Placental Cell Type Specific Transcriptional Responses to Maternal Obesity: Implications for Fetal Growth

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Maternal obesity is associated with increased infant birth weight, elevating the risks of long-term diseases in offspring. Despite this, the specific strategies employed by placental cells in response to maternal obesity for modulating placental or fetal growth remain elusive.

Our study delves into the distinctive responses of placental cell types to maternal obesity and their correlation with infant birth weight. Using single-nuclei RNA sequencing, we analyzed human placental samples from a Chilean cohort, stratified into three groups: normal maternal BMI and appropriate baby birthweight for gestational age (N-AGA, n=4); obese AGA (O-AGA, n=4) with maternal BMI 30⩽ BMI<35; and obese with large baby birthweight for gestational age (O-LAGA, n=4).

Thirteen major cell types were identified and all cell types presented differentially expressed genes (DEGs). Notably, in syncytiotrophoblast, gene expression increased in both obese groups, with a more pronounced effect in the O-AGA group. Conversely, in cytotrophoblast cells, the gene expression decreased in obese groups, with a more significant decrease in the O-AGA group. Fibroblasts from the O-LAGA group exhibited 87 DEGs compared to N-AGA, while the O-AGA group had 43 DEGs.

Pathway analysis revealed perturbations in hormonal response and secretion in syncytiotrophoblasts, modulation of nutrient sensing and tissue growth regulating pathways in cytotrophoblasts, and altered responses to oxygen-containing molecules in fibroblasts from placentas of obese mothers. These results help advance our understanding of the placenta's role in fetal development and shed light on the potential adverse effects of maternal obesity on both maternal and fetal health.

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