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ABSTRACT BOOK

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IMPROVE AND ENHANCE EDUCATION DELIVERY AND THE ROLE OF TECHNOLOGY IN THE SICKLE CELL TRANSITION POPULATION

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Improvements in healthcare has improved the lifespan of adolescents with sickle cell disease (SCD). The goal of a transition program is to provide a seamless transition from the pediatric to the adult health care system. It is important to develop novel and impactful teaching tools to engage teens with chronic health care needs in developing health self-efficacy. We hypothesize that the use of technology will engage patients and improve retention of transition topics in patients ages 13-18 enrolled in the Duke University sickle cell transition program compared to traditional learning techniques. All patients in the transition program complete an American Society of Hematology Transition Readiness Assessment Form, a 26-question tool assessing 5 key components of transition. To understand baseline knowledge, we performed a retrospective analysis utilizing assessments completed from June 2020-June 2021 and identified a knowledge gap in understanding insurance. Our SMART aim was to increase baseline knowledge of insurance understanding from an average of 21% to our goal of 50% within four weeks of implementing a new teaching tool. We performed two "Plan, Do, Study, Act" (PDSA) cycles. In PDSA cycle 1, a pre-survey identifying learning preferences was given to sequential patients over a two-week period. 10/12 (83%) learn best using videos and 5/12 (41%) learn best using PowerPoints. A multimedia presentation utilizing PowerPoint, videos, and song was developed. For PDSA cycle 2, sequential patients were presented the insurance teaching tool. Qualitative assessment of interest, acceptability, and information retention was performed after each presentation. Of the patients shown the presentation, 9/12 (75%) found the tool enjoyable and engaging and were able to teach back information from the presentation. Our multimedia approach improved knowledge retention of insurance information in adolescents with SCD. The next steps will include developing similar teaching tools for other areas needing improvement and link to a comprehensive website centered on transition education topics.

2

A POLYCYSTIC OVARY SYNDROME DIAGNOSIS IS A MARKER OF SOCIOECONOMIC ADVANTAGE

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Polycystic ovary syndrome (PCOS) is a chronic, public health burden that costs over $5.3 billion to treat annually in females of reproductive age. PCOS affects up to 21% of females, but the heterogeneous symptomology and the arduous two-year or longer diagnosis process are two important reasons why approximately 75% of women with PCOS remain undiagnosed. Currently, little is known about how socioeconomic status (SES) contributes to PCOS and its clinical diagnosis process. Therefore, we aimed to understand how social determinants of health, including poverty, can affect PCOS diagnosis. We tested the association between the area deprivation index (ADI) and PCOS case status. The ADI is a neighborhood

deprivation measurement that captures the socioeconomic position of a community. We fitted multivariable regression models with PCOS diagnosis as the outcome and ADI as the predictor variable in 1,297 PCOS cases and 21,039 controls, adjusting for median age, race, and body mass index. PCOS patients had significantly lower ADI (OR=0.20, 95%CI = 0.12-0.33, p=1.03e-09), indicating higher SES. Patients in the highest ADI quartile had the lowest rate of PCOS diagnosis (OR=0.58, 95%CI=0.49-0.69, p=4.86e-10), showing that as the ADI increased, the diagnosis rate for PCOS decreased. This was also observed among White females in the top two quartiles, who ranged from having 28% to 44% lower odds of being diagnosed. However, Black females in the top two quartiles had 48% to 42% lower odds of receiving a PCOS diagnosis. This may be due, in part, to the baseline ADI of our sample population, where Black females had statistically higher deprivation indices compared to White females irrespective of their PCOS status ($p<0.001$). PCOS has a diagnostic odyssey that can be a barrier to individuals with low SES. These inequities could be an unrecognized cause in the high rate of undiagnosed women. Further investigations are needed to establish the role of social determinants of health on PCOS and its outcomes.

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NORMAL BONE MARROW BIOPSY RATES AMONG BLACK VERSUS WHITE INDIVIDUALS UNDERGOING A BIOPSY FOR NEUTROPENIA

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Healthy individuals identified as having a Black race are more likely to have lower neutrophil counts than individuals identified as having a White race. These lower counts could result in Black individuals receiving more diagnostic testing for neutropenia, including a bone marrow (BM) biopsy, that does not identify pathology, as compared to White individuals. The lower neutrophils are largely attributable to homozygosity for the benign genetic variant rs2814778-C in the Duffy antigen/chemokine receptor gene (DARC/ ACKR1). Up to 65% of African Americans are homozygous for the rs2814778-C variant, while homozygosity is rare among White individuals. The study comprised individuals without a hematological diagnosis who underwent a BM biopsy at VUMC to investigate neutropenia. We compared the proportions of BM biopsies that did not identify pathology between Black and White individuals. The study measurements included clinical indications for the BM biopsy and the presence of comorbidities. The proportion of normal biopsies between Black and White individuals was compared using multivariable logistic regression. Out of 351 individuals with a BM biopsy to investigate neutropenia, 163 (46%) were males, 67 (19%) were Black and the median age was 40.4 (interquartile range, 11.2 - 61.5) years. Overall, 224 (64%) had a normal BM biopsy result. A higher proportion of Black individuals (57 of 67 [85%]) had a normal biopsy, as compared to White individuals (167 of 284 [59%]). Black race was significantly associated with a normal biopsy result (odds-ratio=3.7, 95% CI [1.8 - 8.4], $p<0.001$) after adjusting for age, gender, and comorbidities**.** In conclusion, Black individuals were significantly more likely than White individuals to have a normal result for a BM biopsy performed to evaluate neutropenia.

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NEURODEVELOPMENTAL SCREENING IN YOUNG CHILDREN WITH SICKLE CELL DISEASE

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Children with sickle cell disease (SCD) have an increased risk of neurological complications; however, co-occurrence rates of SCD and neurodevelopmental disorders (NDD)s remain lower than expected. It is important to prioritize early childhood neurodevelopmental (ND) screenings in accordance with the American Society of Hematology (ASH) and American Academy of Pediatrics (AAP) guidelines, in order to improve quality of life for people with SCD and NDDs. We hypothesize that the risk of NDDs is lower than expected in children with SCD due to low ND screening and surveillance rates among healthcare providers. Therefore, we conducted a retrospective chart review to identify clinical characteristics and examine the frequency of ND screening and surveillance among children under 5 years old with SCD. Patients were screened primarily by pediatricians and hematologists. ND Results: 214 participants qualified for inclusion and 148 participants (70%) were assessed for ND. *Ages and Stages Questionnaire-3* (32%) and other non-standardized screening tools (85%) were most used. Of the ND assessed patients (N=148), 37 (25%) were diagnosed with NDDs. Among the not assessed ND patients (N=66), 16 (24%) were diagnosed with NDDs. ASD Results: 207 participants qualified for inclusion and 39 participants (19%) were assessed for ASD. *Modified Checklist for Autism in Toddlers* was the most utilized screening tool (92%). No patients had ASD. Of the ASD assessed patients (N=39), 9 (23%) were diagnosed with NDDs. Among the not assessed ASD patients (N=168), 41 (24%) were diagnosed with NDDs. In conclusion, children with SCD are not being appropriately screened, particularly for ASD. Among screened children, most were screened with non-standardized tools or outside the age recommendations by ASH and AAP. These results are consistent with our hypothesis and can inform future studies examining how the rates of screening and surveillance have changed since the release of the new guidelines in mid-2020.

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COVID-19 INFECTION AND DIABETES IN PREGNANCY

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Problem Statement: Is the risk of severe COVID-19 infection increased among patients with diabetes in pregnancy compared to pregnant patients without diabetes? Background: Diabetes is associated with a more severe SARS-CoV-2 infection phenotype in non-pregnant individuals. However, there is a limited information about this relationship in pregnancy. Our objective is to determine whether pregnant patients with diabetes are more likely to have severe COVID-19 infection than pregnant patients without diabetes.

