MedicalXpress

Malnutrition during pregnancy may affect the health of future generations

May 1 2014

New research reveals how environmental factors in the womb can predispose not only the mother's own offspring but also the grandoffspring to metabolic disorders like liver disease. Researchers reporting in the Cell Press journal *Cell Metabolism* found for pregnant mice that are malnourished—experiencing a 50% caloric restriction during the last week of pregnancy—that their offspring are at first growth restricted and have low birth weight but then go on to become obese and diabetic as they age. Strikingly, in a domino effect, the offspring of the growth-restricted males also inherit the predisposition to metabolic abnormalities.

To investigate how these effects may be arising, leading author Dr. Josep Jiménez-Chillarón, of the Hospital Sant Joan de Déu in Spain, and his colleagues looked at the patterns of gene expression in mice. They found that in utero malnutrition of males influenced the expression of the gene LXR, which regulates fat and cholesterol metabolism in the livers of the males' offspring. This was partly due to an epigenetic change called DNA methylation. Such a change affects gene activity without changing the DNA's underlying sequence. The same pattern of methylation could be found in the sperm of the male mice that experienced in utero malnutrition. "This may contribute, in part, to the transmission of diabetes risk from parents to offspring," says Jiménez-Chillarón.

The findings indicate that in a fetus' reproductive cells, in utero malnutrition causes epigenetic changes that are subsequently transmitted to cells of the next generation. If these findings hold true for humans,

what a woman eats while pregnant may have some effects on health and disease in her future grandchildren.

"Current dogma proposes that the vast majority of epigenetic modifications in the sperm and eggs are erased precisely to avoid transmission of environmentally derived changes. But our data suggest that a few environmentally induced epigenetic modifications may be passed and stably maintained in the next generation," says Jiménez-Chillarón. This opens up the possibility that predisposition for some complex diseases might be inherited independently from one's genetic sequence. However, Jiménez-Chillarón notes that it is important not to fall into the temptation of "blaming" one's parents (or even grandparents) for disease: "Our view is that we inherit some predisposition, but it is our own lifestyle that will determine whether inherited risk will truly translate into disease. Hence, a healthy lifestyle is the best way to prevent any potentially inherited or newly acquired obesity or diabetes predisposition."

More information: *Cell Metabolism*, Martinez et al.: "In utero undernutrition in male mice programs liver lipid metabolism in the second-generation offspring involving altered Lxra DNA methylation." http://www.cell.com/cell-metabolism/abstract/S1550-4131(14)00160-0

Provided by Cell Press