MSc Departmental Seminar – Chem 6001

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Title: NMR metabolomics: from preterm placentas to plastic-exposed brains

Abstract

Introduction: NMR metabolomics is a promising field of research in the study of pregnancy. This talk will describe two uses of NMR-based metabolomics to illustrate the potential for diagnosis and improved understanding of the etiology and underlying mechanisms of pregnancy complications. Preterm birth (PTB) poses significant challenges in maternal and neonatal health, yet the understanding of its etiology remains incomplete. Here, we explore whether there are alterations in placental metabolism in human PTB. With the recent discovery of plastics in the placenta, concerns have escalated regarding the impact of plastics on pregnancy and fetal development.
The health impacts of these plastics, particularly on fetal brain development, remains poorly understood. Using an animal model of pregnancy, we determine whether maternal exposure to nanoplastics alters metabolism in the fetal brain.

Methods: ^{1}H NMR experiments on unprocessed placental tissue samples from term and preterm human pregnancies collected at Eastern Health (n=9/group) were performed using a 500 MHz spectrometer and a comprehensive multiphase magic angle spinning (MAS) NMR probe (University of Toronto). Data was analyzed using spectral editing techniques. Pregnant mice were exposed to polystyrene nanoplastics (10^{6} ng/L in their drinking water) throughout gestation and fetal brain tissue samples were collected at the end of pregnancy (n=18-21/group/sex). A 600 MHz spectrometer and a standard solid-state MAS NMR probe was used (Memorial University). The spectra were processed and analyzed as described previously by our group [1]. Multivariate analysis was conducted using principal component analysis in MetaboAnalyst.

Results: Our findings revealed significant alterations in the placental metabolome of PTB pregnancies, shown by the decreased concentrations of valine, glutamate, and creatine, alongside elevations in the concentrations of alanine, choline, and glucose [2]. Pathway analysis demonstrates disruptions in glycine, serine, and threonine metabolism, aminoacyl-tRNA biosynthesis, and valine, leucine, and isoleucine biosynthesis pathways. Maternal exposure to polystyrene nanoplastics resulted in altered fetal brain metabolism, notably decreasing the relative concentrations of gamma-aminobutyric acid (GABA), creatine, and glucose [3].
Nanoplastic exposure also impacted asparagine levels dependent on fetal biological sex.

Conclusion: Using a NMR metabolomics approach, our findings were able to highlight altered placental metabolism associated with PTB and altered fetal brain metabolism following maternal exposure to nanoplastics. These insights advance our understanding of PTB etiology, provide promising placental metabolic biomarkers of PTB, and highlight the impact of plastics on fetal brain development.

[1] C.M. Schneider, K.L. Steeves, G.V. Mercer et al. *Metabolomics* **2022**, 18(10)
[2] G.V. Mercer et al. *Placenta* **2023**, 143:80-86
[3] G.V. Mercer et al. *Metabolomics* **2023**, 19(96)