Approach: We conducted a retrospective cohort study of all patients delivering at Barnes-Jewish Hospital from June 2020–May 2021 that had a positive COVID-19 test during pregnancy. The labor and delivery unit offered universal SARS-CoV-2 testing to all patients. Patient characteristics, including diabetes in pregnancy, were extracted from the medical record. Descriptive statistics were used to characterize the cohort and Mann Whitney U, chi-square, and Fisher's exact were used to compare patients with severe COVID-19 disease (defined by WHOOSCI and NCPERET criteria) to patients with non-severe disease. Results: There were 197 patients with a positive COVID-19 test during pregnancy: 18 (9.1%) had diabetes in pregnancy, and 49 (24.9%) had severe COVID-19 disease. Compared to those with non-severe disease, patients with severe COVID-19 were more likely to have a c-section (46.9% vs 31.1%, p=0.04) and diagnosed with COVID-19 at an earlier gestational age (30 weeks vs 34 weeks, p=0.03). Patients with severe COVID-19 were not more likely to have diabetes (10.2% vs. 8.8%, p=0.78). Post-hoc power analyses revealed we were underpowered to see a difference between the groups. Impact: Findings from this analysis may inform clinical management of pregnant patients with diabetes during the ongoing COVID-19 pandemic. Conclusion: In this cohort, diabetes in pregnancy did not confer additional risk of severe COVID-19 disease. Similar analyses in larger samples may provide greater understanding regarding the association between severe COVID-19 and diabetes in pregnancy.

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RARE GENE VARIANTS IN AFRICAN POPULATIONS

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The known human genome is derived from samples that are mainly from European populations with little global representation and thus, information on genetic diversity, pathologies, and their prevalence is missing and incomplete in the study of genetics. Rare variants found in this population may be misrepresented due to the homogeneity of the tested population. Six hundred publicly available whole genome sequences of six African populations are currently being studied from the 1000 Genomes Project, HapMap Project, and the Montgomery Lab. By using genetic data from the African population, we can have a more diverse, heterogenic population that may be a better representative of human genetic variation. The RNA sequencing data has been normalized to show the distribution of gene expression for 15854 genes in the population. The goal is to make this RNA and ATAC sequencing data accessible to the scientific community to aid in the interpretation of genome-wide association studies of complex traits and diseases. By finding gene outliers in the sequenced African population, rare variants can be identified. Sifting through the variants to find functional RNA sequences will give greater insight into the prevalence of disease and genetics. Some of these variants can be matched up to known rare diseases to verify already known genetic data. The outliers have been found in the rare functional variant data to separate them from the other common variables to be compared. Considering the large amount of outliers found, checking to see which genes have variants that affect the gene's outcome is important in determining how that allele may affect transcription in an individual with disease. Further research includes finding the relative risks for the alleles that have been separated by frequency and their association with disease.

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ANALYSIS OF MODERN HUMAN VARIATION WITH RESPECT TO CRANIOFACIAL AND MASTICATORY FUNCTION

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The linkage of craniofacial shape, diet, and bite force has been a topic of discussion within dental anthropology and biological anthropology. Studies have shown that with dietary change there is a difference in human craniofacial shape These changes in craniofacial shape have been linked to present-day dental issues with malocclusion and crowding of teeth. Given this, the aim of this study was to examine variation in estimated bite force among and within human populations. A total of 61 skulls (29 males, 32 females) from three different populations of modern humans were examined. Skulls were not included in the study if they did not have adequate number of dentitions or if they had extensive antemortem tooth loss. For each, a three-dimensional model of the skull was generated and 43 landmarks placed onto each skull. From these landmarks we then calculated masseter and temporalis muscle vectors as well as measurements of each individual bite point on the mandible. Muscle vectors, estimates of muscle size, and bite force lever arms were then used to calculate an estimated bite force. These bite forces were then compared between sexes and populations. Results suggest that there was significant variation in bite force estimates between sexes and population. These findings indicate that population and sex do influence bite force which ultimately can be tied back to dietary differences among populations. These findings are important for understanding the effects of diet, sex, and craniofacial shape as it relates to the presence of modern-day dental issues and human evolution.

8

ENDING SPINAL FUSIONS AT L4 IN IDIOPATHIC SCOLIOSIS: MOTION FROM L4 TO SACRUM ON PREOPERATIVE FLEXIBILITY STUDIES IMPACTS OUTCOME AFTER SPINAL DEFORMITY SURGERY

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There is controversy among the Pediatric Orthopedic Surgeon community regarding posterior spinal fusion surgery in patients with Idiopathic Scoliosis (IS). Posterior spinal fusion surgery is the gold standard in correcting scoliosis in patients with AIS once the curve is more than 50°. Ending the fusion at L4 is said to optimize correction of the deformity and "obtain global sagittal and coronal balance." The desired outcome of this surgery is leveling of the inferior endplate of the LIV, because the vertebrae distal to the LIV will "spontaneously correct and permit global coronal and sagittal position." However, range of motion between L4 and S1, and morphology of the vertebrae ("specifically poor L4-S1 motion and/or L5 or S1 vertebral wedging) will compromise the outcome. This study aims to show the benefits of fusing the spine to level L4 and aims to determine how the alignment between L4 and the sacrum before surgery and lowest instrumented vertebra in the operating room affects spinal alignment post-operatively. The clinical data will include radiographic images of both preoperative and postoperative views of the patient's spine, and the curves will be measured. Additionally, the alignment between L4 and the sacrum will be obtained. All

values will be compared preoperatively and postoperatively to evaluate correction. It is our aim to estimate the percent correction of the spine with surgical enhancement. Patients will be excluded from the study if they have not had posterior spinal fusion surgery to L4. This is a retrospective study. Patients included in the study had preoperative x-rays no more than 6 months prior to the surgery. Postoperative imaging was taken at approximately 6 week and 2 years following surgery. This study has been approved by the Institutional Review Board. Results and conclusions will be analyzed once data is obtained from the biostatistician.

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DIETARY ROLE OF DAILY GLYCEMIC INDEX AND SELECT NUTRIENTS IN PROSTATE CANCER RISK

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Prostate cancer is the most common cancer in men and is expected to cause 34,130 deaths in 2021, estimated by the American Cancer Society. Prior research has established age, race, a family history, and vasectomy as the most relevant risk factors for developing Prostate Cancer [Pienta & Esper, 1993]. Newer studies have shown that total fat, carbohydrates, and dairy can increase cancer risk. On the other hand, nutrients in soy, cruciferous vegetables, and antioxidants have been associated with protection. The aim of this research is to assess for potential prostate cancer triggers in diet by analyzing consumption of various nutrients in African American men in the US. This research is a secondary data analysis of "Dietary Risk Factors of Prostate Cancer among Men of African Descent" (Flora A. M. Ukoli). Data analyzed was acquired from BLOCK food frequency questionnaires that covered intake of 110 dietary items. Questionnaire data was then used to estimate nutrient levels. This data was collected from African American men with prostate cancer and controls, this is a Case-Control Study. Differences between the groups and intake patterns were assessed using Independent Sample t Tests, Chi Square Tests, Mean Comparison, Correlations, and Descriptive Statistics. The results support claims that multivitamins and high carbohydrate intake are associated with higher risk of prostate cancer. It also added evidence to claims that lycopene and some carotenoids have a protective effect. Most other nutrients had no significant difference between groups and did not show any patterns, despite previous research. These included dairy, total fat, and protein intake. In conclusion, different foods can provide a level of protection while others may contribute to prostate cancer risk. Significant relationships between diet and Prostate Cancer can be used to make dietary recommendations to assist in reducing the risk of Prostate Cancer development and progression.

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MAPPING THE CELLULAR COMPOSITION OF RESECTED CORTICAL TUBERS AND PERITUBERAL TISSUES

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Clinical symptoms of tuberous sclerosis complex (TSC) include developmental delay, intellectual disability, and epilepsy. Mutations in TSC2 are often associated with increased symptom severity. Unfortunately, epilepsy associated with mutations in TSC1/2 is often refractory to drug treatment, requiring surgical resection. Within resected brain tissues from patients with TSC, detection of enlarged "balloon" cells is diagnostic for this disorder. Analysis of tubers and perituberal tissues indicates seizures in TSC originate in the perituberal tissues, and "balloon" cells may contain loss of heterozygosity (LOH) of TSC1/2 compared to surrounding tissue. Though mutations in TSC1/2 produce epilepsy and cause mTORC1 hyperactivation, unified criteria to identify "balloon" cells and infer their lineage are lacking. These diagnostic cells have not been studied across large TSC cohorts at the protein level. In addition, how "balloon" cells influence their microenvironment to produce epileptogenic foci is poorly understood. High-dimensional approaches like imaging mass cytometry (IMC) and cyclic immunostaining offer the opportunity to directly assess more than thirty proteins and/or signaling events in single cells while documenting spatial relationships within the tissue. We have developed a custom imaging panel and computational workflow to identify "balloon" cells within archived cortical tubers. We are currently mapping cytoarchitecture and signaling perturbations within these samples, with a specific focus on "balloon" cells and their immediate neighbors. These data will represent a rich dataset for understanding the abundance, structure, and signaling activity of neuronal, glial, and immune cells within archived tubers and perituberal tissues, enabling quantitative comparison of TSC with other mTORopathies.

