



# Postpartum circulating microRNA enhances prediction of future type 2 diabetes in women with previous gestational diabetes

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## Abstract

**Aims/hypothesis** Type 2 diabetes mellitus is a major cause of morbidity and death worldwide. Women with gestational diabetes mellitus (GDM) have greater than a sevenfold higher risk of developing type 2 diabetes in later life. Accurate methods for postpartum type 2 diabetes risk stratification are lacking. Circulating microRNAs (miRNAs) are well recognised as biomarkers/mediators of metabolic disease. We aimed to determine whether postpartum circulating miRNAs can predict the development of type 2 diabetes in women with previous GDM.

**Methods** In an observational study, plasma samples were collected at 12 weeks postpartum from 103 women following GDM pregnancy. Utilising a discovery approach, we measured 754 miRNAs in plasma from type 2 diabetes non-progressors ( $n = 11$ ) and type 2 diabetes progressors ( $n = 10$ ) using TaqMan-based real-time PCR on an OpenArray platform. Machine learning algorithms involving penalised logistic regression followed by bootstrapping were implemented.

**Results** Fifteen miRNAs were selected based on their importance in discriminating type 2 diabetes progressors from non-progressors in our discovery cohort. The levels of miRNA miR-369-3p remained significantly different ( $p < 0.05$ ) between progressors and non-progressors in the validation sample set ( $n = 82$ ; 71 non-progressors, 11 progressors) after adjusting for age and correcting for multiple comparisons. In a clinical model of prediction of type 2 diabetes that included six traditional risk factors (age, BMI, pregnancy fasting glucose, postpartum fasting glucose, cholesterol and triacylglycerols), the addition of the circulating miR-369-3p measured at 12 weeks postpartum improved the prediction of future type 2 diabetes from traditional AUC 0.83 (95% CI 0.68, 0.97) to an AUC 0.92 (95% CI 0.84, 1.00).

**Conclusions** This is the first demonstration of miRNA-based type 2 diabetes prediction in women with previous GDM. Improved prediction will facilitate early lifestyle/drug intervention for type 2 diabetes prevention.

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