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Gene causing birth defects in mice discovered

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Cornell researchers report that they have identified a gene that causes neural tube defects (NTDs) in laboratory mice. NTDs, also known as spina bifida and anencephaly, are one of the most common birth defects in the United States, occurring every 1 in 1,000 births.

Women who are at risk potential of having babies with NTDs cannot be identified because the genes causing this birth defect have not been evident.

The new study, published in the American Journal of Clinical Nutrition (February 2011), provides evidence that the so-called Shmt1 gene and most likely the entire folate pathway for thymidylate synthesis in which Shmt1 participates, is responsible for human NTDs.

"Although it must be proven through human studies, based on the similarity of folate metabolism in mice and humans, it is likely that this gene is associated with human NTDs," said Patrick Stover, professor in the Division of Nutritional Sciences.

Certain women are genetically prone to having a child with an NTD, and maternal folic acid consumption before and during pregnancy can reduce the risk up to 70 percent, Stover said. Women who do not know they are susceptible to this birth defect may not take the necessary measures to protect their unborn child, he said; the defect can form as early as 28 days after conception.

In this study, Stover and Cornell colleagues disrupted a gene known to

interact with folate and showed that it resulted in folate-responsive neural tube defects. They discovered that deletion of just one copy of the Shmt1 gene in mice resulted in 50 percent less Shmt1 protein expression and in folic acid-responsive neural tube defects.

"This is the first example of a genetically altered mouse model that exhibits folate-responsive NTDs when a folate-metabolizing gene is knocked out, where as many other folate-related genes have been knocked out and not resulted in NTDs," said Stover. "This tells us which pathway in folate metabolism leads to NTDs."

The findings also suggest that other types of nutritional interventions, such as nucleotide supplementation, may be more effective than folic acid to prevent NTDs, but this would have to be verified experimentally. In the 1990s, the U.S. government fortified the food supply with folic acid to prevent human NTDs.

Provided by Cornell University