A drug-screening platform for autism spectrum disorders using human astrocytes

Grant Award Details

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Grant Type: Early Translational IV

Grant Number: TR4-06747

Project Objective: This project is a CFP collaboration between Muotri and the Ferrer lab at NIH which is part of the NCATS and has expertise in high throughput screening technologies. The project is examining astrocyte dysfunction in autism spectrum disorders (ASDs) and specifically Rett syndrome (RTT). They are using iPSCs from RTT and control patients to differentiate astrocytes and look for phenotypic differences that could be used to screen for drugs and therapeutics that can rescue the cellular and molecular readouts.

Investigator:

Name:	Alysson Muotri
Institution:	University of California, San Diego
Type:	PI

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Name:	Marc Ferrer
Institution:	National Institutes of Health
Type:	Partner-PI

Disease Focus: Autism, Neurological Disorders, Pediatrics, Rett's Syndrome

Collaborative Funder: NIH

Human Stem Cell Use: iPS Cell

Award Value: $1,656,456

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: A drug-screening platform for autism spectrum disorders using human astrocytes

Public Abstract: Autism spectrum disorders (ASD) are complex neurodevelopmental diseases that affect about 1% of children in the United States. Such diseases are mainly characterized by deficits in verbal communication, impaired social interaction, and limited and repetitive interests and behavior. The causes and best treatments remain uncertain. One of the major impediments to ASD research is the lack of relevant human disease models. Reprogramming of somatic cells to a pluripotent state (induced pluripotent stem cells, iPSCs) has been accomplished using human cells. Isogenic pluripotent cells are attractive from the prospective to understanding complex diseases, such as ASD. The main goal of this project is to accelerate drug discovery to treat ASD using astrocytes generated from human iPSC. The model recapitulates early stages of ASD and represents a promising cellular tool for drug screening, diagnosis and personalized treatment. By testing whether drugs have differential effects in iPSC-derived astrocytes, we can begin to unravel how genetic variation in ASD dictates responses to different drugs. Insights that emerge from our studies may drive the development of new therapeutic interventions for ASD. They may also illuminate possible differences in drug responsiveness in different patients and potentially define a molecular signature resulting from ASD variants, which could predict the onset of disease before symptoms are seen.

Statement of Benefit to California: Autism spectrum disorders, including Rett syndrome, Angelman syndrome, Timothy syndrome, Fragile X syndrome, Tuberous sclerosis, Asperger syndrome or childhood disintegrative disorder, affect many Californian children. In the absence of a functionally effective cure or early diagnostic tool, the cost of caring for patients with such pediatric diseases is high, in addition to a major personal and family impact since childhood. The strikingly high prevalence of ASD, dramatically increasing over the past years, has led to the emotional view that ASD can be traced to a single source, such as vaccine, preservatives or other environmental factors. Such perspective has a negative impact on science and society in general. Our major goal is to develop a drug-screening platform to rescue deficiencies showed from brain cells derived from induced pluripotent stem cells generated from patients with ASD. If successful, our model will bring novel insights on the dentification of potential diagnostics for early detection of ASD risk, or ability to predict severity of particular symptoms. In addition, the development of this type of pharmacological therapeutic approach in California will serve as an important proof of principle and stimulate the formation of businesses that seek to develop these types of therapies (providing banks of inducible pluripotent stem cells) in California with consequent economic benefit.