A mouse Mecp2*-null mutation causes neurological symptoms that mimic Rett syndrome*

Jacky Guy[1], Brian Hendrich[1], Megan Holmes[2], Joanne E. Martin[3] & Adrian Bird[1]

Nature Genetics **27**, 322 - 326 (2001)

doi:10.1038/85899

The MECP2 gene provides instructions for making a protein (MeCP2) that is essential for normal brain development. This protein seems to be important for the function of nerve cells in the brain and is present in high levels in mature nerve cells.

Studies suggest that the MeCP2 protein plays a role in forming connections (synapses) between nerve cells, where cell-to-cell communication occurs.

Source: http://ghr.nlm.nih.gov/gene/MECP2

Abstract

Rett syndrome (RTT) is an inherited neurodevelopmental disorder of females that occurs once in 10,000–15,000 births[1, 2]. Affected females develop normally for 6–18 months, but then lose voluntary movements, including speech and hand skills. Most RTT patients are heterozygous for mutations in the X-linked gene *MECP2* (refs. 3–12), encoding a protein that binds to methylated sites in genomic DNA and facilitates gene silencing[13, 14, 15, 16, 17]. Previous work with *Mecp2*-null embryonic stem cells indicated that MeCP2 is essential for mouse embryogenesis[18]. Here we generate mice lacking *Mecp2* using Cre-*loxP* technology. Both *Mecp2*-null mice and mice in which *Mecp2* was deleted in brain showed severe neurological symptoms at approximately six weeks of age. Compensation for absence of MeCP2 in other tissues by MeCP1 (refs. 19,20) was not apparent in genetic or biochemical tests. After several months, heterozygous female mice also showed behavioral symptoms. The overlapping delay before symptom onset in humans and mice, despite their profoundly different rates of development, raises the possibility that stability of brain function, not brain development *per se*, is compromised by the absence of MeCP2.