**BASIC SCIENCE**

**Abstracts 10-19**

10. **Maternal obesity impacts fetal neuroinflammation in a murine model of preterm birth**

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**OBJECTIVE:** Maternal obesity is associated with increased adverse outcomes in premature offspring; the molecular mechanisms for this remain poorly understood. Our prior examination suggests fetal neuroinflammation is compounded by maternal obesity. To understand the molecular mechanisms of preterm brain injury in relation to maternal weight, we analyzed the abundance of immune related mRNA in fetal brains using the murine model.

**STUDY DESIGN:** A high-fat diet was given to generate/maintain obese dams in parallel to normal dams given a standard diet. Sires were on a normal diet. To induce preterm birth, bacterial endotoxin (LPS) was injected intrauterine on embryo day 15.5. Controls received the vehicle (PBS). The NanoString Neuroinflammation panel was used to quantify 757 mRNAs normalized to the internal references from n=14 fetal brains per condition: normal or obese diet given either PBS or LPS. The log fold change and significance between LPS vs. PBS for each diet condition were analyzed using nSolver. Pathway-functional analysis was conducted using IPA.

**RESULTS:** Irrespective of diet, the majority of target genes were upregulated with LPS. With maternal obesity, gene expression was substantially greater (Figure1). Expression patterns linked to similar pathways/functions (Figure2), with notable exceptions; MYD88, IL1A, autophagy and hematopoiesis of mononuclear leukocytes were linked whereas TNFR1, TWEAK and SOCS1 were absent with obesity compared to normal.

**CONCLUSION:** Maternal obesity compounds fetal neuroinflammatory responses related to prematurity. Enhanced responses with obesity strongly associated with autophagy and MYD88 signaling, both of which mediate brain injury. Neuroinflammatory injury with maternal obesity may involve Interleukin signaling, more so than TNF and its inducer TWEAK. Protective effects from SOCS1 pathway, that suppresses IL1B signaling, may also be diminished with maternal obesity. Altogether, these signaling mechanisms may exaggerate inflammation and worsen neurological outcomes in preterm infants born to obese mothers.

11. **Epigenome-wide DNA methylation in maternal blood and preterm birth (PTB)**

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**OBJECTIVE:** PTB is a multifactorial condition with poorly understood pathophysiology and challenges in prediction. Epigenetics may provide additional insight into the underlying pathogenesis. We sought to evaluate whether CpG methylation in maternal blood differs among those delivering preterm.

**STUDY DESIGN:** Planned primary analysis of a prospective observational cohort study that recruited patients at a single, tertiary University-based hospital carrying singleton, non-anomalous gestations who were at high risk for spontaneous PTB due to a high-risk obstetric history or current pregnancy complication. Placental CpG methylation at ~850,000 CpG sites genome wide in maternal blood was interrogated by the Illumina® MethylationEPIC BeadChip. The primary outcome was PTB < 37 weeks’ gestation. Secondary outcomes were PTB < 34 and < 28 weeks’ gestation. We compared CpG methylation at each gestational age cutoff. Statistical analysis included logistic regression models (controlling a priori for maternal age, insurance status, smoking, male fetal sex, and gestational age at blood sampling) with Bonferroni correction. A q-value < 0.10 was considered statistically significant.