MedicalXpress

Paternal obesity impacts child's chances of cancer

February 5 2013

A father's obesity is one factor that may influence his children's health and potentially raise their risk for diseases like cancer, according to new research from Duke Medicine.

The study, which appears Feb. 6 in the journal *BMC Medicine*, is the first in humans to show that paternal obesity may alter a genetic mechanism in the next generation, suggesting that a father's lifestyle factors may be transmitted to his children.

"Understanding the risks of the current Western lifestyle on future generations is important," said molecular biologist Adelheid Soubry, PhD, a postdoctoral associate at Duke Cancer Institute and the study's lead author. "The aim of this study was to determine potential associations between obesity in parents prior to conception and epigenetic profiles in offspring, particularly at certain gene regulatory regions."

Researchers looking at health outcomes in newborns have historically focused on pregnant women. Studies have shown that nutrition and environmental factors during pregnancy can affect children's health and may raise their risk of chronic diseases. However, little has been done to uncover how paternal factors can affect children.

The Duke research team sought to determine associations between obesity in parents and changes in DNA methylation at the insulin-like growth factor 2 (IGF2) gene among offspring. DNA methylation

regulates the activity of certain genes, which can reflect a higher risk for some diseases. Decreased DNA methylation at the IGF2 gene has been associated with an increased risk of developing certain cancers, including colorectal and ovarian cancers.

"Our genes are able to adapt to our environment. However, we adjust in a way that may be problematic later," said Cathrine Hoyo, PhD, MPH, a cancer epidemiologist at Duke Medicine and the study's senior author. "It is not a change in the sequence of the DNA itself, but how genes are expressed. Some genes may get 'shut off' as a result of environmental trauma."

To gather data on newborn health outcomes, the researchers followed families enrolled in the Newborn Epigenetics Study (NEST), a research program developed by Hoyo and funded by the National Institutes of Health to test the influence of environmental exposures on genetic profiles in newborns.

Researchers gathered information about the mothers and fathers using questionnaires and medical records. They then examined DNA from the umbilical cords of 79 newborns to determine potential associations between the offspring's DNA methylation patterns and parental obesity before conception.

DNA methylation at the IGF2 gene in the offspring of obese fathers was significantly lower than in the children of fathers who were not obese. This suggests that paternal obesity may be associated with an increased risk of children developing certain cancers.

The researchers noted that the changes in DNA methylation could have been a result of something related to obesity, such as eating a certain diet or having diabetes, that was not measured in this study.

Additional research is underway to see if these changes in DNA methylation at the IGF2 gene remain as the children grow older. Future studies may also determine if certain interventions – similar to women taking folic acid while pregnant to prevent birth defects – can be used prior to or after conception to prevent irregular methylation profiles.

"This study is an important start in looking at the effects of environmental exposure on children, not only through the mother but also through the father," said Soubry. "Although we cannot define at this point which obesity-related factor may cause an epigenetic effect, we measured in this study a significant association between paternal obesity and aberrant methylation profiles in the offspring."

More information: Paternal obesity is associated with IGF2 hypomethylation in newborns: results from a Newborn Epigenetics Study (NEST) cohort Adelheid Soubry, Joellen M Schildkraut, Amy Murtha, Frances Wang, Zhiqing Huang, Autumn Bernal, Joanne Kurtzberg, Randy L Jirtle, Susan K Murphy and Cathrine Hoyo, *BMC Medicine*, (in press)

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