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## Time restricted feeding in diet induced obesity mouse model reduces aortic stiffness and inflammatory T cells

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OBJECTIVES/GOALS: Time restricted feeding (TRF) in diet induced obesity (DIO) has several health benefits, including improved metabolic rhythms and inflammation. Our lab has shown that TRF in DIO significantly reduces renal and aortic damage. The main goal of our research is to understand how TRF impacts aortic function, organ damage, and T cell activation in DIO. METHODS/ STUDY POPULATION: We will use a 20-week DIO model, where mice will be on 20 weeks of normal fat diet (ND) or high fat diet (HFD). During weeks 18-20, mice will go through TRF intervention where food is restricted to the 12-hour active period or continue ad libitum feeding. At the end of the 2-week TRF intervention or continued ad libitum feeding, aortic stiffness will be measured via pulse wave velocity measurements. We will also collect kidney, aorta, and small intestine at the end of the 20-week protocol for flow cytometric analysis of tissue T cell activation as well as histological assessments. This will allow us to determine the relationship with organ damage, organ function, and the T cell response. We will also analyze tissue and circulating levels of inflammatory T cell-derived cytokines such as interleukin-17A (IL-17A) via ELISA. RESULTS/ANTICIPATED RESULTS: DIO mice showed significantly increased aortic stiffness (measured by pulse wave velocity) compared to mice on ND. Interestingly, TRF intervention in DIO mice reduced aortic stiffness compared to DIO ad libitum. Histological assessments also showed that TRF abolished aortic and kidney fibrosis suggesting a role for the timing of feeding in regulating aortic function and organ damage from chronic HFD. We have several ongoing experiments to determine the T cell response with TRF in DIO mice. We predict that TRF in DIO mice will significantly decrease inflammatory T cells and reduce cytokine abundance in target organs. DISCUSSION/ SIGNIFICANCE: Our lab has shown that TRF reduces aortic thickness and aortic and kidney fibrosis, but the driving mechanisms are unknown. We propose that TRF reduces T cell activation in DIO mice leading to reduced organ damage. Our work will provide insight on how TRF in DIO regulates the T cell response and may improve inflammation in the kidney and aorta.

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## Galectin-3 as a Biomarker and Potential Therapeutic Target in Biliary Atresia\*

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OBJECTIVES/GOALS: Biliary atresia (BA) is a progressive congenital disease that is characterized by periductular inflammation and fibrosis that leads to bile duct destruction and cholestasis in neonates. Galectin-3 (Gal3) plays a key role in inflammation and fibrosis. The

aim of this study was to evaluate plasma Gal3 levels in early and late BA. METHODS/STUDY POPULATION: Samples from our institutional Pediatric Liver Biobank were used for this study. Patients were categorized as early BA (at diagnosis), late BA (at liver transplant), early other cholestatic liver disease (CLD), late other CLD, or controls without cholestasis or structural liver disease. Plasma Gal3 levels were measured by standard ELISA. Inflammatory cytokines were measured in a subset of samples using MSD Proinflammatory Panel 1 multiplex ELISA. Liver fibrosis was categorized as none (Ishak or METAVIR 0), mild (Ishak 1-2 or METAVIR 1), moderate (Ishak 3-4 or METAVIR 2-3), and severe (Ishak 5-6 or METAVIR 4) based on histology. Data are presented as median (IQR) and compared using Kruskal-Wallis test. Spearmans correlation was used to assess the relationship between Gal3 and clinical and inflammatory markers. RESULTS/ANTICIPATED RESULTS: Samples from 10 controls, 26 early BA, 24 late BA, 13 early other CLD, and 8 late other CLD patients were used for this study. Gal3 levels in late BA (20.8 [12.4-30.5] ng/mL) and late other CLD (21.8 [16.9 - 27.2] ng/mL) were significantly higher than in controls (10.2 [7.6 - 14.5] ng/ mL, p < 0.02) and early BA (11.3 [8.7 - 16.8] ng/mL, p < 0.01), but not significantly different from early other CLD (15.7 [11.9 -21.4] ng/mL, p > 0.05). Gal3 positively correlated with fibrosis score (rho 0.3, p = 0.01), total bilirubin (rho 0.3, p = 0.002), ALT (rho 0.3, p = 0.002),= 0.01), AST (rho 0.3, p = 0.005), and APRI score (rho 0.3, p =0.009), and negatively correlated with albumin (rho -0.3, p =0.01). Out of the 10 cytokine proinflammatory panel, Gal3 was significantly correlated with IL-6 (rho 0.3, p = 0.006). DISCUSSION/ SIGNIFICANCE: Gal3 is elevated in late BA and other CLD at time of transplant and correlated with degree of fibrosis, suggesting it may play a role in disease progression to cirrhosis. If targeted in the early disease stage, blocking Gal3 in pediatric cholestatic liver diseases may help delay the progression to cirrhosis and need for transplant.

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## Is miR let-7c protective against Acute Chest Syndrome in Sickle Cell Disease?

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OBJECTIVES/GOALS: We have shown that small extracellular vesicles (exosomes) isolated from patients with a history of ACS disrupt the endothelium in vitro. Sequencing of miRNA contents of these vesicles suggested that miR let-7c was differentially expressed. The current study was designed to determine the relationship between miR let-7c levels and ACS. METHODS/STUDY POPULATION: We identified 16 subjects from the SCD Lungomics biobank at the University of Chicago Comer and La Rabida Childrens Hospitals who had samples obtained at baseline. Among them, 9 had a history of ACS (ACS(+)) and 7 did not (ACS(-)). For all subjects, we reviewed clinical data relevant to their SCD and laboratory data (including hemoglobin, absolute reticulocyte count, white blood cell count) obtained at the same time as the baseline samples. RNA was isolated from the plasma and miR let7c was quantified using quantitative RT-PCR. RESULTS/ANTICIPATED RESULTS: Subjects were similar clinically, except that those with a history of ACS were more likely to be on hydroxyurea (p<0.05) and to have obstructive sleep apnea (p<0.05). Hematologic laboratory values were similar irrespective of