

Placental DEPTOR inhibition restores maternal vasodilation in fetal growth restricted mice.

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Abstract

Fetal growth restriction (FGR) is a gestational complication characterized by a reduction in expected fetal growth and is a leading factor of fetal and neonatal morbidity and mortality. The mechanistic target of rapamycin (mTOR) kinase is a central regulator of cellular growth, homeostasis, and aging. DEP-domain-containing mTOR-interacting protein (DEPTOR) is an endogenous inhibitor of mTOR signaling that downregulates mTOR complex 1 and 2 activities. Previous studies have shown that silencing DEPTOR in the placenta increases trophoblast amino acid transport and mitochondrial respiration. We hypothesized that placental DEPTOR silencing prevents the effects of maternal nutrient restriction-evoked FGR on the vasodilation of maternal uterine artery (UtA). We assessed vascular function through wire myography and structural characteristics by histology in pregnant maternal UtA at gestational day 18.5. Vasoactive responses were tested for increasing concentrations of phenylephrine, acetylcholine, bradykinin, and sodium nitroprusside (SNP). Placental DEPTOR silencing restores the vasodilatory responses to SNP in maternal UtA in mice with FGR pregnancies. No significant structural differences were observed in vascular structure. These observations highlight a role for placental mTOR signaling in the regulation of maternal uterine vasculature during pregnancy.