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OBJECTIVES/GOALS: Antibiotic treatment sets the stage for intestinal domination by Candida albicanswhich is necessary for development of invasive disease, but the resources driving this bloom remain poorly defined. We sought to determine these factors in order to design novel prophylaxis strategies for reducing gastrointestinal (GI) colonization. METHODS/STUDY POPULATION: We initially developed a generalizable framework, termed metabolic footprinting to determine the metabolites C. albicanspreferentially uses in the mouse GI tract. After identifying the metabolites C. albicansutilizes, we usedin vitro growth assays in the presence and absence of oxygen to validate out metabolomics findings. We next determined if a probiotic E. coli that utilizes oxygen would reduce C. albicanscolonization compared to a mutant E. coli that could not respire oxygen. Finding that oxygen was a necessary resource, we utilized germ-free mice to determine if Clostridiaspp. known to reduce GI oxygen would prevent C. albicanscolonization. Lastly, we sought to see if 5-aminosalicylic acid (5-ASA) could prevent C. albicanscolonization. RESULTS/ANTICIPATED RESULTS: We found that C. albicans preferentially utilizes simple carbohydrates including fructo-oligosaccharides (e.g., 1-kestose), disaccharides (e.g., β-gentiobiose), and alcoholic sugars (e.g., sorbitol) and is able to grow in vitro on minimal media supplemented with either of these nutrients. However, in the hypoxic environment that is found in the "healthy" colon, C. albicans cannot utilize these nutrients. We next found that pre-colonization in a mouse model with a probiotic E. coli significantly reduced C. albicanscolonization, but the mutant E. coli had no effect on colonization. We next showed that Clostridia supplementation restored GI hypoxia and reduced C. albicanscolonization. Remarkably, we found that 5-ASA significantly reduced GI colonization of C. albicans. DISCUSSION/SIGNIFICANCE: We have shown that C. albicans requires oxygen to colonize the GI tract. Importantly, we found that 5-ASA can prevent an antibiotic mediated bloom of C. albicans by restoring GI hypoxia, which warrants additional studies to determine if 5-ASA can be used as an adjunctive prophylactic treatment in high risk patients.

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Mechanisms of a Dynamic Stability Protocol for Persons with Thumb Osteoarthritis†

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OBJECTIVES/GOALS: Our aims are to 1) describe changes in thumb Carpometacarpal (CMC1) joint stability following an 8-week clinic-based dynamic stability exercise program using computerized tomography (CAT) and 2) to evaluate the agreement between ultrasound and CAT (reference standard) when quantifying thumb CMC stability. METHODS/STUDY POPULATION: Aim 1: We have enrolled 13/49 participants in a prospective pre-post interventional study of an 8-week clinic-based occupational therapy dynamic stability program. The primary outcome will be change in stability (thumb metacarpal subluxation in mm) when forcefully loading the thumb as per CAT from pre-treatment to post-treatment at 9 weeks. Aim 2: Same 49 participants are undergoing a one-time ultrasound during baseline assessment. Agreement of ultrasound and CAT measurements (thumb metacarpal subluxation in mm) will be assessed by the Bland-Altman method. RESULTS/ANTICIPATED RESULTS: Exercise is a first-line treatment of CMC1 OA yet there is insufficient evidence to support this. Progression of CMC1 OA is characterized by altered joint mechanics. Joint replacement surgery may reduce pain but often worsens thumb mechanics and overall hand function. This study is the first to test the sustained biomechanical effects of non-invasive thumb exercises. Should these benefits exist, this will further support exercise as a first-tier intervention. Should ultrasound be a suitable proxy for CAT, therapists/physicians could monitor thumb CMC mechanics in response to treatment without risk of radiation exposure. We anticipate 1) a statistically significant reduction in thumb CMC subluxation at 9 weeks follow up and 2) high agreement between sonographic and CAT measures of thumb stability. DISCUSSION/SIGNIFICANCE: This study will lay the foundation for future work and may offer critical support for the use of a non-pharmacological and non-surgical approach as first-line treatment of a highly disabling disease. Future study should include controlled trials where hand function, activity limitation, disease progression, and costs are the outcomes in interest.

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A CTS Team Approach to Identifying Risk of Neonatal Hypoglycemia and its Relationship with Endothelial Dysfunction*

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OBJECTIVES/GOALS: Neonatal hypoglycemia is seen in 65% of maternally diabetic pregnancies, and can lead to severe neurological damage. Neonatal glycemia may also be an indicator of placental function in these pregnancies. The purpose of this study is to identify patterns of neonatal glycemia, and associated endothelial dysfunction, by maternal diabetes subtype. METHODS/STUDY POPULATION: Pregnancies with maternal Type 1 (T1DM), Type 2 (T2DM), and gestational diabetes mellitus (GDM) are being enrolled. Maternal hemoglobin A1c (HbA1c) and umbilical cord insulin/glucose are being collected from 20 pregnancies in each group, 10 of which also undergo placental/umbilical cord tissue collection. Following delivery, neonatal blood glucose levels are also collected every 3-4 hours (4+ measurements) to determine rate of glycemic change. Linear regression modeling will be used to determine associations with placental and umbilical endothelial RNA expression, umbilical cord insulin levels, and maternal HbA1c within each diabetic subtype and between normoglycemic and hypoglycemic neonates. Endothelial gene expression will be compared using paired t-tests with Benjamini-Hochberg correction. RESULTS/ANTICIPATED RESULTS: Thus far, 5 T1DM, 10 T2DM, and 13 GDM samples have been collected. Gestational age at delivery and birth weight were similar between groups (38.1 ± 1.05 weeks; 3.6 ± 0.59 kilograms) and delivery method is evenly distributed (Cesarean section or vaginal delivery). Currently, with limited cohort size, no association is evident between maternal HbA1c and

