Reference: IR 2156

Publications

Nagai M., Re D.B., Nagata T., Chalazonitis A., Jessell T.M., Wichterle H., Przedborski S. "Astrocytes expressing ALS-linked mutated SOD1 release factors selectively toxic to motor neurons" Nature Neuroscience. 15 April 2007; 10 (5) 615-622.

Web Links

WIPO: WO/2008/127974

Application area

Development and discovery of the underlying molecular mechanisms causing ALS and other degenerative motor neuron diseases

Discovery platform for identifying novel biomarkers of ALS for use in diagnostic testing

Platform for the discovery of molecules with therapeutic potential against ALS

Initial assessment of the therapeutic index of neuroprotective compounds, as stem cells can be differentiated into non-neuron cell types

Transferable to a wide number of neurological diseases as the expression of mutant proteins in astrocytes or motor neurons can be easily modified

Advantages

Low cost as stem cells can be propagated and expanded into large numbers for thorough testing

Applicable to HTS or other highly parallel processes as fluorescence monitoring of cell viability and number can be readily quantified

Operationally straightforward, avoiding many of the difficulties associated with primary neuron cultures

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