Brazilian Zika Virus Cellular Models

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BACKGROUND

Zika Virus (ZIKV) is an arbovirus of the genus Flavivirus Flaviviridae linked to microencephaly, as one form of congenital malformation, and also Guillain–Barré syndrome, and other severe neurological diseases. Dr Alysson Muotri and coworkers recently published in the journal Nature results of research using cellular models of the Brazilian Zika virus strain causing birth defects.This drug screening platform represents a useful human model of microcephaly due to Zika virus in a mouse model.

TECHNOLOGY DESCRIPTION

Researchers have created a human/mouse platform to test the impact of the zika virus in the nervous system, discovering that the Brazilian strain of Zika virus can cross the placenta and infect the fetus. The results also indicate that this phenomenon is dependent on genetic variation. The researchers have created a human platform using pluripotent stem cells, to test the impact of Zika during cell proliferation, aggregation, formation of neurospheres, neuronal maturation, and structural brain organization using cerebral organoids in vitro.

The suspected link between infection by Zika virus (ZIKV), a re-emerging flavivirus, and microcephaly is an urgent global health concern. The direct target cells of ZIKV in the developing human fetus are not clear. The recent publication in Nature indicates that a strain of the ZIKV, MR766, serially passaged in monkey and mosquito cells efficiently infects human neural progenitor cells (hNPCs) derived from induced pluripotent stem cells. Infected hNPCs further release infectious ZIKV particles. Importantly, ZIKV infection increases cell death and dysregulates cell-cycle progression, resulting in attenuated hNPC growth. Global gene expression analysis of infected hNPCs reveals transcriptional dysregulation, notably of cell-cycle-related pathways. These results identify hNPCs as a direct ZIKV target. In addition, researchers have established a tractable experimental model system to investigate the impact and mechanism of ZIKV on human brain development and provide a platform to screen therapeutic compounds.

ADVANTAGES

This is a unique platform, never described before. Using potential therapeutic interventions, such as drugs or vaccines, laboratories around the world can use this system to investigate whether a putative anti-Zika candidate actually works, potentially utilizing this model to generate data relating to the efficacy of the therapeutic candidate in human/mouse models.

STATE OF DEVELOPMENT

These materials are available to academic and non-profit research groups under a Material Transfer Agreement. These materials are also available under a commercial license

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OTHER INFORMATION

KEYWORDS

Zika virus Drug screening Human model, mouse model Microcephaly

CATEGORIZED AS

- Research Tools
  - Animal Models

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▶ The Brazilian Zika virus strain causes birth defects in experimental models Fernanda R. Cugola, Isabella R. Fernandes, Fabiele B. Russo, Beatriz C. Freitas, João L. M. Dias, Katia P. Guimarães, Cecília Benazzato, Nathalia Almeida, Graciela C. Pignatari, Sarah Romero, Carolina M. Polonio, Isabela Cunha, Carla L. Freitas, Wesley N. Brandão, Cristiano Rossato, David G. Andrade, Daniele de P. Faria, Alexandre T. Garcez, Carlos A. Buchpigel, Carla T. Braconi, Erica Mendes, Amadou A. Sall, Paolo M. de A. Zanotto, Jean Pierre S. Peron, Alysson R. Muotri Nature (2016) doi:10.1038/nature18296 Received 08 March 2015 Accepted 04 May 2016 Published online 11 May 2016

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