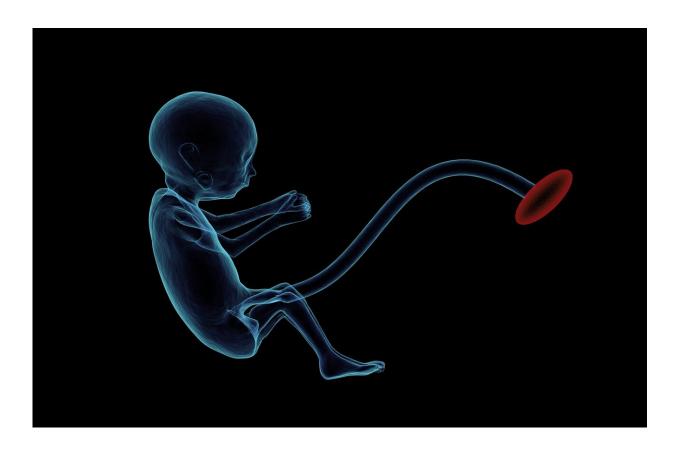


New study focuses on the placenta for clues to the development of gestational diabetes

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A new study led by the Harvard Pilgrim Health Care Institute has identified that a deficit in the placental expression of the gene insulinlike growth factor 1 (IGFBP1) and low IGFBP1 circulating levels are associated with insulin resistance during pregnancy, highlighting a



potential risk factor for the development of gestational diabetes.

The study, "Placental IGFBP1 levels during early pregnancy and the risk of insulin resistance and gestational diabetes," appears in the April 16, 2024 edition of *Nature Medicine*.

Gestational diabetes, a disease that can lead to multiple pregnancy and delivery complications, is the most common pregnancy metabolic complication, affecting 1 in 7 pregnancies. Existing research has shown that excess insulin resistance in pregnancy contributes to gestational diabetes, but the exact causes of this resistance remain unclear.

"The placenta—the major driver of changes in insulin physiology in pregnancy—is likely a key source of hormones involved in the development of gestational diabetes," says Marie-France Hivert, Harvard Medical School associate professor of population medicine at the Harvard Pilgrim Health Care Institute and lead author of the study. "Our goal was to discover novel placental factors that are implicated in gestational diabetes, by studying all proteins expressed in placenta tissues, across the <a href="https://doi.org/10.1007/journal.org/10.100

The study builds on Dr. Hivert's extensive research into the determinants of gestational diabetes using genetics and other omics approaches, and their interaction with lifestyle and <u>environmental factors</u>. The study team conducted genome-wide RNA sequencing on maternal-facing placental tissue samples, and measured identified proteins in blood collected in multiple pregnancy cohorts with diverse backgrounds.

The team identified 14 genes whose placental RNA expression levels were associated with insulin resistance, finding the strongest association with gene IGFBP1. By measuring the IGFBP1 protein levels in



circulation, they found that IGFBP1 levels rise over the course of pregnancy and are 5 times higher in pregnant people compared to outside of pregnancy, arguing for the placenta being one of the major sources of this protein during pregnancy.

Results also show that low levels of circulating IGFBP1 in early pregnancy could predict who is likely to develop gestational diabetes in late second trimester of pregnancy. Finally, the team found that the trajectory of IGFBP1 levels across pregnancy differs in people who have a subtype of gestational diabetes characterized by <u>insulin resistance</u> previously shown more likely to develop pregnancy complications.

"Identifying a novel protein that characterizes a subtype of gestational diabetes is one additional step towards developing precision medicine for gestational diabetes," adds Dr. Hivert. "It's possible that measuring IGFBP1 in the first trimester could help identify people at risk of developing gestational diabetes early in pregnancy, potentially offering a window for prevention. We hope to conduct future research to address whether this protein plays a causal role in gestational glycemic regulation."

More information: Placental IGFBP1 levels during early pregnancy and the risk of insulin resistance and gestational diabetes, *Nature Medicine* (2024). DOI: 10.1038/s41591-024-02936-5

Provided by Harvard Pilgrim Health Care Institute

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