Identification of early transcriptome signatures in placenta exposed to insulin and obesity

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Objective

The purpose of this study was to investigate the effects of insulin on human placental transcriptome and biological processes in first-trimester pregnancy.

Study Design

Maternal plasma and placenta villous tissue were obtained at the time of voluntary termination of pregnancy (7-12 weeks) from 17 lean (body mass index, 20.9 ± 1.5 kg/m^2) and 18 obese (body mass index, 33.5 ± 2.6 kg/m^2) women. Trophoblast cells were immediately isolated for in vitro treatment with insulin or vehicle. Patterns of global gene expression were analyzed using genome microarray profiling after hybridization to Human Gene 1.1 ST and real time reverse transcription–polymerase chain reaction.

Results

The global trophoblast transcriptome was qualitatively separated in insulin-treated vs untreated trophoblasts of lean women. The number of insulin-sensitive genes detected in the trophoblasts of lean women was 2875 ($P < .001$). Maternal obesity reduced the number of insulin-sensitive genes recovered by 30-fold. Insulin significantly impaired several gene networks regulating cell cycle and cholesterol homeostasis but did not modify pathways related to glucose transport. Obesity associated with high insulin and insulin resistance, but not maternal hyperinsulinemia alone, impaired the global gene profiling of early gestation placenta, highlighting mitochondrial dysfunction and decreased energy metabolism.

Conclusion

We report for the first time that human trophoblast cells are highly sensitive to insulin regulation in early gestation. Maternal obesity associated with insulin resistance programs the placental transcriptome toward refractoriness to insulin with potential adverse consequences for placental structure and function.