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THE EFFECT OF METFORMIN ON DIABETIC RETINOPATHY PROGRESSION IN TYPE 2 DIABETICS

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Diabetic Retinopathy is one of the leading causes of irreversible vision loss in adults in the United States. Diabetic Retinopathy can progress from the non-proliferative form (NPDR), to the vision threatening proliferative form (PDR). Another complication of diabetic retinopathy, diabetic macular edema (DME), is the leading cause of vision loss in patients with DR. Both of these processes can lead to blindness, and patients with NPDR or PDR can develop DME. Many patients with diabetes are treated with metformin. Studies show that use of metformin can slow the progress of NPDR to PDR, but do not discuss the confounding effects of DME. The objective of our research was to analyze the effect of metformin on the progression of diabetic retinopathy to diabetic macular edema. Patient disease status was identified by

phenotyping through the synthetic derivative, a de-identified database. Then, ICD-9 and ICD-10 codes were used to review metformin use within those patients. **We found that …** These results are **consistent/not consistent** with the hypothesis that at least one year of metformin use will be associated with a reduction in odds of diabetic retinopathy progression to PDR or DME after adjusting for confounders.

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SURVIVAL-TIME FREE OF CARDIOVASCULAR DISEASE IN OLDER WOMEN – A SUB-ANALYSIS OF THE WOMEN'S HEALTH INITIATIVE

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Cardiovascular disease (CVD) is the leading cause of death among Americans. Although the risk factors such as diabetes, HTN, and high cholesterol are well documented as major contributors to CVD, fewer studies have defined protective factors that promote vascular health. Even fewer studies have evaluated these factors in elderly women. The objective of our research was to determine years lived free of cardiovascular disease stratified by risk profile in a cohort of women recruited from the WHI. We performed survival analysis of 1,687,925 person-years from 145,034 women during the years 45 through 75 from data generated in the Women's Health Initiative. All participants free of cardiovascular disease at baseline were included in the analysis. Baseline risk factors included hypertension (treated or untreated), high cholesterol requiring pills, diabetes, smoking status, physical activity (< 7.5 met hrs/week), and obesity as well as total cardiovascular disease outcome were analyzed. We found that after 45, lifetime risk estimates for total CVD increased (1). For example, there was a Meta-analysis from 18 cohort studies who risks factors for CVD were measured at 45, 55, 65, and 75 years where BP, cholesterol level, smoking status, and diabetes were used to stratify people. This will help with informing health policy objectives by estimating projection of the overall burden of cardiovascular disease in women. This will also improve communication of cardiovascular disease risk between patients and clinicians. Moreover, data on predictors of poor survival in older women is sparse and this analysis will further our ability to better manage elderly women.

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ZAR1L/ATP6V0A4 DRIVEN METASTASIS IN BREAST CANCER CELLS

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Novel protein, Zygote Arrest 1 Like (ZAR1L), is an RNA-binding, C4 zinc finger containing protein that has been shown to cause transcriptional gene silencing of the BRCA2 gene in breast cancer cells. The presence of the vacuolar proton-translocating ATPase (V-ATPases) on the cell surface is known to increase the invasive phenotype of breast cancer by reducing the pH. ATP6V0A4 subunit is known to locate the V-ATPase on the plasma. We observed that knocking down ZAR1L in breast cancer cell line MCF7 results in upregulation of the subunit of vacuolar ATPase, ATP6V0A4. The molecular mechanism of ZAR1L mediated ATP6V0A4 expression regulation is unclear. This study aims to establish a trend between ZAR1L

and ATP6V0A4 in breast cancer cells. ZAR1L is a novel protein and due to the lack of validated reagents, we started by expressing the recombinant human ZAR1L protein to validate the commercial antibody used in the study. Breast cancer cells were subjected to siRNA-mediated knockdown of ZAR1L. We found that levels of ATP6V0A4 were elevated in the ZAR1L knockdown cells. We also observed that the cells with ZAR1L knockdown are more invasive. This inverse relationship strongly suggests that ZAR1L may play a role in regulating the invasiveness of breast cancer cells via regulating the ATP6V0A4 levels. This study hopes to elicit a new area of research interest that further explores a possible target site for metastatic tumor management/treatments.

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EFFECTS OF BORTEZOMIB ON CHROMATIN REMODELING REGULATOR PHF19 IN CD8$^+$T CELLS AND CANCER CELLS

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T cell exhaustion and senescence are major causes for concern when considering host immune responses to cancer. Enhancement of immune system antitumor functionality by inhibition of CD8+ T cell senescence and exhaustion by regulation of epigenetic operators is a way for this concern to be addressed. PHD finger protein 19 (PHF19) is a polycomb group protein that functions as an accessory subunit of the polycomb repressor complex 2 (PRC2), which represses target gene expression. Research has shown that when PHF19 is over expressed in CD8+ T cells those cells have enhanced proliferation, limited differentiation and less exhaustion promoting antitumor activity. The objective of our research was to demonstrate that Bortezomib epigenetically regulates antitumor immunomodulatory CD8+ T cells via Phf19. Bortezomib's effects on cell senescence and downstream effects were done with dose-dependent treatments and subsequent gene expression. We found that bortezomib demonstrated significant dose-dependent effects on tumor cell viability on lung and breast cancer cell lines. The expression of PHF19 and the downstream PRC2 complex genes were significantly decreased with bortezomib treatment. Notably, bortezomib increased the expression of PHF19 and the downstream PRC complex in CD8$^+$ T cells. These results are consistent with the hypothesis that bortezomib has an effect on downstream events as well as senescence activity of the T cells.

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INVESTIGATION OF ENDOTRACHEAL TUBE VERSUS LARYNGEAL MASK AIRWAY EMERGENCE TIMES FOR SURGICAL PATIENTS

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General Anesthesia is used for surgical patients which requires an airway for adequate ventilation during the procedure. The three parts of general anesthesia are induction which is when the airway is placed. Providers usually use an Endotracheal tube (ETT) or laryngeal Mask (LMA). The ETT is a protected airway while the LMA is quicker to remove. Next part is maintenance, which keeps the patient under, and the last is emergence which is when the patient wakes up. During induction and emergence, there is a higher risk for adverse events such as aspiration, cardiac /respiratory failure, and airway obstruction. The ETT has been found to increase hoarse voice, laryngospasm, coughing, and sore throat when compared to the LMA. This study aims to see if there is a difference in emergence times between the ETT and LMA while also looking at factors such as sleep apnea, ASA score, smoking status, and BMI. A retrospective chart review using a database from OhioHealth will be performed using 2071 patients. Data will be collected about the patient's demographics and factors mentioned before including the airway type, emergence time, total operative time, and procedure duration. Data will be summarized using descriptive statistics. Preliminary data using just emergence time (ET) and airway type showed an ET was around 2 minutes faster for the LMA. Decreasing the time, the patient is in the emergence stage could decrease adverse events when using an LMA. The results are consistent with the hypothesis, but further chart review and analysis must be performed for factors that could alter the emergence times in surgical patients.

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THE ROLE OF THE CALCIUM-SENSING RECEPTOR IN PROMOTING CALCIUM-INDUCIBLE GENES

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Cancer-induced hypercalcemia (CIH) is common in cancer patients with metastatic disease and in up to 30% of cases without metastasis. In the course of breast cancer progression, the secretion of parathyroid hormone-related protein (PTHrP) by tumor cells and the associated destruction of bone tissues, leads to a progressive increase in systemic calcium or CIH. The increase in circulating Ca^{2+} is sensed by the calciumsensing receptor (CaSR), which plays a significant role in maintaining Ca^{2+} homeostasis. Interestingly, high circulating Ca^{2+} is associated with aggressive tumors in premenopausal women and larger tumors in postmenopausal women; however, the contribution of the CaSR in cancer progression

remains poorly understood. Unlike SNPs at rs1801726, up to 20% of breast cancer patients with SNPs at rs1801725 may be predisposed to higher circulating Ca^{2+} in the course of their disease. Since breast cancer frequently metastasizes to Ca^{2+} rich skeletal tissues, we hypothesize that the development of CIH and subsequent desensitization of the CaSR by sustained high Ca^{2+} is critical for both the adaptation of TNBC cells to CIH in Ca^{2+} rich microenvironments and TNBC progression. Our preliminary data reveal the expression level and mutational status of the CaSR is cell type-specific, and that sustained high Ca^{2+} desensitizes the receptor, but promotes tumor cell growth and motility. Sustained high Ca^{2+} also triggers the expression of metastasis promoting genes, including the cancer/testis antigen, MAGEC2, potentially via the early response genes FOS/FOSB. Our data provide novel insights into not only the adaptation of TNBC cells at high Ca^{2+}, but also suggests that screening of patients with Exon 7 CASR variants, could lead to improved management of calcium associated comorbidities and potentially, better therapeutic interventions for women with metastatic breast cancer, for which there is no cure.

