

Human Gestational Diabetes is Prevented by a Protein Found in Mice

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Researchers have discovered a protein that induces changes in adipose tissue in vitro and in pregnant mice, suggesting that it could help people avoid gestational diabetes. A foetus needs fuel and a mother's body changes dramatically during pregnancy to ensure that it receives it. One alteration is a decrease in insulin sensitivity, which means cells become less sensitive to insulin signals instructing them to collect glucose from the bloodstream. In 5% to 9% of pregnancies in the United States, cells become so resistant to insulin that they are much less effective in controlling blood glucose levels. GDM (gestational diabetes mellitus) is a transitory condition in which mothers and their children are at an increased risk of developing type 2 diabetes and other problems later in life [1].

Raziel Rojas-Rodriguez, a PhD student in Silvia Corvera's lab at the University of Massachusetts at the time, observed variations in the fat, or adipose tissue, of pregnant women with and without GDM some years ago. Although increases in fat mass are common during pregnancy, pregnant women with GDM had larger fat cells around their organs and reduced expression of specific genes implicated in insulin signalling in their fat tissue, according to genetic assays. The researchers asked if there was a link between fat remodelling and the development of insulin resistance during pregnancy. They focused their investigation on PAPP-A, a protein generated mostly by the placenta that helps regulate insulin signalling and rises in the bloodstream throughout pregnancy. PAPP-A is involved in the remodelling of human adipose tissue and stimulates vascularization, according to in vitro tests. Pregnant animals without PAPP-A exhibited more fat around their livers and lower insulin sensitivity than pregnant wild type mice, according to Rojas-Rodriguez [2,3].

The researchers also looked at hospital records from 6,361 pregnant women who had PAPP-A testing in the first trimester and glucose tests in the third trimester (the protein is also used to determine foetal aneuploidy). Even after controlling for BMI and age, the researchers discovered that low PAPP-A was linked to an increased risk of GDM, implying that the protein may protect

against the disease. The findings, according to Thomas Buchanan of the University of Southern California, provide new insight into adipose tissue remodelling during pregnancy and the significance of PAPP-A. Because there may be confounding factors impacting a person's GDM risk that aren't recorded in this study, and because the PAPP-A-knockout mice don't reproduce all the aspects of human pregnancy, he believes the link between PAPP-A levels and GDM is uncertain. Although the knockouts had lower insulin sensitivity than wild types, they had better glucose tolerance [4].

According to Corvera, this appears to be due to the mice's muscular tissue using unusually huge amounts of glucose. "We have no idea why," she says. "Perhaps the mice are moving around more." Tissue-specific knockouts, she adds, could help pinpoint exactly what's going on. The team would like to measure PAPP-A longitudinally during pregnancy, adds Rojas-Rodriguez, who is currently a postdoc at Tufts University, and notes that the protein could be used as a biomarker. "Obviously, additional research is needed," she says, "but this protease has the potential to be employed in the diagnosis of gestational diabetes" [5].

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