Medical Xpress

# Researchers 'grow Rett syndrome' in a Petri dish

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A groundbreaking study published Friday in the leading scientific journal, *Cell*, revealed that a team of investigators had successfully generated nerve cells using skin cells from four individuals with Rett syndrome. The study was led by Dr. Alysson Muotri at the University of California, San Diego -- a leading researcher in the stem cell field.

The article, titled 'A Model for Neural Development and Treatment of Rett Syndrome Using Human Induced Pluripotent Stem Cells,' describes how the team used a newly-devised procedure to reprogram the skins cells - literally winding back their developmental clock to an earlier state and transforming them into stem cells. The researchers then employed a second novel technique, taking the newly-formed stem cells and driving them along a developmental path to form nerve cells. When Dr. Muotri and his team examined these new nerve cells closely, they observed characteristic hallmarks of nerve cells with Rett syndrome, including fewer synapses, smaller cell bodies and changes in the cells' signaling capabilities.

The group then took their work a step further; testing several drugs previously shown to be effective in mouse models of Rett syndrome, they provided evidence of functional rescue, using human cells. In 1999, the laboratory of Dr. Huda Zoghbi at Baylor College of Medicine, made a seminal discovery, identifying a causative link between mutations in the gene methyl-CpG-binding protein 2 (MeCP2) and Rett syndrome. This led to further work showing the MeCP2 protein is critical for the proper functioning of nerve cells.

In 2007 another study in the laboratory of Dr. Adrian Bird at the University of Edinburgh, Scotland showed that restoration of MeCP2 function in a mouse model of the disease reverses the neurological symptoms in adult mice. This finding provided a critical proof of concept that symptoms of the disorder may be reversible in humans. However, to date, no effective pharmacological treatments have been developed.

The main limitation for human studies and thus, drug development, has been the inaccessibility of live neurons from human patients. To get around this issue, the use of induced pluripotent stem cells (iPSCs) to establish a human cell-based model of Rett syndrome is key to the development of high throughput drug screens and therefore has been an area of the highest priority for IRSF who provided a post-doctoral fellowship Award to Dr. Cassiano Carromeu, a member of the team and a co-author of the current study. The study's principal author, Dr. Alysson Muotri, said, "Dr. Bird's data shows that you can reverse symptoms in a mouse model, now we've shown that this could be done using human cells." "I think the future is to push this in a high throughput screening platform to develop new drugs," he continued.

IRSF recently provided funding to support a new program for Rett syndrome-specific drug development, titled the "Selected Molecular Agents for Rett Therapeutics" (SMART) Initiative. The SMART Initiative will assemble a collection of brain-specific drugs that target select biological mechanisms important in RTT and make the compound collection available to researchers worldwide. IRSF's Chief Scientific Officer, Dr. Antony Horton said "IRSF has been proactive in moving iPSC technology forward for the purpose of drug screening, which is aligned well with the new SMART Initiative." "With the publication of this study, a major hurdle has been overcome in our quest to develop and test new medicines for the benefit of people living with Rett syndrome." added Dr. Horton.

Provided by International Rett Syndrome Foundation