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AUTOLOGOUS NEUTRALIZATION DYNAMICS IN THE LATENT RESERVOIR OF HIV-1

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HIV-1 can infect activated CD4+ T cells as they return to a resting memory state and stably integrate into the host cell genome – forming a latent reservoir of infected, transcriptionally silent T cells. The latent reservoir can be reactivated and begin releasing virus at any time – presenting a major barrier to HIV cure. If an individual stops ART, reactivation of this latent reservoir results in rebound viremia. Recent studies have shown that the viruses present after rebound often differ from the viruses detected by the quantitative viral outgrowth assay (QVOA) – the gold standard for quantifying the size of the latent reservoir. This discrepancy could be a result of autologous neutralizing antibodies (anAbs). In this study, the impact of anAbs on the landscape of rebound viruses was explored. A modified QVOA in which a patient's anAbs were added to the culture media was performed alongside a standard QVOA without the addition of anAbs. Outgrowth viruses from the QVOA were sequenced for HIV *env* to identify relevant mutations conferring sensitivity or resistance to anAbs. Longitudinal samples were also collected from patients and anAbs from each timepoint were tested in a TZM-bl neutralization assay against viruses isolated from the supernatant of the QVOAs to assess the IC50 and neutralization capacity of the patient's anAbs over time. There are a variety of outcomes anticipated for the experiments. One outcome is that the neutralization capacity of anAbs from later timepoints will increase when tested against viral isolates from earlier samples. Another outcome is the opposite occurring in which the neutralization capacity of anAbs from later timepoints decreases. A final outcome is that there is no significant change in neutralization capacity. Identifying characteristics of anAb-resistant viruses and the impact of anAbs on the viral landscape may provide insight on reservoir dynamics and guide HIV cure strategies.

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HIGHER BRAIN EXTRACELLULAR GLUTAMINE LEVELS CORRELATE WITH SEIZURE-FREE OUTCOME IN PATIENTS WITH DRUG-RESISTANT EPILEPSY

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Glutamine is critical for numerous brain functions, such as ammonia detoxification and synthesis of the neurotransmitters glutamate and gamma-aminobutyric acid (GABA). Glutamine synthetase (GS) is the only enzyme capable of forming significant amounts of glutamine in mammals. In patients with drug-resistant epilepsy (MTLE), the enzyme is severely deficient in the seizure focus of the brain. Furthermore, these findings highlight the importance of glutamine regulation in epilepsy. To this extent, we measured the glutamine levels in patients who eventually underwent epilepsy surgery and compared glutamine levels in patients who had seizure-free outcomes with patients with Engel class II, III, and IV outcomes. Twenty-nine patients with drug-resistant focal epilepsies of different types were implanted with intracranial depth electrodes for seizure localization. A microdialysis catheter was inserted into the lumen of the depth electrodes. Glutamine was quantified in the dialysis samples using liquid chromatography-tandem mass spectrometry. Postoperative seizure outcome was assessed using the Engel scale. Extracellular fluid was collected from 66 depth electrodes from 29 patients. The patients were followed for a median period of 5.3 years. Eleven patients reported Engel class I outcomes. Next, we compared the basal glutamine levels between the two groups. Glutamine levels were significantly higher in patients with seizure-free outcomes versus other Engel class outcomes (791.3 vs. 510.6 μM, P = 0.021). Logistic regression reveled the patient with higher glutamine levels has significantly better odds of obtaining seizure-free outcomes (OR: 1.001, P = 0.027). This pilot study implements basal glutamine levels with epilepsy surgery outcomes. Higher glutamine levels in patients with Engel class I outcomes underscore the importance of glutamine maintenance in epileptogenesis. Further studies in various animal models can help in understanding the role of glutamine homeostasis in epilepsy

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EXPLORING THE PSYCHOLOGICAL IMPACT OF AXILLARY HYPERHIDROSIS IN SUBJECTS BEING TREATED WITH NOVEL TOPICAL INVESTIGATIONAL DRUG

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Hyperhidrosis is a clinical condition in which there is an excess in sweat production that is well beyond the physiological need of the patient's body. This condition arises due to the sweat glands becoming overactive and in turn, an individual experiences an overabundance of sweat. The burden of this condition is related to the impact it has on an individual's quality of life. The excessive sweating may impede on one's daily life activities and thus greatly impact an individual's physiological state in a negative manner. The objective of our research was to observe an improvement in subjects' quality-of-life measurements, exhibited by a decrease in questionnaire scores, during the study as subjects experience a decrease in axillary sweat production. Quality of life measurements were determined by the completion of the Hyperhidrosis Disease Severity Measure- Axillary (HDSM-Ax) and Dermatology Life Quality Index- Axilla (DLQI) questionnaires. Axillary sweat production was determined by using the Gravimetric Sweat Production Measurement (GSP) testing in each axilla, in mg, which is recorded at each visit. We found that subjects displayed a general trend in a decrease in the quality-of-life scores, both HDSM-Ax and DLQI, which corresponds to an improvement of their quality-of-life measurements. Subjects also displayed a trend towards producing less milligrams of sweat in the GSP testing by the end of the study. These results are consistent with the hypothesis that as subjects experience an improvement in their axillary hyperhidrosis symptoms (decrease in mg of sweat), they will exhibit an improvement in their quality-of-life measurements (decrease in questionnaire scores).

This project was supported, by Meharry Center of Excellence Grant.

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RECIPROCAL EDUCATION AS A CONDUIT TO BUILD TRUST AND SKILLS IN BLACK BIRTH WORKERS

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Black women experience a maternal mortality rate three times higher than their white counterparts. Studies show that black women are also more likely to have a detrimental birthing outcome as a result of perceived racism. These health disparities explain the plight of mistrust between black birthing individuals and their obstetric healthcare providers. Due to these unfavorable outcomes, black women have begun using doulas as a means of support and advocacy throughout their pregnancy. Doulas are trained individuals whose role is to provide emotional, mental, and physical support leading to, during, and after their client's delivery. Unfortunately, many women have become reliant on doulas for insight on topics requiring medical expertise, which is beyond the scope of doula training. In an attempt to fortify doulas, we have constructed a collaborative training session conducted by Ob-Gyns and midwives to equip doulas with medical knowledge on how to recognize and respond to common pregnancy complications within the black birthing community. This two-hour informational session covers topics regarding postpartum warning signs, gestational hypertension, gestational diabetes mellitus (GDM), and breastfeeding. We assessed the doulas' mastery of these topics using a case-based, multiple-choice questionnaire before and following the educational session. Based on this trial, it is supported that this medical training forum significantly improves doulas' knowledge base on postpartum warning signs, GDM, gestational hypertension, and breastfeeding ($P<0.0001$). Additionally, one of the trained doulas reported a client testimonial which she believed to be successful due to the tools she acquired during this seminar. Using this educational format, we can enhance doula proficiency in postpartum maternal care while simultaneously strengthening the trust between black women and obstetric healthcare professionals. This novel model serves as a dynamic framework for improving the quality of the birthing process for black women.

This project was supported by the Reaching Our Sisters Everywhere Community-Engaged Research Program Mini-Grant (Meharry Vanderbilt Alliance).

