Renal Tubular Complement C9 Deposition is Associated with Renal Tubular Damage and Fibrosis in Lupus Nephritis

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OBJECTIVES/GOALS: Tubulointerstitial damage in lupus nephritis (LN) is a strong predictor of progression to chronic kidney disease and end stage renal disease (ESRD). While complement activation mediates glomerular injury, the role of complement in renal tubular damage has not been evaluated. We investigated the association between complement activation and tubulointerstitial fibrosis.

METHODS/STUDY POPULATION: Patients with LN were selected randomly between July 2014 - July 2016. Chromogenic immunohistochemistry was performed on formalin-fixed, paraffin-embedded, 4-μm human renal biopsy sections using unconjugated, murine anti-human Complement C9 (Hycult Biotech, clone X197) as a marker of the terminal complement activation. Positive control is anti-human C9- patients: median (IQR) 6.2g (3.3-13.1) vs. 2.4g (1.3-4.6), p<0.01. The differences persisted at 6 months post biopsy. Bivariate associations were assessed at time of biopsy and 6 months post biopsy. Multivariable logistic regression was used to control for other covariates.

RESULTS/ANTICIPATED RESULTS: Renal biopsies from 30 LN patients had significantly higher urine protein, compared to C9- patients: median (IQR) 6.2g (3.3-13.1) vs. 2.4g (1.3-4.6), p<0.01. The differences persisted at 6 months after induction therapy: 1.08g (1.0-8.3) in C9+ vs. 0.68g (0.2-2.1) in C9- patients, p = 0.06. There was no significant difference in creatinine at renal biopsy between the two groups. Tubular C9 deposition was associated with interstitial fibrosis: 49% had severe interstitial fibrosis vs. none in the C9- group, p = <0.01. Higher proportion of C9+ patients had moderate NIH Chronicity index: 42.9% vs 8.7% in the C9- group, p = 0.07. DISCUSSION/SIGNIFICANCE OF IMPACT: Tubular C9 deposition is significantly associated with proteinuria, interstitial fibrosis and increased chronicity which predict progression to ESRD and high mortality. This finding suggests that complement activation in the tubules may be linked to proteinuria and contribute to mechanism in tubulointerstitial damage in LN.
(20 females) matched for age and IQ. Children received a diagnostic evaluation using the K-SADS. Pre-processing was conducted using FreeSurfer. For ROI analyses, multivariate GLM models were conducted in SPSS for estimates of GMV to examine the main effects of diagnosis and sex, and sex-by-diagnosis interactions. Whole-brain analyses were conducted in FreeSurfer. Associations were examined between structure and parent ratings of callous-unemotional (CU) traits using the Inventory of Callous-Unemotional Traits in regression analyses in the DBD group, while controlling for the variance in aggressive behavior using the Child Behavior Checklist Aggressive Behavior Scale. All analyses controlled for differences in intracranial volume. RESULTS/ANTICIPATED RESULTS: Relative to controls, children with DBD showed reduced GMV in the bilateral amygdala (left: \( p = 0.004 \); right: \( p = 0.04 \)). Sex-by-diagnosis interactions were observed in the left ventromedial prefrontal cortex (\( p = 0.004 \)), right insula (\( p = 0.001 \)), right inferior frontal gyrus (\( p = 0.02 \)), and bilateral anterior cingulate (left: \( p = 0.02 \); right: \( p = 0.01 \)) in which DBD males showed lower and DBD females showed higher GMV relative to respective controls. For whole-brain analyses, a significant sex-by-diagnosis interaction was observed in the left ventromedial prefrontal cortex and supramarginal gyrus indicating that DBD males showed lower and DBD females showed higher cortical thickness relative to respective controls. Sex-by-CU traits interactions were observed for left amygdala and ACC volumes. DISCUSSION/SIGNIFICANCE OF IMPACT: The current study provides evidence of reduced amygdala volume in children with DBD, and interactions between sex and diagnosis in the ventromedial prefrontal cortex and supramarginal gyrus, which may have implications for identifying sex-sensitive neural biomarkers. CONFLICT OF INTEREST DESCRIPTION: Disclosures: Dr. Sukhodolsky receives royalties from Guilford Press for a treatment manual on CBT for anger and aggression in children. Drs. Ibrahim, He, Pelphrey, McCarthy, and Mr. Li have no biomedical financial interests or potential conflicts of interest to declare related to this present study.

