Placental Small Extracellular Vesicle MiRNA and Proteomic Profile Reveals a Role in Regulation of Glucose Metabolism in Gestational Diabetes Mellitus

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Background
Small extracellular vesicles (sEVs) are membrane-bound vesicles derived from variety of cells and are enriched in selected proteins and miRNAs. The aim of the present study is to identify the functional roles of miRNA and protein profile in placental cells and their secreted sEVs, in the pathophysiology of Gestational Diabetes Mellitus (GDM).

Methods
Primary trophoblast cultures were developed from placentas at term obtained from healthy pregnant women and women with GDM. sEVs were isolated from the primary trophoblast culture conditions media by differential ultracentrifugation. Using quantitative proteomic analysis, we identified the specific set of proteins significantly different in placental cells and sEVs in GDM compared to healthy pregnancy. Also, using next generation sequencing we identified the set of miRNAs differentially expressed in placental cells and sEVs in GDM compared to healthy pregnancy. Using Ingenuity Pathway Analysis (IPA) analysis we identified the miRNA-gene interactions and created a network that linked with the down- and up-regulated pairs of miRNA-proteins.

Conclusion
miRNA and protein profile of trophoblast cells are reflected in the content of sEVs derived from them. Trophoblast-derived sEVs in GDM can modify the metabolic response of their target cells and might contribute to regulation of maternal metabolism in GDM.