and wild-type controls treated with a 4% high-salt (HS) diet. Male C57BL6, B129S1, and PPAR-α KO mice (12 weeks old) will be treated with 4% HS diet for 28 days. Systolic blood pressure is measured by tail cuff. GFR is measured by transdermal FITC-Inulin radioactive fluorescence. Inflammatory biomarkers will be measured by cytokine array and western blot. Sodium transporter expression will be measured by western blot. RESULTS/ANTICIPATED RESULTS: Baseline SBP was 146 ± 31 mmHg (C57), 140 ± 24 mmHg (B129), and 153 ± 23 mmHg (KO). After 21 days of normal (control diet) or treatment (HS diet), control systolic pressures were 139 ± 18 mmHg (C57), 107 ± 23 mmHg (B129) and 147 ± 34 mmHg (KO), while HS systolic pressures were 166 ± 23 mmHg (C57) and 119 ± 34 mmHg (B129). We are collecting blood pressure for the KO HS group. Baseline GFR was 1194 ± 140 μL/min/g (C57), 1167 ± 279 μL/min/g (B129), and 1191 ± 157 μL/min/g (KO). DISCUSSION/SIGNIFICANCE OF IMPACT: We hypothesize significantly higher SBP, inflammatory marker expression, and renal sodium transporter expression in KO and B129 mice on a HS diet. We predict that PPAR-α expression in the kidney will be higher in C57 compared to B129. We predict that PPAR-α activity plays a vital role in reducing high-salt-induced hypertension and inflammatory markers.

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The effect of a novel inhibitor of Slc7a5 on remyelination in MS

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OBJECTIVES/GOALS: This study aims to first understand the expression of the L-type amino acid transporter, Slc7a5, in demyelinated plaques in postmortem multiple sclerosis (MS) CNS tissue. It also seeks to understand the effect of a novel inhibitor of Slc7a5 on remyelination in mice with experimental autoimmune encephalomyelitis. METHODS/STUDY POPULATION: Using single-cell RNA sequencing (scRNA-seq), we will examine the expression of Slc7a5 in demyelinated plaques in postmortem CNS tissue of patients with MS compared to non-lesioned regions (n = 3/group). Using visually evoked potential (VEP) on mice with experimental autoimmune encephalomyelitis (EAE), we will determine the ability of the Slc7a5 allosteric inhibitor OKY-034 to promote remyelination compared to EAE-only controls (n = 10/group). Lastly, we will use spatial transcriptomics with scRNA-seq to map transcriptional activity within different populations of cells to determine how OKY-034 changes gene expression in specific cell types compared to EAE-only controls (n = 3/group). RESULTS/ANTICIPATED RESULTS: A conditional knockout of Slc7a5 showed that microglial activation and oligodendrocyte differentiation were affected in demyelinated lesions. This suggests that it plays a role in numerous cell types in active demyelinated plaques, which is what we expect to find from our scRNA-seq data in post-mortem CNS tissue of patients with MS. Measuring VEP is a noninvasive way to measure remyelination in both clinical and research settings. OKY-034 increases oligodendrocyte differentiation suggesting remyelination, so we expect that administration of OKY-034 in mice with EAE will lead to restored VEP compared to control and EAE-only mice. Lastly, because OKY-034 reduces inflammation, we expect to see a decrease in gene expression for genes involved in an immune response. DISCUSSION/SIGNIFICANCE OF IMPACT: Completion of this study will lead to understanding what the effect the allosteric Slc7a5 inhibitor OKY-034 has on remyelination and whether it may serve as a novel therapeutic drug that can be administered orally for the treatment of MS. This could lead to its further development as a treatment for progressive MS.

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Novel inflammatory gene expression changes occur within the occluded vasculature of large vessel ischemic stroke

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OBJECTIVES/GOALS: We hypothesized that the bulk transcriptomic profiling of blood collected from within the ischemic vasculature during an acute ischemic stroke with large vessel occlusion (LVO) will contain unique biomarkers that are different from the peripheral circulation and may provide much-needed insight into the underlying pathogenesis of LVO in humans. METHODS/STUDY POPULATION: The transcriptomic biomarkers of Inflammation in Large Vessel Ischemic Stroke pilot study prospectively enrolled patients ≥ 18 years of age with an anterior circulation LVO, treated with endovascular thrombectomy (EVT). Two periprocedural arterial blood samples were obtained (DNA/RNA Shield™ tubes, Zymo Research); 1) proximal to the thrombus, from the internal carotid artery and 2) immediately downstream from the thrombus, by puncturing through the thrombus with the microcatheter. Bulk RNA sequencing was performed and differential gene expression was identified using the Wilcoxon signed rank test for paired data, adjusting for age, sex, use of thrombolytics, last known well to EVT, and thrombolysis in cerebral infarction score. Bioinformatic pathway analyses were computed using MCODE and reactome. RESULTS/ANTICIPATED RESULTS: From May to October 2022, 20 patients were screened and 13 were enrolled (median age 68 [SD 10.1], 47% male, 100% white). A total of 608 differentially expressed genes were found to be significant (p-value) DISCUSSION/SIGNIFICANCE OF IMPACT: These results provide evidence of significant gene expression changes occurring within the ischemic vasculature of the brain during LVO, which may correlate with larger ischemic infarct volumes and worse functional outcomes at 90 days. Future studies with larger sample sizes are supported by this work.

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Evaluating fibroblast growth factor receptor (FGFR) pathway mRNA expression and protein activation in cholangiocarcinoma tumors

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OBJECTIVES/GOALS: Personalized cancer therapy based on genomic testing is advancing patient care. Genomic alterations in fibroblast growth factor receptor (FGFR) predict response to FGFR inhibitors; however, the role of RNA expression and protein activation is not known. We propose to examine the

https://doi.org/10.1017/cts.2024.1106