

 METABOLISM

DLK1 levels predict fetal growth restriction

In pregnancy, elevated circulating levels of delta-like homolog 1 (DLK1) are required for the increased fatty acid metabolism needed during gestation. According to new research, these levels can be used to predict fetal size before birth and might enable the development of a simple blood-based test to predict complications in pregnancy, such as fetal growth restriction (FGR).

The investigators first used a mouse model lacking *Dlk1* (*Dlk1KO*) to show that the elevated maternal levels of DLK1 are derived from the fetus. In normal circumstances, elevated DLK1 levels lead to increased fatty acid metabolism in the mother. However, in mice with a *Dlk1KO*

pregnancy, circulating ketone levels did not increase and these mice were hyperglycaemic compared with controls, despite having similar levels of insulin. As *Dlk1KO* embryonic mice were smaller than controls, the team hypothesized that DLK1 levels might predict birth-weight in humans.

The team measured maternal plasma levels of DLK1 at a mean of 36 weeks and 1 day of gestational age in samples from the Pregnancy Outcome Prediction study, which included 4,512 women having a first pregnancy. Women with infants who were small-for-gestational age (SGA) had lower levels of DLK1 (-9.44 ng/ml; $P = 0.001$) than matched controls. The association

was not significant when comparing levels of DLK1 in mothers with infants who were healthy and those who had infants born SGA. However, DLK1 levels were significantly lower in mothers with infants with FGR compared with controls (-13.33 ; $P < 0.0001$).

The authors believe their findings could have use in the clinic for differentiating pregnancies that might need intervention from healthy SGA pregnancies.

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ORIGINAL ARTICLE Cleaton, M. A. M. et al. Fetus-derived DLK1 is required for maternal metabolic adaptations to pregnancy and is associated with fetal growth restriction. *Nat. Genet.* <http://dx.doi.org/10.1038/ng.3699> (2016)