High levels of specific DNA methylation are linked to greater birth weight and higher adiposity

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A*STAR researchers uncover evidence that the relationship between HIF3A methylation levels and weight begins before birth. Their findings may hold significant implications regarding the development of weight-related disorders such as obesity later in life. Credit: janulla/iStock/Thinkstock

The theory that weight gain is partly predetermined by our DNA, and not just a result of adult habits, has gained traction among obesity researchers. Now, scientists at A*STAR have discovered that epigenetic variations at a genetic region linked to obesity are directly linked to birth weight and an infant's 'adiposity' or baby fat.

Our DNA sequence is specified at conception, while epigenetic factors controlling DNA are modified by environment in utero and after birth. Variations in DNA methylation levels—the mechanism used by cells to regulate gene expression—have been linked to the development of certain diseases. A recent study of Caucasian adults found a link between methylation levels of the hypoxia inducible factor 3 gene (HIF3A)—a gene that responds to decreases in cellular oxygen levels—and body mass index.

"We wanted to build on this study to see if variations in HIF3A methylation levels in babies are linked to birth weight," says Joanna Holbrook, who led an international team of scientists with her colleague Neerja Karnani at the A*STAR Singapore Institute for Clinical Sciences. "If it did, it would suggest that the path to obesity starts early and is not just a consequence of adult behaviors."

The team used DNA samples collected from the umbilical cords of 991 participants in the ongoing Growing Up in Singapore Towards healthy Outcomes (GUSTO) project—a large-scale study of Asian families in Singapore conducted by KKWCH, NUHS, and SICS, which examines influences on childhood health and development from pregnancy onwards that started in 2008.

As in the adult study, Holbrook, Karnani and co-workers focused on HIF3A, also examining genetic variants linked with the gene. They found that higher HIF3A methylation was associated with greater birth weight and infant adiposity. The correlation between weight and HIF3A was significant across all genotypes, but the association was strongest in the CC-genotype. This indicates that some people's weight may be linked more strongly to higher HIF3A methylation levels than others.

"HIF3A levels and weight are already connected at birth," says Holbrook. "Something happens between conception and birth to dictate this, but so far we have not pinpointed the exact cause."

The breakthrough suggests that HIF3A could be a useful biomarker for metabolic development. Holbrook adds that a more beneficial breakthrough

would be to find a biomarker that shows whether or not an intervention to alter developmental trajectory has been successful.

"Obesity is a complex disorder, and this finding is just the tip of the iceberg," says Karnani. "It highlights the need for an exhaustive investigation of the epigenome both at birth and in the early years."

More information: Hong Pan et al. association with adiposity: the story begins before birth , *Epigenomics* (2015). DOI: 10.2217/EPI.15.45

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