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Genes linked to low birth weight, adult shortness and later diabetes risk

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An international team of genetics researchers has discovered four new gene regions that contribute to low birth weight. Three of those regions influence adult metabolism, and appear to affect longer-term outcomes such as adult height, risk of type 2 diabetes and adult blood pressure.

"This large study adds to the evidence that genes have a strong influence on fetal growth," said one of the co-authors, Struan F.A. Grant, Ph.D., associate director of the Center for Applied Genomics at The Children's Hospital of Philadelphia. "The cumulative effect of the genes is surprisingly strong; it's equivalent to the effect of maternal smoking, which is already recognized as lowering a baby's weight at birth. We already know that a low birth weight increases the risk of health problems in adult life."

The article, published today in Nature Genetics, was the second major study on birth weight by the Early Growth Genetics (EGG) Consortium, composed of groups of scientists from multiple countries, including the United Kingdom, Finland, the Netherlands, and the United States. Earlier this year, Grant was the lead investigator of an EGG study—the largest-ever genome-wide study of common childhood obesity—which found two novel gene variants that increase the risk of that condition.

The lead investigator of the current study was Rachel M. Freathy, Ph.D., a Sir Henry Wellcome Postdoctoral Fellow from the University of Exeter Medical School in the U.K.

The meta-analysis and follow-up study encompassed nearly 70,000 individuals, of European, Arab, Asian and African American descent, from across 50 separate studies of pregnancy and birth. In addition to confirming that three previously discovered genetic regions increased the risk of low birth weight, the consortium discovered four new regions: genes HMGA2, LCORL, ADRB1, and a locus on chromosome 5.

Two of the previously identified gene regions are connected to a risk of type 2 diabetes, while two of the newly found regions confer a risk of shorter adult stature. A third region, ADRB1, is associated with adult blood pressure—the first time that scientists have found a genetic link common to both birth weight and blood pressure. The biological mechanisms by which the identified genetic regions function to influence early growth and adult metabolism remain to be discovered, although, said Grant, these regions offer intriguing areas on which to focus follow-up research.

Freathy, the study's lead investigator, summed up the study's findings by saying, "These discoveries give us important clues to the mechanisms responsible for the control of a baby's growth in the womb, and may eventually lead to a better understanding of how to manage growth problems during pregnancy."

"This study demonstrates that genes acting early in development have important effects on health both in childhood and beyond," added Grant. "While we continue to learn more about the biology, an important implication is that designing prenatal interventions to improve birth weight could have lifelong health benefits."

More information: "New loci associated with birth weight identify genetic links between intrauterine growth and adult height and metabolism," *Nature Genetics*, advance online publication, Dec. 2, 2012. doi:10.1038/ng.2477

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