A Human Model for Studying and Treating Rett Syndrome and Other Autism Spectrum Disorders

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BACKGROUND

Mutations and duplication of the X-linked MeCP2 gene are observed in several disorders, such as Rett Syndrome (RTT), Autism, severe neonatal encephalopathy, schizophrenia and X-linked mental retardation. As MeCP2 plays an important role in the pathogenesis of multiple mental disorders, the investigation of MeCP2 function and regulatory pathways may show promise for developing broad-spectrum therapies. Downstream MeCP2 target genes, such as the calcium channel TRPC6, can have a secondary impact on the cell and predispose the individual to autism.

TECHNOLOGY DESCRIPTION

UCSD researchers have demonstrated that RTT-derived neurons, deriving from patients carrying different MeCP2 mutations, can recapitulate some of the disease aspects, such as decreased in spine density, reduced glutamatergic synapses and defective neuronal networks. They also found drugs able to rescue synaptic deficiency in RTT neurons, as a proof-of-principle for a future drug screening platform. Together, such results suggest that RTT, and likely other neurological disorders can be modeled using induced pluripotent stem cells (iPSC) technology to investigate the molecular mechanisms underlying their abnormalities. The same technology can be combined with genomics to study idiopathic (sporadic) types of autism.

APPLICATIONS

This cellular model has the potential to lead to the discovery of new compounds to treat RTT, autism and other neurodevelopmental diseases. As another exemple, this plataform was used to detect alteration in TRPC6 expression in an autistic patient. Using iPSC-dervied neurons, it was possible to design a personalized medicine using nutritional complements in patient's diet.

ADVANTAGES

Automated and high through screening system with highly efficient neuronal and astrocyte differentiation protocol for a cellular and molecular read outs, such as synapse formation.

Stage of development: Screening system with several iPSC cell lines carrying different MeCP2 and TRPC6 mutations have been used to identify promising regulatory pathways and potential drug candidates.

STATE OF DEVELOPMENT

Screening system with several iPSC cell lines carrying different MeCP2 and TRPC6 mutations have been used to identify promising regulatory pathways and potential drug candidates.

INTELLECTUAL PROPERTY INFO

Patent pending. PCT application WO 2013163455 A2 titled "A drug screening platform for Rett syndrome"

RELATED MATERIALS

- Available upon request. Tang, X., Zhou, L., Wagner, A.M., Marchetto. M.C.N., Muotri, A. R., Gage, F.H., & Chen, G. Astroglial cells regulate the developmental timeline of human neurons differentiated from induced pluripotent stem cells. Stem Cell Research. 2, 743-57 (2013). - 09/01/2013
- Available upon request. Tang, X., Zhou, L., Wagner, A.M., Marchetto. M.C.N., Muotri, A. R., Gage, F.H., & Chen, G. Astroglial cells regulate the developmental timeline of human neurons differentiated from induced pluripotent stem cells. Stem Cell Research. 2, 743-57

CONTACT

University of California, San Diego
Office of Innovation and Commercialization
innovation@ucsd.edu
tel: 858.534.5815.

OTHER INFORMATION

KEYWORDS

Rett Syndrome, Autism Spectrum Disorders, Neurodevelopmental, Drug screening, MeCP2, TRPC6

CATEGORIZED AS

- **Medical**
  - Disease: Central Nervous System
  - Screening
- **Research Tools**
  - Screening Assays

RELATED CASES

2011-281-0

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▶ Available upon request. Marchetto MC, Carromeu C, Acab A, Yu D, Yeo GW, Mu Y, Chen G, Gage FH, Muotri AR. A model for neural development and treatment of Rett syndrome using human induced pluripotent stem cells. Cell. 2010 Nov 12;143(4):527-39. - 11/12/2010

University of California, San Diego
Office of Innovation and Commercialization
9500 Gilman Drive, MC 0910, ,
La Jolla,CA 92093-0910

Tel: 858.534.5815
innovation@ucsd.edu
https://innovation.ucsd.edu
Fax: 858.534.7345