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THE ONCOGENIC ROLE OF EPIGENETIC FACTOR, SNF2L IN PROSTATE CANCER

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Prostate cancer (PCa) is the second-leading cause of cancer mortality in the United States and is the most commonly diagnosed malignancy in African American men. Epigenetic regulation including chromatin remodeling plays a crucial role in the development and progression of many human diseases such as cancers. Epigenetic alterations contribute to the development and progression of PCa. These alterations may cause drug resistance to readily available treatment options for human cancers including PCa. Nucleosome-remodeling factor (NURF) consists of bromodomain-PHD finger transcription factor (BPTF), sucrose non-fermenting-2-like (SNF2L), and pRBAP46/48, controls the chromatin remodeling machinery. One of NURF's major function is to regulate histone modifications and gene expression. Epigenetic factor, SNF2L serves as the energy transducing subunit in NURF and is encoded by the *SMARCA1* gene. SNF2L is a ubiquitously expressed transcription activator and its elevation is associated with cancer development. However, the role of SNF2L on PCa progression is still elusive. Therefore, there are unmet needs to understand the role of SNF2L in PCa in order to develop effective therapeutic approaches of controlling this malignancy. The objective of this project is to assess the impact of SNF2L loss on PCa progression. We hypothesized that SNF2L knockout (KO) will inhibit the proliferation of androgen-sensitive and castration-resistant PCa cells and targeting SNF2L or SMARCA-1 gene may be beneficial for controlling cancer progression. We have generated SNF2L KO PCa cells with CRISPR-Cas9 technology and inhibited SMARCA1 gene via transient transfection application. Our results showed that SNF2L loss resulted in a reduced proliferation and altered morphology of PCa cells. SNF2L KO destabilizes the NURF complex and impairs chromatin remodeling and histone modifications for cell growth and survival. Thereby, Targeting SNF2L may serve as a novel therapeutic regime in PCa control.

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RADIATION INDUCES UPREGULATION OF CD38 ON HUMAN GLIOBLASTOMA CELLS

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Glioblastomas (GBMs) are aggressive and malignant brain tumors that are almost always fatal (Levy, et al. 2012). Patients have low survival rates and high tumor recurrence despite the gold standard treatments of chemotherapy, radiation, and surgical excision (Levy, et al. 2012). Neurologists and surgeons have observed a significant increase in biomarkers that are present on GBM cells of recurrent tumors. Specifically, CD38 has been shown to be overexpressed in the recurrent GBMs of patients who've undergone radiation therapy (Burns, Terry M.D., Ph.D., Mayo Clinic). When compared to the primary tumor of pre-irradiated human GBM, recurrent GBMs have increased surface CD38 enzymes. CD38 is a transmembrane and ecto-enzyme on innate and adaptive immune cells (Chini et al. 2019). It functions as a NAD+ glycohydrolase and regulates NAD+ metabolism by using the NAD+ substrate to form adenosine diphosphate ribose (ADPR), cyclic ADPR, and nicotinamide (Chini et. al. 2019). These CD38 enzyme products mobilize calcium, a second messenger that has many physiological roles, including vesicle release within the synaptic cleft, muscle contraction, and cell growth (Chini et al. 2019). Interestingly, increased levels of CD38 are seen in situations such as infection, age-related pathologies, and tumorigenesis (Chini et al. 2019). We radiated human glioblastoma cells (GBM6) using 10 Gy. After 14 days there was a significant increase in CD38 expression and activity compared to 0 Gy GBM6 cells. Next, we treated GBM6 cells with TNF-alpha, IL-6, and TNF-alpha plus IL-6. Using a reverse cyclase assay, we discovered that TNF-alpha upregulated CD38 activity, but IL-6 did not. Finally, we saw TNF-alpha plus IL-6 treated cells had a synergistic effect that significantly increased CD38 activity.

This project was supported, in part, by the 2021 Dean's Scholar Summer Research Fellowship.

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EFFECTS OF THE ADIPOKINE ITHMIN ON LIPID ACCUMULATION IN NAFLD MICE LIVER

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With the increasing prevalence of type 2 diabetes and non-alcoholic fatty liver disease (NAFLD), there is still an unmet need to better treat hyperglycemia and hyperlipidemia. Isthmin (Ism1) is a recently identified adipokine that promotes glucose uptake in adipocytes while suppressing lipid production in hepatocytes. The mechanism by which Ism1 controls lipid metabolism is still unknown but the data show that Ism1 treatment induces a signaling pathway that counteracts lipid production, which could be directly related to its function in reversing hepatic steatosis. Different mechanisms are known to be responsible for the development of hepatosteatosis, including enhanced *de novo* lipogenesis, impaired fatty acid oxidation or impaired lipid transport. The hypothesis is that Ism1 signaling affects one or several of these mechanisms to control lipid metabolism and reduce hepatosteatosis. The objective of this research was to identify the different lipid species that are controlled by Ism1 treatment or are altered in livers from mice lacking the Ism1 gene, to better understand which of the lipid pathways are regulated by Ism1. To do so, we used a NAFLD mouse model in which mice were pharmacologically treated with Ism1 or in which Ism1 was genetically knocked out. We quantified the liver lipid content by mass spectrometry. We observed that Ism1 treatment and Ism1 loss of function impacted the quantity of many lipids in NAFLD mice liver including diglycerides, triglycerides, and fatty acids, consistent with a major role for Ism1 in regulating *de novo* lipogenesis. Although Ism1's mechanism of action needs to be identified, these results suggest that Ism1 may have a therapeutic potential to treat NAFLD.

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5 MINUTE MOMENT FOR RACIAL JUSTICE

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Systemic racism has roots in American healthcare and medical education. There are few curricula or approaches on how to teach anti-racism in the clinical environment. The objective of our research is creating a curriculum to teach structural racism during bedside rounds, emphasizing historical narratives and healthcare disparities. The Five-Minute Moment for Racial Justice is a 5-step framework highlighting: context, current standards, historical narrative, health disparities, and steps to equity in medical diagnostics, evaluation, and treatment. This framework and curriculum were presented to physicians at University of Alabama Birmingham School of Medicine and Stanford Medical School, where feedback was taken. Additionally, we led discussions with a Community Advisory Board around challenges to teaching anti-racism at the bedside and solicited feedback from the Community Advisory Board members. To date, we have interviewed nine faculty physicians and conducted one Community Advisory Board meeting. Open-ended responses by physicians identified discomfort with the subject, lack of knowledge, or inadequate time as barriers to discussing race and racism with patients at the bedside and with learners. Qualitative responses from both the faculty interviews and the Community Advisory Board discussion groups showed positive and favorable feedback to the framework structure and language. These preliminary observations are indicative of the necessity of building a curriculum to teach the topic of race as a social determinant of health at the bedside with patients and with learners (residents and medical students).

This project was supported in part by the Stanford-Meharry summer research program.

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PTEN EXPRESSION IN ENDOMETRIAL CARCINOMA

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Endometrial cancer is the fourth most common cancer among women in the United States (1). The Cancer Genome Atlas (TCGA) study on endometrial cancer resulted in molecular classifications that have both prognostic and potential predictive significance. These four classifications include: *POLE* mutated, microsatellite instability (MSI), No Specific Molecular Profile (NSMP), and copy-number high/"serous-like" (P53). Phosphate and tensin homolog (*PTEN)* is a tumor suppressor gene that is involved in cell cycle regulation, and is frequently altered in endometrial endometrioid cancers. The objective of our project was

to evaluate *PTEN* expression. In the future we plan to evaluate *PTEN* loss within the context of molecular status, as this analysis may provide additional prognostic significance. *PTEN* expression was assessed using digitally scanned tissue microarrays (TMA's) stained immunohistochemically with a *PTEN* antibody. The TMAs were constructed from a series of 325 endometrial endometrioid carcinomas from the Intermountain Biorepository that had previously undergone TCGA molecular classification. The digitally scanned slides of the *PTEN* stained TMAs were assessed using Objective Pathology software. Overall of the 316 evaluable TMA's, 48.4% demonstrated loss of *PTEN* expression, 44.6% demonstrated retained expression, 2.5% demonstrated decreased expression, and 4.4% demonstrated subclonal expression. In the future we plan to evaluate *PTEN* expression patterns within the context of specific molecular groups. We are hopeful that these findings provide further insight into heterogeneity of clinical behavior within a particular molecular subgroup.

This project was supported by the Stanford-Intermountain Collaboration Grant Program and MD Anderson Gynecologic SPORE Career Enhancement Program (CEP) Award (NIH sponsored).

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THE PARADIGM SHIFT IN MENISCAL SURGERY: MENISECTOMY VS MENISCAL REPAIR

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Orthopaedic surgeons have begun to experience a paradigm shift in the classical treatment of meniscal tears. Specifically, between meniscal repair (MR) and meniscectomy (MT) in that MT is decreasing while MR is increasing in an inverse relationship to each other. This shift was recognized heuristically among the specialty, however, there existed little published data that used epidemiological statistics to define this shift in surgical treatment. The purpose of our study was to analyze this shift on a macro-scale using patient information from the Nationwide Ambulatory Surgery Sample (NASS) database. From there we drew conclusive statements about these general trends in our patients and their procedures from the NASS database. The data for both MT and MR was mined from the database via Current Procedural Terminology codes. With the data, we calculated averages, confidence intervals, and p-values. We found that the heuristic belief of the shift in surgical treatment was true statistically and that our research was congruent with the previous literature. In addition, we elucidated other statistically significant findings for MT and MR in areas like gender, cost, location, and age.

