**48 Early-life Lactobacillus rhamnosus GG Supplementation of High-risk for Asthma Infants Reprograms Gut Microbiota Development and promotes regulatory T-cells**

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**Rationale:** Neonatal gut microbiome perturbation is associated with childhood allergic asthma development. Daily *Lactobacillus rhamnosus* GG supplementation of high-risk (HR) for asthma infants from birth may impact the compositional and functional development of the gut microbiome in a manner that promotes immune tolerance.

**Methods:** Longitudinal stool samples from 25 HR infants (randomized to receive 1x10^10 LGG or placebo daily, from birth to 6mo), and 29 healthy control (HC) infants were subjected to 16s rRNA-based microbiota and un-targeted liquid chromatography mass spectrometry metabolic profiling. A dendritic-cell/T-cell co-culture assay was used to assess the capacity of sterile fecal water from a subset of 6mo and 12mo samples to promote T-regulatory cell populations and IL10 production.

**Results:** Compared to healthy controls, placebo-treated HR subjects exhibited delayed bacterial diversification over the first year of life, which was abrogated in LGG supplemented subjects. Compared to the placebo arm, LGG supplementation was associated with gut bacterial communities and fecal metabolic profiles more similar to healthy control subjects. At 6 months LGG-supplemented subjects exhibited enrichment of a range of anti-inflammatory metabolites, and sterile fecal water prepared from these participants promoted expansion of CD4+CD25+Foxp3+ (T-regulatory) cells and IL10 production.

**Conclusions:** Daily LGG supplementation in early life partially rescues gut microbiota and metabolome deficiencies associated with high-risk for asthma subjects. Sustained supplementation or supplementation with a cocktail of bacteria typically depleted in HR infants may be necessary to prevent allergic asthma in childhood.

**49 Surfactant Protein-D (SP-D) Is A Lung Specific Regulator of Group 2 Innate Lymphoid Cells (ILC2)**

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**Rationale:** We previously showed that ILC2 were required for recruitment of neutrophils and eosinophils into the lung following ozone (*O3*) inhalation. SP-D is an immunoprotective protein released by airway epithelial cells. We found that presence of SP-D was necessary to resolve airway inflammation after O3. The relationship between SP-D and ILC2 in the lung has not been investigated before. We hypothesized that SP-D suppresses ILC2 activation by O3.

**Methods:** C57BL/6 (WT) and SP-D−/− mice were exposed to 3 ppm O3 for 2 hours and euthanized 12 hours later. Bronchoalveolar lavage (BAL) was collected and measured for inflammatory cell influx and cytokines (ELISA). Lungs were harvested and gene expression (qPCR) of ILC-activating cytokines (IL-33, TSLP, IL-25) and ILC transcription factors (GATA-3, Bcl11b, RORγt) was analyzed from whole lung and isolated ILC2. Expression of ILC2 surface markers was measured via flow cytometry.

**Results:** SP-D−/− mice had heightened and prolonged airway neutrophilia after O3 exposure, that corresponded with significantly increased ILC2 count in the BAL. O3 induced ILC2-activating cytokines in the lung (qPCR) and inhibited ILC2 suppressor IFNγ in the BAL of both WT and SP-D−/− mice. Lack of SP-D was associated with increased lung IL-33 mRNA expression elevated ILC2 counts and higher ST2 (IL-33 receptor) GATA-3, Bcl11b and lower RORγt expression by ILC2.

**Conclusions:** We propose that in the absence of SP-D, ILC2 are “primed” for response to O3, explaining why SP-D−/− mice are more susceptible to the effects of O3 than WT mice.

**50 Effects of Annona muricata L. (soursop) seeds oil improves in model in vivo and in vitro of type 1 diabetes mellitus**

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**Rationale:** Type 1 diabetes mellitus (T1D) is a metabolic disorder caused by an autoimmune reaction against pancreatic β cells. *Annona muricata* L. has several medicinal properties, such anti-diabetic effects. In this work, we hypothesized that the *A. muricata* seeds oil (AmSO) possess immunomodulatory and can improve inflammatory markers in T1D in vivo and in vitro.

**Methods:** Fatty acid profile to AmSO was evaluated by gas chromatography. Spleenocyte viability exposure to AmSO was evaluated by MTT-tetrazolium and Resazurin. Whole blood cell viability exposure to AmSO was evaluated by Resazurin. AmSO was given orally in Balb/c mice for 48 days and mice were randomly divided into four groups; control group, Stz group, Stz-AmSO (1.0 mg/Kg) and AmSO group (1.0mg/Kg). T1D was STZ-induced intraperitoneally (3x-100 mg/Kg). Blood glucose, serum insulin, area of pancreatic islets, ALT, creatinine, histopathological analysis were evaluated. IL-10, IL-4, and IL-17 production in splenocyte cultures upon AmSO exposure from diabetic mice was determined by ELISA. IFN-γ and IL-10 also was determined in whole blood cells culture from 12 T1D diabetes patients upon AmSO exposure.

**Results:** AmSO contain 39% of oleic acid and 33% of linoleic. AmSO showed anti-hyperglycemic effect (p<0.01), preservation of the area of pancreatic islets (p<0.001), preservation of liver tissue and partial recovery glycogen, increase of IL-4 and IL-10 in splenocytes culture (125µg/mL, p<0.01) and decrease of IFN-γ (125, 62.5 and 31µg/mL, p<0.05) in whole blood cell from T1D patients.

**Conclusions:** AmSO has immunomodulatory potential for the treatment and/or prevention of T1D.