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umbilical cord glucose/insulin (p=0.114) or neonatal hypoglycemia diagnosis (p=0.674) when controlled for gestational age and infant birthweight. We hypothesize that, with pending analyses, maternal HbA1c and umbilical cord insulin levels will correlate negatively with the rate of neonatal glycemic change, and positively with the level of inflammatory and angiogenic transcription identified in placental and umbilical endothelium. DISCUSSION/SIGNIFICANCE: Characterization of postnatal glucose control is key to prognosis and risk stratification of infants of diabetic mothers. Understanding placental response to glucose, as well as sequela in the fetal endothelium, is also critical to understanding the pathogenesis of neonatal hypoglycemia and other adverse outcomes of diabetic pregnancy.

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The OGT/O-GlcNAc Axis Regulates Fibrosis Resolution in Idiopathic Pulmonary Fibrosis

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OBJECTIVES/GOALS: Idiopathic pulmonary fibrosis (IPF) is a chronic lung disease characterized by dysregulated collagen accumulation in the lung parenchyma. Our goal is to investigate the role of O-linked N-Acetylglucosamine (O-GlcNAc) transferase (OGT) in pulmonary fibrosis to ultimately discover novel therapies for fibrosis resolution. METHODS/STUDY POPULATION: Lung tissue from IPF and non-IPF donors was subjected to immunohistochemistry (IHC) to assess O-GlcNAc levels. Primary human lung fibroblasts were treated with OGT or O-GlcNAcase (OGA) inhibitors followed by transforming growth factor-beta 1 (TGF-β1) stimulation to assess O-GlcNAc regulation of fibroblast-to-myofibroblast transition (FMT) markers [alpha smooth muscle actin (α-SMA) and type 1 and type 3 collagen (COL1α1, COL3α1)] In Drosophila melanogaster, OGT knockdown (KD)/overexpression (OE) was conditionally induced to assess pericardin, a type IV collagen-like protein, regulation by immunofluorescence. Lastly, a mouse model of bleomycin-induced pulmonary fibrosis was examined following OGT KD and assessed for fibrosis resolution via histology, hydroxyproline assay, and western blotting. RESULTS/ANTICIPATED RESULTS: O-GlcNAc staining was increased in IPF lung tissue compared to non-IPF control lungs. In primary human lung fibroblasts, TGF-α1 administration resulted in increased FMT markers (α-SMA, COL1α1, and COL3α1), which were reduced or increased by OGT or OGA inhibition, respectively. Genetic manipulation in the Drosophila models showed decreased pericardin expression with OGT KD compared to the wild-type, whereas OGT OE increased pericardin compared to control. Additionally, OGT KD in bleomycin treated aged mice resulted in reduced collagen levels at the transcript and protein level and concurrent fibrosis resolution as assessed by Masson's trichrome staining and total hydroxyproline analysis. Collectively, showing OGT/O-GlcNAc regulating collagen in fibrosis resolution. DISCUSSION/SIGNIFICANCE: These data suggest that the OGT/O-GlcNAc axis regulates collagen deposition in pulmonary fibrosis, and we show that O-GlcNAc is implicated in the pathogenesis of IPF. We identified OGT as a therapeutic target to overcome current drug limitations, opening new horizons for biomedical treatment.

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Automated Prediction of Bone Volume Removed During Cortical Mastoidectomy Using Deep Learning

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OBJECTIVES/GOALS: Patient-specific definition of extent of surgical excision is foundational to the safety offered by computer assisted interventions. Consequently, this study aims to develop a pipeline for automated segmentation of bone removed during cortical mastoidectomy, a technically complex otologic surgery. METHODS/STUDY POPULATION: A simulator, previously developed in our lab, allows fully immersive simulation of mastoidectomy using segmented temporal bones generated from CT data. Using the simulator, one attending surgeon will perform three trials of mastoidectomy on 20 different temporal bones. From the simulator we will obtain data on the volume of bone removed for a specific anatomy, averaged between trials. No new U-net (nnU-net), an open-source three-dimensional segmentation network, will then be trained to predict the volume of bone removed using segmented pre-operative CT imaging. Segmentation accuracy will be evaluated with the Dice coefficient, modified Hausdorff distance (mHD), sensitivity and specificity. RESULTS/ANTICIPATED RESULTS: We expect the mean pairwise Dice coefficient to be high indicating relative similarity of volume removed between trials. Moreover, we predict that following five-fold cross-validation the best model will result in a Dice coefficient, mHD, sensitivity, and specificity indicative of volume removed predictions consistent with surgeon-generated data. Finally, given that network training will penalize overlap of the predicted excised bone segment and previously segmented anatomic structures, we expect that no critical anatomical structures will be marked as tissue removed. DISCUSSION/SIGNIFICANCE: We hope to show that deep learning architectures can accurately predict bone removed during mastoidectomy. These predictions can be used for preoperative planning, as clinical endpoints in surgical simulators, or be used in conjunction with surgical robots, all ultimately improving patient safety.

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Improving Patient Outcomes through Design of Biodegradable Implants for Long Bone Fractures

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OBJECTIVES/GOALS: Current long bone fracture standard of care uses inert metal intramedullary nails (IMN), 10x stiffer than femur cortex. Consequent "stress-shielding" bone loss sees >5% of patients

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