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Special Delivery: Home Delivery of Healthy Food to Young Women during Pregnancy*
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OBJECTIVES/GOALS: Most pregnant youth (ages 14-24) gain more weight during pregnancy than recommended by clinical guidelines. We aim to describe the feasibility and acceptability of home grocery delivery of fruits, vegetables, and healthy snacks to promote healthy weight gain in this vulnerable population. METHODS/STUDY POPULATION: Participants were low-income pregnant youth in Michigan. Each participant was sent biweekly grocery deliveries consisting of $35 worth of fresh fruits, vegetables, and healthy snacks via the app-based delivery service, Shipt. Between deliveries, participants were prompted to respond to weekly text message-based surveys of a 24-hour food recall. This validated nutritional assessment quantifies consumption of fruit and vegetable servings. In addition, participants were asked to send daily photos and descriptions of foods they were eating. This study was approved by the University of Michigan Institutional Review Board. RESULTS/ANTICIPATED RESULTS: To date, 27 participants have been enrolled. Thirteen participants have completed their participation, 4.3 months on average, and were sent an average of 10 grocery deliveries each. In total, over 200 deliveries have been sent with 86% confirmed by the study participant (179/207). Additional outcomes to be assessed include: 1) text message response rates by participants and 2) content from photos and text descriptions of food eaten by participants. The 24-hour recall and text and photo messaging provided in-context data about grocery utilization. DISCUSSION/SIGNIFICANCE OF IMPACT: Grocery delivery is both feasible and acceptable to our youth participants. Use of grocery delivery constitutes a novel intervention to promote healthy weight gain in pregnancy for vulnerable populations through improving access to healthy food options.

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Stepping Stones for Success in T3-T4 Translation: Building Collective Impact
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OBJECTIVES/GOALS: We will investigate the influence of multisector partnerships in T3-T4 research associated with advances in delivery systems, patient/population outcomes and health policy and the translational processes linked to these improvements. METHODS/STUDY POPULATION: We are using both quantitative and qualitative data to measure and analyze partnership characteristics linked to successful translation into practice & policy. We aim to complete 100 surveys of investigators who have conducted CTSA-supported T3-T4 research to examine partnerships, conditions of collective impact, and quantifiable changes in delivery systems, health outcomes, and policy. Using rigorous criteria, we will select projects for more in-depth interviews to understand the practices of successful translation and roadblocks and barriers that challenge translation. RESULTS/ANTICIPATED RESULTS: The anticipated research products include: (i) an analytic report on partnership structure and processes and the statistical associations to stages of change outcomes, (ii) a series of vignettes to describe the impact stories and translational processes, (iii) cross-project analysis of the data and vignettes to produce generalizable information to improve T3-T4 translation, and (iv) peer-reviewed manuscript(s) for publication. DISCUSSION/SIGNIFICANCE OF IMPACT: The study will inform and improve researcher competencies and accelerate translation in CTSA hubs that emphasize T3-T4 research. We will develop novel definitions of the T3-T4 research impact. Ultimately, the results will inform research training to better address real-world priorities and needs.

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Stromelysin-1 as a biomarker for acute lung injury
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OBJECTIVES/GOALS: Acute lung Injury (ALI) has long been considered a proceeding event to the development of Acute Respiratory Distress Syndrome (ARDS). Diagnosis of classical ALI and ARDS remains difficult relies on clinical components of the Berlin Criteria, interpretation of radiographs and exclusion of pulmonary