

# **PREECLAMPSIA RISK STRATIFICATION EARLY IN PREGNANCY: LEVERING A PROMISING METABOLOMICS DISCOVERY INTO A LC-MS BASED CLINICAL ASSAY**

## **Authors**

Liz Bond<sup>1,5</sup>, Caroline Nolan<sup>1,5</sup>, Katy Hyland<sup>1,5</sup>, Charline Lenaerts<sup>2</sup>, Phil Baker<sup>3,5</sup>, Louise Kenny<sup>4,5</sup>, **Robin Tuytten**<sup>1,5</sup>

<sup>1</sup>Metabolomic Diagnostics, Little Island, Cork, Ireland

<sup>2</sup>Lab. of Pharmaceutical Analysis, Faculty of Medicine & Pharmacy, University of Mons, Belgium

<sup>3</sup>Gravida: National Centre for Growth and Development, The University of Auckland, New Zealand

<sup>4</sup>The Irish Centre for Fetal and Neonatal Translational Research, Cork University Maternity Hospital, Cork, Ireland

<sup>5</sup>on behalf of the IMproved Pregnancy Outcomes by Early Detection consortium (IMPROvED)

## **Objectives**

Unbiased metabolite biomarker discovery has revealed that combinations of blood-borne metabolites have the potential to predict preeclampsia accurately at ca. 15 weeks of gestation (Kenny et al., 2010). Our aim is to deploy a dedicated translational effort bringing the merits of de-novo biomarker research to health care providers and patients.

## **Methods**

To exploit the widespread availability of quadrupole mass spectrometers (QqQ-MS) in clinical laboratories world-wide, a platform migration to QqQ-MS was performed. To support the further refinement of the metabolites-based pre-eclampsia prediction algorithm, and the technical and clinical validation of the test, access to appropriate patient samples from prospective cohorts is warranted. A public-private partnership involving supranational government funding, clinicians and dedicated small and medium sized companies, collaborated to establish a pregnancy biobank.

## **Results**

Thus far, a simple metabolite extraction and a targeted LC-QqQ-MS approach using stable isotope labelled metabolites for relative quantification has been developed. The (semi-) quantitative analysis of circa 40 metabolites with very disparate physicochemical characteristics is achievable in a single 10 minute run.

The company is engaged in 2 dedicated public-private initiatives, i.e. SCreening fOr Pregnancy Endpoints (SCOPE) (North et al, 2011) and IMproved Pregnancy Outcomes by

Early Detection (IMPROvED) (Navaratnam et al, 2013). These collaborations are instrumental for the further clinical and technical validation of the test under development.

### **Conclusion**

Development of a dedicated translational effort to further exploit newly discovered biomarkers relevant to the prediction of preeclampsia has already resulted in an analytical method ready for testing in clinically relevant patient cohorts. Public-private biobanking efforts have proved to be a cost-efficient means enabling both additional basic biomarker research and progression of biomarkers to market.

### **Acknowledgment**

The authors gratefully acknowledge funding from the EU-HEALTH Project IMPROvED (305169) of the Seventh Framework Programme (FP7).

1. Kenny, L. C. *et al.* Robust early pregnancy prediction of later preeclampsia using metabolomic biomarkers. *Hypertension* **56**, 741–9 (2010).
2. North, R. A. *et al.* Clinical risk prediction for pre-eclampsia in nulliparous women: development of model in international prospective cohort. *BMJ* **342**, d1875 (2011).
3. Navaratnam, K. *et al.* A multi-centre phase IIa clinical study of predictive testing for preeclampsia: improved pregnancy outcomes via early detection (IMPROvED). *BMC Pregnancy Childbirth* **13**, 226 (2013).