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PERCEPTUAL INFERENCE AND PHENOMENOLOGY OF AUDITORY VERBAL HALLUCINATIONS

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Auditory verbal hallucination (AVH) is a perceptual or auditory-like experience lacking corresponding external stimuli. This phenomenon, commonly investigated in patients with schizophrenia, can be further characterized using variables such as voice clarity, presence or absence of acoustic characteristics, and length of occurrence. Little is known about whether a diversity of phenomenological features corresponds to a diversity of mechanisms leading to the emergence of AVH or whether subsets of these features may signal differential response to treatments. Although many features of AVH may be thought to signal differences in pathophysiology, the clarity of AVH—how 'voice-like' versus 'thought-like' the AVH are—has long been thought to be an important feature. Therefore, the objective of our research was to explore perceptual and clinical correlates as they relate to voice-like (VLV) and thought-like (TLV) AVH subtypes. These correlates were determined using a Computerized binary Scale of Auditory Speech Hallucinations and an Auditory Conditioned Hallucinations Task. No perceptual differences between the clinical groups where identified while investigating conditioned hallucination rates, confidence rates, the weighting of priors vs. sensory evidence, and the ability of subjects to update their beliefs. Meanwhile, clinical differences were found when measuring susceptibility to delusions and distress due to voices. These results suggest that characteristics like clarity may correlate to clinical outcomes and overall functioning, but not perception.

This project was supported by a NARSAD Young Investigator Award from the Brain and Behavior Research Foundation, a K23 Career Development Award from the National Institute of Mental Health (K23 MH115252-01A1), a Career Award for Medical Scientists from the Burroughs-Wellcome Fund, and by the Yale University School of Medicine and Department of Psychiatry.

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MIR125B IS REGULATED VIA DNMT MEDIATED PROMOTER HYPERMETHYLATION

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The ongoing HIV/AIDS pandemic has resulted in more than 72 million infections worldwide and over 40 million deaths. In the absence of an effective vaccine, a combination of inhibitors against HIV-1 enzymes are the only treatment option available to curb the global disease burden. However, the emergence of drug-resistant viruses, cellular toxicity and co-morbidities of the current antiretroviral drugs require identification of novel therapeutic targets. Therefore, new knowledge on the mechanisms of HIV-1 infection is critical to identify such antiviral targets. Micro RNAs (miRNAs) are small non-coding RNAs which have been identified to play a role in HIV-1 infection. Specifically, miR-125b has been shown to be downregulated during HIV-1 infection, however, the underlying mechanism of this regulation remains unclear. Mature miRNAs are generated from primary miRNA transcripts within the host chromosomes. Our *in silico* analysis suggest that the promoter of miR-125b contains DNA methylation sites identified by the presence of CpG-rich sites. DNA methyltransferases (DNMTs) are the primary enzymes responsible that carry out CpG methylation of promoters. The majority of these methylations are carried out by DNMT1, however, accumulating evidence also suggests contributions by DNMT3a and DNMT3b. Therefore, in this study, we examined the effect of DNMT overexpression on regulation of miR-125b. Our results indicate that DNMT1 and DNMT3a overexpression is correlated with the downregulation of miR-125b.

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SCREENING ABDOMINAL RADIOGRAPHS IN SUSPECTED INTUSSUSCEPTION

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Intussusception is the most common abdominal emergency among the 9 to 24 month and male infants. The condition is an introversion of proximal bowel into a distal segment at the ileocecal junction. Clinical presentation of intussusception is non-specific.[1]The intussusception triad is observed in less than 50% of cases. Ultrasonography is highly specific and sensitive, challenging radiography as the first-line imaging modality in screening for intussusception. The hallmark finding for intussusception on ultrasound is the target sign. Despite evidence for ultrasonography as the intussusception screening tool, some sources assert radiography as the preferred modality. Our project assessed the utility of ultrasonography in comparison to radiography in screening for intussusception. A retrospective cohort study was conducted among children with suspected intussusception over a two period at Vanderbilt University Medical Center's pediatric emergency department. A chart review of 719 cases was performed to collect data including: patient demographics and history, physical exam, and radiologic results. Of the 719 cases reviewed, #(%), #(%), and #(%) received radiographs, ultrasonography or both imaging modalities respectively. Among the 688 ultrasounds 69 (10.03%) were read as positive for intussusception. Of the 714 radiographs 57 (7.98%) were concerning for intussusception. Among the 719 cases reviewed 67 (9.32%) had a final diagnosis conclusive for intussusception. The results of our study demonstrate the utility of ultrasonography in comparison to radiography in screening for intussusception. There were 67 (9.32%) true positive cases. Ultrasonography identified 69 (10.03%) positive cases. In contrast, radiography identified 57 (7.98%) concerning cases despite there being more of this type of study performed amongst the cohort. Given the severity and low prevalence of intussusception an imaging modality that maximizes positive indicators while minimizing risk of radiation exposure should be preferred when screening for this condition.

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IMPACT OF RACE ON GRAFT SURVIVAL IN PATIENTS UNDERGOING LIVER TRANSPLANTATION

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Liver transplantation is a life saving measure for patients with end stage liver disease, however, implicit biases and racial disparities are prevalent in the liver transplantation process. The objective of our research was to determine the impact of donor and recipient race on post-transplant liver graft survival and biologically, to examine whether donor and recipient race matching results in better liver transplant outcomes. Clinical data concerning donor recipient characteristics and transplant outcomes for 18,443

patients 18 years of age and older, whose liver transplants were performed in the US from 2016-2018 were extracted from the OPTN (Organ Procurement and Transplantation Network) database. The primary outcome of the study is graft failure stratified by donor and recipient race. Graft failure was defined by recipient death or re-transplantation within one year of liver transplantation. The data set was then compiled and analyzed using R code. The results indicate that white liver Tx recipients have better 1-year graft survival outcomes in comparison to AA patients, and that there is a significant decline in 1-year graft survival when AA patients are matched by race. Whether this is driven by the recipient or donor characteristics by race is unclear. AA patients are also underrepresented in the recipient population and over-represented in the donor population, highlighting the existing inequality in healthcare and society in general. In turn, our results strongly suggest that racial disparities in liver transplant highlights the need for equity and justice within the entire liver transplantation process in regards to AA transplant recipients and donors.

This project was supported, in part, by the Stanford-Meharry Initiative.

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EXAMINING THE COMBINED PIWI-INTERACTING RNA AND MICRO RNA SIGNATURE IN PRIMARY HUMAN CARDIAC MYOCYTES DURING EARLY PHASE *TRYPANOSOMA CRUZI* INFECTION

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Chagas disease is caused by the parasite *Trypanosoma cruzi*. About 40% of infected individuals develop cardiovascular, neurological, or gastrointestinal pathologies. *T. cruzi* infection triggers extensive changes in the gene expression of affected host cells through mechanisms that are not well defined. Small non-coding RNA (sncRNA) play significant roles in regulating gene expression. However, their role in *T. cruzi* induced gene regulation remains unknown. *Our study aims* examined the expression profiles of PIWI-interacting RNAs (piRNAs) and micro RNAs (miRNAs) during the early phase of infection. We challenged primary human cardiac myocytes (PHCM) with *T. cruzi trypomastigotes, extracted RNA,* and conducted small RNA-sequencing to evaluate changes in sncRNA expression. Reads were aligned to the hg38 reference genome and sncRNA databases using Bowtie. Piano and miRDeep2 were used to predict novel piRNAs and miRNAs, respectively. NOISeq was used to determine *differentially expressed (DE)* piRNAs and miRNAs. DE scnRNAs were queried against human coding transcripts to predict potential targets using miRanda, RNA22, and TargetScan. Enrichment mapping to KEGG pathways was done using WebGestalt. *Our results* identified 29 and 217 unique DE miRNAs and piRNAs, respectively. Among the DE miRNAs, 11 were known, and 18 were putative and potentially novel. Of the DE piRNAs, 6 were known, and 211 were novel. The DE piRNAs and miRNAs had established Chagas Disease genes (TGFβ1, NFATC2, FOSB, and NR4A1) as their targets. Among the enriched KEGG pathways were focal adhesion, regulation of actin cytoskeleton, and MAPK signaling pathways. In comparison, miRNA-associated enriched KEGG pathways were calcium signaling, dilated cardiomyopathy, and MAPK signaling. *In summary,* through *in silico* analysis of small RNA sequencing data, we identified sncRNAs dysregulated in PHCM during early *T. cruzi* infection. These findings serve as a major step toward identifying the piRNA-miRNA signature profile contributing to infection and altered gene expression in host tissues.

