Medical Xpress

Undernutrition during pregnancy changes lung-specific gene expression

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Children born to women pregnant during the Dutch famine were more likely to have a constellation of health problems including cardiovascular disease and asthma, but the exact mechanisms that cause this epigenetic inheritance have not been fully explored. Now researchers at Jefferson show how a mother's diet can affect epigenetic markers of her offspring and result in changes to genes that regulate lung health.

"The findings paint a clearer picture of how a mother's nutrition and environment can affect her child's health," says senior author pulmonologist Jesse Roman, MD, Professor and CEO of the Jane & Leonard Korman Respiratory Institute - Jefferson Health and National Jewish Health. "Epigenetic mechanisms are powerful in biology and we're really still scratching the surface in trying to understand them." The research was published in the journal *Nutrition Research.*

Epigenetic changes may allow for a mother's experiences to be passed to the offspring. Genetically, it's not possible for mutations in skin or liver cells acquired over the course of a lifetime to be passed to a child. Children get a clean genetic slate. But, epigenetic changes can be passed down.

If a person's genome is a set of blueprints or plans for building an organism, then a genetic mutation would be penciling in a new wall, or erasing a floor from those plans. Rather than change the blueprint, epigenetic changes leave the blueprint intact, but instead, roll up a page into a tight and inaccessible bundle. The plans, or genes, on those rolled

pages, can't be read by the cell's architects. Other types of epigenetic changes prevent pages from getting rolled at all, causing many more of that architectural element, or protein, to be made than needed.

When Dr. Roman, together with first author Igor Zelko, Ph.D., from the University of Louisville, Kentucky and colleagues, examined the lung-related genes in offspring of mice whose diet was limited during the second and third trimesters of gestation, they saw that a handful of them had a different expression level than mice who ate freely.

In particular, the expression of two genes were turned up via epigenetic mechanisms that in this case, kept the blueprint open longer than needed, producing more of that protein. The researchers found higher levels of fibronectin in mice born to malnourished mothers. Fibronectin is a connective tissue molecule that provides a substrate on which cells can organize. However, its fragments may attract neutrophils, an immune cell that can exacerbate inflammatory reactions, like asthma. Expression of the Selplg gene was also turned up. Higher levels of Selplg may predispose blood vessels to inflammation as well as clotting.

"The work represents a first step in understanding how gene expression is affected by the environment. In this case, malnutrition resulted in changes in gene expression through epigenetic changes that could be potentially transferred down through the generations," says Dr. Roman. "The next steps would be to understand how these genes might affect lung function in these offspring and what other factors can influence these events."

More information: Igor N. Zelko et al, Maternal undernutrition during pregnancy alters the epigenetic landscape and the expression of endothelial function genes in male progeny, *Nutrition Research* (2018). DOI: 10.1016/j.nutres.2018.10.005

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