Maternal-Fetal Metabolic Communication During Gestation

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Summary

Pregnancy exerts an extreme metabolic demand that necessitates coordinated adaptations between mother and fetus to ensure that the energetic and biosynthetic requirements of the rapidly growing fetus are met without compromising maternal health and fecundity. To determine maternal and fetal contributions to metabolic flexibility during gestation, pregnant mice with genetic impairments in mitochondrial carbohydrate and/or lipid metabolism were subjected to nutrient deprivation. Due to the incredible demand for glucose during gestation, fasting during pregnancy results in an accelerated starvation response that is characterized by an earlier and more exaggerated shift to ketone body utilization. The maternal fasting response initiated a fetal liver transcriptional program marked by up-regulation of lipid- and Pparα-regulated genes. Impaired maternal lipid metabolism altered circulating lipid metabolite concentrations and enhanced the fetal response to fasting, which was largely dependent on fetal Pparα. Maternal fasting also improved metabolic deficits in fetal carbohydrate metabolism by increasing the availability of alternative substrates. Impairment of both carbohydrate and lipid metabolism in pregnant dams further exacerbated the fetal liver transcriptional response to nutrient deprivation. Together, these data demonstrate a regulatory role for mitochondrial macronutrient metabolism in mediating maternal-fetal metabolic communication particularly when nutrients are limited.