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MUTATIONS IN THE NSD1 GENE ARE ASSOCIATED WITH POLYCOMB REGULATED GENES IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

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NSD1 is an enzyme that regulates gene expression. A mutation in the *NSD1* gene disrupts the normal function of *NSD1* enzyme thereby preventing NSD1 from regulating other genes properly. Germline (inborn) *NSD1* mutations cause Sotos syndrome. Somatic *NSD1* gene mutations frequently occur in Head and Neck Squamous Cell Carcinoma (HNSCC). The objective of our research is to explore the genes that are differentially expressed by *NSD1* mutations in both Sotos syndrome and Head and Neck cancer. We analyzed TCGA gene expression and somatic mutation data to find the most differentially expressed genes that are abnormally expressed specifically in *NSD1* mutated cancers and used gene set enrichment analysis to characterize the types of genes that are deregulated due to *NSD1* mutations. Identification of the genes is important as it helps us to understand the mechanism through which *NSD1* mutations regulate gene expression and may identify transcriptional pathways that are altered in *NSD1*-mutated cancers. We found that *NSD1* mutations were associated with deregulated genes that are controlled by polycomb mediated silencing. This could explain the role of NSD1 in cancer since polycomb mediated silencing is a known cause of cancer.

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EFFECTS OF DENTAL TREATMENT ON CIRCULATORY CYTOKINE AND CHEMOKINE LEVELS IN HIV+ PATIENTS

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Objectives: The Human Immunodeficiency Virus (HIV) infection has historically been associated with reduced CD4 T-helper cells and increased inflammation with relatively high levels of circulating cytokines. Periodontal Disease (PD) is highly prevalent among HIV+ patients and is characterized by increased inflammation and oxidative stress. Uncontrolled PD may result in the systemic spread of inflammatory products, enhance inflammatory burden, and contribute to the unresolved inflammation often observed in the individuals with undetectable viral loads who continue to experience morbidities. We hypothesize that local dental treatment attenuates the abnormal circulating cytokines and inflammatory burden while improving PD status in HIV+ patients. **Methods:** Sixteen HIV-positive virally suppressed African Americans (AA) with a median age of 41 were divided into two groups (n=8 each) based on their interface with dentistry: Group 1 had been receiving ongoing regular dental care and Group 2 participants had not

received routine dental care prior to the study. The periodontal status was assessed and periodontal therapy along with oral hygiene education were provided at baseline, 3 months, 6 months, and 12 months. Blood was collected at each visit from both groups from which serum was extracted and stored at -80^{0}C. Serum samples were analyzed for an array of human inflammatory cytokines/chemokines and receptors by qPCR. Statistical comparisons between two groups and at different visits were performed using multiple comparison tests. **Results:** Proinflammatory cytokine/chemokine levels were significantly ($p<0.05$) higher in Group 2 (n=75) compared to Group 1 at baseline. Across longitudinal visits, dental treatment for each group significantly reduced several cytokines: TNFα, IFN-γ, IL-5, 7, 8, 13, 15, 17A, IL 1A, IL 1B and BMP 2 and chemokines: CCL 2, 3, 5, 8, 11, 20, 22, 23 in our study cohort. **Conclusion:** Dental treatment effectively suppressed circulating pro-inflammatory cytokines, thus improving inflammatory burden in virologically suppressed HIV+ patients.

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TRANSMEMBRANE DOMAINS AND STRUCTURAL MOTIFS ARE LINKED TO MITOCHONDRIAL PROTEIN LOCALIZATION AND PROTEIN-PROTEIN INTERACTIONS OF TIM17 IN TRYPANOSOMA BRUCEI

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Trypanosoma brucei (*T. brucei*) is a eukaryotic parasite responsible for the sub-Saharan disease, African Trypanosomiasis. Like yeast and humans, this single-celled organism contains a tubular mitochondrion with canonical features, despite having only one. Additionally, most mitochondrial proteins are nuclear-encoded and require localization and import into the mitochondrion after cytosolic transcription. Our lab as well as others have shown that *T. brucei* contains species-specific import machinery which consist of an archaic translocase of the outer membrane (ATOM) and one translocase of the inner membrane (TbTIM) in contrast to yeast and humans which contain two (TIM 23 and TIM22) with very specific functions. Our lab has also determined that TbTim17 is the only translocase in the ~1,000 kDA TbTIM protein complex capable of performing both functions of TIM23 and TIM22. However, it is unclear how this protein interacts with other proteins in the complex making this possible. Like most mitochondrial proteins, TbTim17 is also nuclear encoded which means it too must be localized and imported into the mitochondrion. It is predicted that TbTim17 consists of four-transmembrane domains (TMDs) similarly to Tim23 and Tim22, but it is unclear which regions of this protein contain targeting signals which allow its localization and import. Using deletion mutants removing the N- and C- termini, and each TMD successively, we have indicated TMD 1 and 4 as important regions necessary for mitochondrial localization. Furthermore, using yeast-two hybrid analysis, we have determined that the C-terminal region of TbTim17 interacts with small TbTims and other TbTims pointing to a possible mechanism of how TbTim17 forms a complex and engages in translocating different nuclear-encoded mitochondrial proteins.

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RETROSPECTIVE ANALYSIS OF PROSTATE CANCER CHARACTERISTICS THAT ARE MISSED BY STANDARD MRI AND MRI ARTIFICIAL INTELLIGENCE MODEL RAPSODI (RADIOLOGY *P*ATHOLOGY *S*PATIAL *O*PEN-SOURCE MULTI-*D*IMENSIONAL *I*NTEGRATION)

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There are numerous studies that have previously studied the accuracy of AI models in comparison to traditional MRI and radiologist readings, the specific characteristics of the prostate cancer and patient that are missed by the AI model have yet to be explored. False positives and negatives are not uncommon regarding prostate cancer, especially aggressive cancers. The continuation of development and perfection of deep learning models can help in increased early prostate cancer detection and therefore decreased death rates. Using the already attained pathology images, we used the histopathology to identify lesions missed by the radiologist and the digital pathologist (AI). The retrospective used data from previous studies done by the Laboratory for Integrative Personalized Medicine at Stanford University. The data consists of 73 patients with aligned the MRI, histopathology images from surgery, and lesions from radiologists. Connected components was used to connect adjacent lesions at least 5ccs identified by both the pathologist and digital pathologist. 3D slicer was then used to manually identify lesions missed by the digital pathologist and radiologist using the lesions identified by the pathologist in the whole mount histopathology from the radical proctectomy as the gold standard. The volume cut off for lesions was at least 150 mm^3. We found that there was a significantly higher percentage of minority patients with missed lesions in comparison to white patients. In addition, the digital pathologist identified significantly more lesions that the radiologist. Lastly, we found that there was a significantly higher lesion intensity on MRI's in minority patients than in white patients. Although the sample of Black, Asian, and Hispanic was too small to make any definitive conclusions, the higher rate of missed lesions and higher intensity is noteworthy and should be further explored in a larger patient population.

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STUDY PARTNERS' PERCEPTIONS OF RESEARCH BURDEN IN LONGITUDINAL ALZHEIMER DISEASE STUDIES

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Study partners are required for participants to enroll in Alzheimer Disease (AD) studies; they provide essential information on their participants' cognitive and functional status over time and can impact participant adherence and retention. Study partners' perception of health risk of the participant, such as side effects from treatment, physical pain and deteriorating health, could negatively impact study partners' decisions to participate, or continue participating, in longitudinal studies. This purpose of this study is to

examine the barriers and facilitators to the retention of study partners in longitudinal Alzheimer disease research. Study partners were recruited from four Alzheimer Disease Research Centers (ADRC). Eligibility requirements included study partners of participants who: 1) were aged 45 years or older; 2) were currently enrolled in longitudinal studies; and 3) had a Clinical Dementia Rating score of <1. Study partners of participants who were institutionalized or lived outside the geographical region of the ADRC were excluded. Study partners completed a 57-item survey with 2 open ended questions about facilitators and barriers to retention in longitudinal studies in-person or via phone. Items were rank on a Likert scale of 1 (strongly disagree) to 5 (strongly agree) unless noted otherwise. The attendance percentage and dropout rate of the study partners were also recorded. Multiple linear regression analysis will be conducted to identify which barriers influenced the study partners' attendance. Approximately 212 study partners completed the survey. Perceived health risks of participating in AD research are associated with high burden procedures such as lumbar punctures or CT scans. Twenty-four percent study partners (n=51) reported "physical harm", "side effects", "physical pain" and "worsening health" as health concerns resulting from their participants' involvement in AD research. There was not an association between study partners' perceived health risk of participants and study partners' attendance rate. Distance and trust in research showed a strong correlation with attendance rates of study partners. The study indicates that study partners attendance is not affected by perceived health risks for participants. However, ADRCs should aim to decrease the physical burden of participants to increase recruitment. Trust in Alzheimer research has potential to improve if individuals know that they will not be physically harmed by procedures and could positively impact attendance and retention. Distance or traveling to research sites affect the attendance rates of study partners. Previous studies have shown that home visits may help alleviate burden on study partners; longitudinal AD studies may benefit from utilizing remote or home visits when possible.

