Medical Xpress

You are what your father ate: Paternal diet affects lipid metabolizing genes in offspring

December 23 2010

Scientists at the University of Massachusetts Medical School and the University of Texas at Austin have uncovered evidence that environmental influences experienced by a father can be passed down to the next generation, "reprogramming" how genes function in offspring. A new study published this week in *Cell* shows that environmental cues—in this case, diet—influence genes in mammals from one generation to the next, evidence that until now has been sparse. These insights, coupled with previous human epidemiological studies, suggest that paternal environmental effects may play a more important role in complex diseases such as diabetes and heart disease than previously believed.

"Knowing what your parents were doing before you were conceived is turning out to be important in determining what disease risk factors you may be carrying," said Oliver J. Rando, MD, PhD, associate professor of biochemistry & molecular pharmacology at UMMS and principal investigator for the study, which details how paternal diet can increase production of cholesterol synthesis genes in first-generation offspring.

The human genome is often described as the set of instructions that govern the development and functioning of life. It's not surprising, then, that most contemporary genetic research focuses on understanding and cataloging how mutations and changes to our DNA—the basis of those "instructions"—cause disease and impact health. A number of recent studies, however, have begun to draw attention to the role epigenetic inheritance – inherited changes in gene expression caused by mechanisms other than changes in the underlying DNA sequence – may play in a host of illnesses. "A major and underappreciated aspect of what is transmitted from parent to child is ancestral environment," said Dr. Rando. "Our findings suggest there are many ways that parents can 'tell' their children things."

To test their hypothesis that environmental influences experienced by the father can be passed down to the next generation in the form of changed epigenetic information, Rando and colleagues fed different diets to two groups of male mice. The first group received a standard diet, while the second received a low-protein diet. To control for maternal influences, all females were fed the same, standard diet. Rando and colleagues observed that offspring of the mice fed the low-protein diet exhibited a marked increase in the genes responsible for lipid and cholesterol synthesis in comparison to offspring of the control group fed the standard diet.

These observations are consistent with epidemiological data from two well-known human studies suggesting that parental diet has an effect on the health of offspring. One of these studies, called the Överkalix Cohort Study, conducted among residents of an isolated community in the far northeast of Sweden, found that poor diet during the paternal grandfather's adolescence increased the risk of diabetes, obesity and cardiovascular disease in second-generation offspring. However, because these studies are retrospective and involve dynamic populations, they are unable to completely account for all social and economic variables. "Our study begins to rule out the possibility that social and economic factors, or differences in the DNA sequence, may be contributing to what we're seeing," said Rando. "It strongly implicates epigenetic inheritance as a contributing factor to changes in gene function."

The results also have implications for our understanding of evolutionary processes, says Hans A. Hofmann, PhD, associate professor of integrative biology at the University of Texas at Austin and a co-author of the study. "It has increasingly become clear in recent years that mothers can endow their offspring with information about the environment, for instance via early experience and maternal factors, and thus make them possibly better adapted to environmental change. Our results show that offspring can inherit such acquired characters even from a parent they have never directly interacted with, which provides a novel mechanism through which natural selection could act in the course of evolution." Such a process was first proposed by the early evolutionist Jean-Baptiste Lamarck, but then dismissed by 20th century biologists when genetic evidence seemed to provide a sufficient explanation.

Taken together, these studies suggest that a better understanding of the environment experienced by our parents, such as diet, may be a useful clinical tool for assessing disease risk for illnesses, such as diabetes or heart disease. "We often look at a patient's behavior and their genes to assess risk," said Rando. "If the patient smokes, they are going to be at an increased risk for cancer. If the family has a long history of heart disease, they might carry a gene that makes them more susceptible to heart disease. But we're more than just our genes and our behavior. Knowing what environmental factors your parents experienced is also important."

The next step for Rando and colleagues is to explore how and why this genetic reprogramming is being transmitted from generation to generation. "We don't know why these genes are being reprogrammed or how, precisely, that information is being passed down to the next generation," said Rando. "It's consistent with the idea that when parents go hungry, it's best for offspring to hoard calories, however, it's not clear if these changes are advantageous in the context of a low-protein diet."

Provided by University of Massachusetts Medical School