Biomarker in saliva predicts childhood obesity risk

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Gloria Guzman Jimenez and her children, Sophia Sapulveda, 8, left, Eduardo Sapulveda, 10, and Andrea Sapulveda, 6, participated in the GROW trial on pediatric obesity. Credit: John Russell

A molecular marker in saliva is associated with the emergence of childhood obesity in a group of preschool-aged Hispanic children.

The intriguing discovery, reported in the journal *BMC Medical Genetics*, supports ongoing efforts to identify biomarkers associated with the emergence of childhood obesity before body mass index (BMI) is designated as obese, said Shari Barkin, MD, MSHS, director of Pediatric Obesity Research at Monroe Carell Jr. Children's Hospital at Vanderbilt.

"Understanding the factors that predispose children to obesity is important and will pave the way toward better prevention and early intervention," said Barkin, William K. Warren Foundation Professor of Medicine and chief of the Division of General Pediatrics.

The prevalence of pediatric obesity has been increasing at an alarming rate, Barkin noted, with a disproportionate burden in Hispanic populations. Pediatric obesity is associated with the onset of later comorbidities including Type 2 diabetes, high blood pressure and cancer.

"Right now, we only have crude markers to predict the emergence of obesity; we wait until the BMI is a certain number to intervene," Barkin said. "We're looking for markers that will allow us to intervene much earlier."

Barkin and her colleagues collected saliva samples at baseline from children who were enrolled in the Growing Right Onto Wellness

(GROW) trial. A total of 610 parent-preschool child pairs, 90% of whom were Hispanic, received high-dose behavioral intervention during a three-year study period. At enrollment, the children were at-risk for obesity, but not yet obese.

"Even though many of the children in our intervention group compared to our control group improved their nutrition, maintained physical activity consistent with guidelines and got sufficient sleep, 30% of them still emerged into obesity," Barkin said. "This sheds new light on how we think about the interaction of behavior and genetics and how that might contribute to health disparities."

The investigators had collected saliva as an easily accessible, non-invasive tissue that they hoped would reveal genetic and epigenetic factors that might predispose a child to obesity.

In a previous study, they analyzed saliva samples from a subset of the enrolled children for methylation of genes associated with obesity. Methylation is an epigenetic "mark" on DNA that regulates gene expression. They found that methylation at 17 DNA sites in the child's baseline saliva was associated with the mother's BMI and waist circumference, suggesting that obesity risk may be transmitted from mother to child.

Now, they have evaluated associations between baseline salivary methylation and objective changes in child BMI after three years in the study.

"At baseline, these children were all non-obese, but based on their maternal BMI, their DNA was methylated differently at 17 sites," Barkin said. "Now we know that some of them emerged into obesity. We asked, 'Could we have predicted that from differences in methylation, even after accounting for maternal BMI and assessing other behavioral

factors?'"

The answer looks like it is "yes." The investigators found that methylation of a gene called NRF1, which has roles in adipose tissue inflammation, was associated with childhood obesity. A child with the NRF1 methylation at baseline had a threefold increased odds of being obese three years later, after controlling for maternal BMI and other factors.

"This is a proof-of-principle study; it needs to be repeated with larger numbers of children," Barkin said. "But even with small numbers, we found a really important signal using salivary epigenetics."

The study demonstrates the utility of using saliva for epigenetic studies and points to at least one gene, NRF1, that should be more extensively studied for its role in the emergence of obesity.

"Most studies have looked for factors in children who are already obese," Barkin said. "Our study demonstrates that there are already changes in the physiology—a pathway to obesity—even before the phenotype of obesity emerges. If we can define a predictive epigenetic signature, we can intervene earlier to reduce health disparities in common conditions like obesity."

More information: Amanda Rushing et al, Salivary epigenetic biomarkers as predictors of emerging childhood obesity, *BMC Medical Genetics* (2020). DOI: 10.1186/s12881-020-0968-7

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