NEWS

Genetics: Prader-Willi syndrome gene is new autism candidate

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Rare risk: A boy with a mutation in the MAGEL2 gene has autism and had trouble feeding as an infant.

Mutations in a single gene in 15q11.13 — a chromosomal region linked to multiple neurological disorders — may increase the risk of autism, according a study published in November in *Nature Genetics*[1].

This gene, called MAGEL2, is expressed only from the paternally inherited chromosome. It may function to enhance the activity of **UBE3A**, which **has been linked to autism**.

The 15q11.13 region is linked to several disorders: Loss of the maternal copy leads to **Angelman syndrome**, duplication of the maternal copy **increases the risk of autism**, and deletion of the paternal copy leads to Prader-Willi syndrome.

Mice lacking MAGEL2 have symptoms that resemble Prader-Willi syndrome, including obesity. No single gene leads to all the symptoms of Prader-Willi in mice, suggesting that the disorder results from loss of multiple genes in the 15q11.13 region.

Infants with Prader-Willi are small with poor muscle tone. Later, they are prone to severe overeating and have developmental delay and intellectual disability. About 20 percent of children with the syndrome also have autism[2].

In the new study, researchers found a 13-year-old boy with a mutation in MAGEL2. The boy has autism, intellectual disability and some symptoms of Prader-Willi. The researchers then looked at the region in 1,248 individuals from the Baylor College of Medicine **Whole Genome Laboratory** sequencing database. They found three more people with mutations in MAGEL2. All three also have autism and intellectual disability.

Each of these individuals has a different set of features of Prader-Willi syndrome; only one meets all the criteria for a full diagnosis.

The results show that alterations in a single paternally expressed gene in the 15q11.13 region lead to some of the symptoms of Prader-Willi syndrome. It also suggests that MAGEL2 is a new candidate gene for autism.

References:

1: Schaaf C.P. *et al. Nat. Genet.* **45**, 1405-1408 (2013) **PubMed**

2: Descheemaeker M.J. *et al. Am. J. Med. Genet. A.* **140**, 1136-1142 (2006) **PubMed**