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How genes link a mother's diet to the risk of obesity in her offspring

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Many research studies have made it clear that a mother's eating habits prior to pregnancy, during pregnancy and during lactation have a profound impact on her offspring and their propensity for developing weight problems, including obesity. However, until now, the mechanisms behind this phenomenon were unclear. According to new research published in the September 2014 issue of *The FASEB Journal*F, scientists using an animal model found an epigenetic link between a mother's diet and an offspring's risk of future obesity. This link hinges on the blocked expression of a gene called Pomc, which manages a discrete area of the brain that controls feeding behavior. Excess methylation on the DNA sequence blocks the ability to express this gene, leading to a late satiety response, increased food intake and eventually to obesity.

"Parental obesity and diet can affect the children's likelihood to overeat and develop obesity. Changes in epigenetic programming have been implicated as one of the mechanisms underlying this phenomenon," said Asaf Marco, Ph.D., a researcher involved in the work from the Faculty of Life Sciences at Bar Ilan University in Ramat-Gan, Israel. "We observed a clear correspondence between a specific epigenetic mechanism and weight gain, potentially allowing for early detection and prevention of obesity."

To make this discovery, Marco and colleagues fed female rats either a high-fat diet or a standard diet from post-weaning to adulthood and in separate groups, throughout pregnancy and lactation. All offspring,

including those of the high-fat treated rats, received standard food after weaning until adulthood. Blood was analyzed for hormone levels and brain sections for epigenetic modification on the specific DNA sequence of interest. Results showed that unmated female rats, chronically fed a high-fat diet, presented obesity associated with disruptions in an epigenetic mechanism that controls the production of Pomc. However, due to the sharp weight loss during lactation, rats who consumed a high-fat diet presented normal weight and a normalized epigenetic mechanism. Because methylation on the genes is typically considered stable and relatively permanent, this opens the door for future drug development. Researchers found that epigenetic malprogramming induced by maternal high-fat diet had a long-term effect on the offspring's vulnerability to develop obesity. These effects were not reprogrammed by providing standard food to the pups after weaning and the offspring maintained their obesogenic phenotype until adulthood.

"Shining light on heritable, epigenetic factors that cause obesity should help us shed unwanted pounds in future generations," said Gerald Weissmann, M.D., Editor-in-Chief of *The FASEB Journal*. "This research shows that being overweight and obese has a direct impact on the genes we use to signal when it's time to stop eating."

More information: Asaf Marco, Tatiana Kisliouk, Tzlil Tabachnik, Noam Meiri, and Aron Weller. Overweight and CpG methylation of the Pomc promoter in offspring of high-fat-diet-fed dams are not "reprogrammed" by regular chow diet in rats. *FASEB J*. September 2014 28:4148-4157; DOI: 10.1096/fj.14-255620

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