Gestational Diabetes Mellitus is characterized by differential protein profile associated with glucose metabolism in skeletal muscle and placenta

Soumyalekshmi Nair1, Andrew Lai1, Katherin Scholz-Romero1,2, Gregory Duncombe1, H David McIntyre3, Martha Lappas4,5, Carlos Salomon1,2,6

1Exosome Biology Laboratory, Centre for Clinical Diagnostics, UQ centre for Clinical Research, Royal Brisbane and Women’s Hospital, Faculty of Medicine + Biomedical Sciences, The University of Queensland. 2Department of Clinical Biochemistry and Immunology, Faculty of Pharmacy, University of Concepción, Concepción, Chile. 3Mater Research Institute-University of Queensland, Translational Research Institute, Woolloongabba, Australia. 4Obstetrics, Nutrition and Endocrinology Group, Department of Obstetrics and Gynaecology, University of Melbourne, Victoria, Australia and Mercy Perinatal Research Centre, Mercy Hospital for Women, Heidelberg, Victoria, Australia.

Background
Abnormal glucose metabolism in skeletal muscles and placenta are central to the pathophysiology of Gestational Diabetes Mellitus (GDM). The aim of the present study is to characterize the changes in proteomic profile in the skeletal muscles and placenta in GDM. Also, the differentially expressed miRNAs in circulating exosomes in GDM was identified. We further identified the proteins and pathways in skeletal muscles which could be targeted by these miRNAs in GDM.

Methods
Primary trophoblast cells and skeletal muscle tissues were obtained from normal pregnant and GDM women, at delivery. Information-dependent acquisition (IDA) of the mass spectra was performed using liquid chromatography, tandem MS and quantitative proteomics performed using the Sequential Windowed Acquisition of All Theoretical Mass Spectra- MS (SWATH-MS). Plasma exosomes were isolated from normal and GDM pregnant women and their miRNA profile was analyzed by next generation sequencing. The circulating exosomal miRNAs and skeletal muscle proteins in GDM were integrated using Ingenuity Pathway Analysis (IPA).

Conclusion
GDM is characterized by differential expression of proteins associated with insulin signaling and glucose metabolism in skeletal muscle and placenta. Circulating exosomes in GDM carry a specific set of miRNAs that target specific pathways associated with skeletal muscle insulin sensitivity and glucose homeostasis.