

our projected sample size is small and may impact the ability to examine this interaction. **DISCUSSION/SIGNIFICANCE:** Black Americans, particularly in the Deep South, are at elevated risk for PAD and critical limb ischemic events, such as amputation. Understanding CV health metrics and SDoH characteristics among adults with PAD is essential to reduce disparities in care and provide valuable information for those at highest risk for complications.

## **The Transcriptional Function of TCF7L2 is Spatially Restricted in Liver and Regulates Zonated Metabolic Pathways Which Contribute to Liver Disease\***

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**OBJECTIVES/GOALS:** Single nucleotide polymorphisms in the transcription factor 7-like 2 (TCF7L2) gene are associated with Type 2 Diabetes (T2D) and nonalcoholic fatty liver disease (NAFLD). The metabolic function of TCF7L2 in the liver remains to be fully elucidated, but we hypothesized that TCF7L2 contributes to NAFLD through regulation of zonal metabolic pathways. **METHODS/STUDY POPULATION:** Using single nuclei RNA sequencing, we examined Tcf7l2 expression in periportal (PP) hepatocytes around the portal triad and pericentral (PC) hepatocytes surrounding the central vein of the liver. To visualize TCF7L2 transcriptional activity we used a TCF reporter mice, which expresses an H2B-eGFP fusion protein downstream of the conserved TCF DNA binding site. We disrupted Tcf7l2 transcriptional activity in mouse liver by breeding mice with a floxed Tcf7l2 exon 11, which encodes part of the DNA binding domain (DBD), to albumin-Cre mice (Hep-TCF7L2ΔDBD). Eight-week-old mice were fed a choline-deficient amino acid-defined high fat (CDAHFD) diet for 8 weeks. In liver samples harvested from these mice, we examined disruption to several key zonated metabolic pathways, and quantified the development of fibrosis. **RESULTS/ANTICIPATED RESULTS:** Single nuclei analysis revealed that Tcf7l2 mRNA was expressed primarily in parenchymal cells of the liver but was ubiquitous across the liver lobule. However, in immunofluorescence analysis of TCF reporter mice, the transcriptional activity of TCF7L2 was highly restricted to PC hepatocytes. Classic PC hepatocyte markers, including glutamine synthetase (Glu), were absent in Hep-TCF7L2ΔDBD mice. Following the CDAHFD, Hep-TCF7L2ΔDBD mice developed more severe fibrosis in histological analysis, and expressed elevated levels of genes involved in fibrogenesis, collagen synthesis and TGFβ signaling. Hep-TCF7L2ΔDBD mice also displayed hepatic cholesterol accumulation following the CDAHFD, which was likely the result of impaired pericentral bile acid synthesis. **DISCUSSION/SIGNIFICANCE:** Our results suggest that TCF7L2 plays an important role in the regulation of zonated metabolic pathways, which may contribute to the development of fibrosis. Ongoing analyses are exploring the mechanisms regulating the zonal transcriptional activity of TCF7L2.

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## **Evaluating serum copper and kidney function in a cohort of bariatric surgery patients**

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**OBJECTIVES/GOALS:** High serum copper (Cu) levels have previously been described in bariatric patients. The kidneys are a target organ for Cu toxic insult but the role of Cu on kidney function (eGFR) is uncertain. This study examines the association between Cu and eGFR in a bariatric population in Southeast Louisiana. **METHODS/STUDY POPULATION:** Seven hundred fifty patients will be recruited from the Bariatric Center of the University Medical Center in New Orleans. Inclusion criteria include: age ≥ 18 years, clinic visit between June 1, 2018 – May 31<sup>st</sup> 2024, and having a serum Cu test result. Covariables such as inflammatory markers and hormonal contraception use will be assessed as potential confounders. Blood pressure will be assessed as a potential effect modifier. Data will be obtained from electronic medical records. Two cohorts will be assembled, a pre-surgery cross-sectional cohort and another followed post-surgery. Separate models will be developed stratified by race-ethnicity. **RESULTS/ANTICIPATED RESULTS:** In a pilot study of bariatric patients 26% had elevated (>155 mcg/dl) serum Cu and pronounced racial differences were noted. Characteristics consisted of a mean BMI of approximately 50 kg/m<sup>2</sup>; 91% were female and 69% were Black. Black patients had approximately double the prevalence (OR 1.98; 95% CI: 1.15, 3.4) compared to white patients. Due to the dual nature of the kidneys' involvement in metabolism via excretion and being the target organ for toxic insult, racial differences in exposure, coupled with the disproportionate rates of chronic kidney disease in Black adults, may be an explanation for the association between elevated Cu levels and eGFR in Black adults in this study. **DISCUSSION/SIGNIFICANCE:** Results from this study will provide insight into the prevalence of Cu and its association with kidney function in a bariatric population. Chronic kidney disease or other forms of renal impairment may result in the need for more conservative guidelines for dietary copper in bariatric medicine.

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## **Avoiding Death From Stimulant Toxicity: Resiliency Among People Who Use Stimulants**

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**OBJECTIVES/GOALS:** The project investigates the role that resiliency may play within individual, interpersonal, social, and structural contexts in protecting against acute lethal stimulant (meth/amphetamine or cocaine) toxicity. Identifying preventative factors is crucial in developing and implementing risk reduction strategies for people who use stimulants. **METHODS/STUDY POPULATION:** This is a qualitative study involving in-depth interviews via questionnaire assessing resiliency factors among persons living in San Francisco