Developmental disease is recreated in an adult model

2 June 2011

A new study published today in the journal *Science* has shown that the childhood disorder Rett syndrome, can be reestablished in adult animals by "switching off" a critical disease causing gene in healthy adult animals. The gene was "switched off" in adult mice by use of a sophisticated genetic trick, resulting in the appearance of behaviors typically seen in Rett syndrome. The leading author Christopher McGraw, MD/PhD student, carried out the study in the laboratory of Dr. Huda Zoghbi, a renowned neuroscientist based at Baylor College of Medicine, and director of the Jan and Dan Duncan Neurological Research Institute at Texas Children's Hospital in Houston TX.

In 1999 Dr. Zoghbi's laboratory made a central discovery, identifying the causative link between mutations in the gene methyl-CpG-binding protein 2 (MeCP2) and Rett syndrome. This work led to other studies showing that MeCP2 protein is critical for the proper functioning of nerve cells during development and into adulthood. In 2007 a further study conducted by Dr. Adrian Bird, at Edinburgh University in the UK, showed the neurological symptoms of Rett syndrome can be reversed by reactivating MeCP2 in an adult mouse where the disease is already established. This work provided a critical proof of concept that symptoms of the disorder may be reversible in humans; however, to-date it was not known whether the early developmental period was important in establishing the course of the disease. This new study argues that early expression of the gene does not protect against the development of symptoms if the disease gene is later inactivated.

Commenting on the study, Dr. Zoghbi said "We did this experiment to see if providing MeCP2 early on in life, during critical periods of brain maturation, would be partially protective from loss of this protein in the adult brain. We were surprised to see that the nervous system had no detectable protection when MeCP2 was lost in adulthood. This affirmed that brain cells must have MeCP2 at all times to function normally."

There have been no effective pharmacological treatments developed to treat the disorder although new therapeutic trials are currently underway. This work suggests that therapies for Rett syndrome may need to be continuously maintained throughout the course of an individual's life.

Provided by International Rett Syndrome Foundation