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TISSUE-SPECIFIC NK CELL ACTIVITY AGAINST TUMORS

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Natural killer (NK) cells play significant roles in cancer immunity largely due to their direct cytolytic and indirect immune regulatory functions. Clinical studies have demonstrated a strong role of NK cells in cancer immunosurveillance. The number of infiltrating NK cells in tumor tissues has also been shown to be a significant relation to cancer prognosis. However, NK cells have yet to be fully harnessed in immunotherapy partially due to the extensive heterogeneity and plasticity seen among them. The origin, phenotype, and functions of tissue-resident vs circulating NK cells remain controversial. The objective of this study is to elucidate tissue-specific NK cell diversity and function in solid lung and breast tumor microenvironments. Based on our preliminary data, we hypothesize that NK cells from different tissue locations display unique genetic and functional profiles that can predict NK effectiveness in these solid tumor microenvironments. Data show the biological diversity among NK cells from distinct locations that reflect differences in NK cell interactions with lung and breast murine tumors. This is supported by the heterogeneity of NK cell specific cluster of differentiation markers and gene expression based on flow cytometry, cytotoxicity, and bioinformatics analyses in mouse tumor models of C57BL/6 LL/2 and BALB/c 4T1.2-HA. We observe significant differences in the expression of activating and costimulatory NKG2D receptor both across tissue locations and in response to the solid tumors *in vivo* and *ex vivo*. Differences in

cytotoxicity and tumor infiltration of NK cells from different tissue locations were also noted. These data underscore the importance of tissue-specific NK cells in solid tumor microenvironments that could lead to advancements in NK-based cancer immunotherapy applications.

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"I WILL LISTEN": TRANSDISCIPLINARY ANTI-RACISM COMMUNICATION DIALOGUE ADAPTED TO MEDICINE

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With evident data on the harmful effects of anti-Black racism on health inequalities and the impact interpersonal racism has on the patient-physician relationship, it is critical to highlight the importance of health communication and racial justice in fostering meaningful connections. Presence 5 (P5) is a communication framework designed to promote meaningful connections with patients through five practices: Prepare with Intention, Listen Intently and Completely, Agree on What Matters Most, Connect with the Patient's Story, and Explore Emotional Cues. This study investigated communication practices and specific language used to combat anti-Black racism in healthcare. We performed a preliminary literature review on anti-racism communication and a secondary qualitative analysis on interviews with 40 individuals from non-clinical fields to identify transdisciplinary anti-racism practices. The secondary analysis focused on excerpts coded for "dialogue," which is relevant to communication practices. Through deductive thematic analysis, emergent themes were identified around specific recommended language and coded for the P5 practices, and anti-racism practices were adapted to the following healthcare scenarios: clinician to patient communication, clinician internal reflection, and clinician to clinician communication. The data was analyzed for anti-racism practices. The distribution of excerpts mapped onto the P5 practices accordingly: Prepare with Intention (24%); Listen Intently and Completely (13%); Agree on What Matters Most (13%); Connect with the Patient's Story (11%); Explore Emotional Cues (9%). Outcomes from this analysis make a strong argument that specific anti-racism language recommended by individuals across non-clinical disciplines can be effective and adapted in healthcare settings. Clinician adoption of anti-racism communication language may promote racial justice in clinical interactions and positively influence patient care and health outcomes through meaningful yet challenging dialogue on the impact of racism on patient's health. Future research should evaluate the effectiveness of anti-racism language on health communication outcomes.

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PATIENT CHARACTERISTICS ASSOCIATED WITH ACCEPTABILITY OF OFFICE HYSTEROSCOPY

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Hysteroscopy is a minimally invasive endoscopic procedure that directly visualizes the uterine cavity to diagnose and treat various uterine pathological conditions. Hysteroscopy is an efficient procedure to perform in an office setting when considering patient age and anxiety levels. Advantages to performing this procedure in an office setting includes less cost, optimization of time and increased safety of the procedure for the patient.[3] Patient acceptability of the procedure exhibits their willingness and adherence to follow up with future hysteroscopies. Various studies have demonstrated high satisfaction to hysteroscopies. However, there are patient characteristics that may reduce patient acceptability of this procedure. For example, patient history of anxiety or abortion may impact preoperative anxiety levels. Consequently, preoperative anxiety levels can influence patient acceptability of office hysteroscopy and patient's willingness to undergo this procedure again in an office setting with general anesthesia in an operating room. Patient characteristics that have yet to be investigated and may influence patient acceptability of the hysteroscopy procedure includes anxiety medications, marijuana use, and history of abortion. We hypothesized that patients who take prescribed anxiety medications, have a history of self-medication with marijuana, and have a history of abortion will have a lower acceptability rating of office hysteroscopy and elect anesthesia in an operating room for their follow up hysteroscopy. After conducting a retrospective chart review and logistic regression analysis, we found patients with an anxiety diagnosis, who self-reported anxiety and have a history of SSRI/SNRI or hydroxyzine use for anxiety are more likely to give lower acceptability rating scores. Patients with a history of abortion and patients with a history of marijuana use gave acceptability ratings similar to patients without a history of abortion or history of marijuana use, respectively. Focusing on the psychophysical interactions of women's healthcare experience helps develop individualized interventions, therapies, and treatments.

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UNDERSTANDING RACIAL DIFFERENCES IN UTERINE LEIOMYOMATA AND ITS CLINICAL PHENOME USING MENDELIAN RANDOMIZATION

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Uterine leiomyomata (ULs) are benign growths of the uterine myometrium that affect approximately 77% of women by the onset of menopause. Risk factors include earlier onset menarche, increasing age, and childbearing history, but African ancestry is the most influential factor. AA women are more likely to develop larger, more numerous ULs with an earlier age of onset compared to European ancestry (EA) women. ULs have also been associated with other morbidities like type 2 diabetes (DM) and obesity and body mass index (BMI); however, it remains unclear whether ULs are the cause or result of these conditions. Nine genome wide association studies (GWAS) have been performed that identified over 30 loci that are associated with ULs; however, none of the loci found in eight studies were detected in AA populations. This project seeks to elucidate the relationship between ULs with phenotypes of DM, BMI, and blood pressure traits (BPT) across racial groups to better understand the clinical phenome surrounding ULs. This was accomplished through systemic investigation using Mendelian Randomization to test for pleiotropy between ULs and the phenotypes of interest. Using summary statistics from previous GWAS on ULs, publicly available resources (BMI, DM), and in-house data (BPT), we assessed for vertical pleiotropy with the inverse variance weighted test and horizontal pleiotropy with the MR Egger test. In evaluating the causal relationship between fibroids and other risk factors, we can increase our understanding of the biological mechanisms that contribute to fibroids and help guide clinical care by understanding the role of these risk factors. Moreover, it opens up the floor to providing precision medicine for an underrepresented population and mitigating the health disparities seen with fibroid cases.

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INTACT MORAL DECISION-MAKING IN ADULTS WITH MODERATE-SEVERE TRAUMATIC BRAIN INJURY

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Individuals with moderate-to-severe traumatic brain injury (TBI) may display a wide range of cognitive impairments, including those related to decision-making and social/emotional cognition. However, less is known about how individuals with TBI perform on moral decision-making tasks, which purportedly tap both social and non-social cognitive processes. In light of this literature gap, the current study sought to probe moral decision-making in a sample of individuals with TBI using a widely employed measure. We administered a set of 50 traditional trolley-type dilemmas to 31 individuals with TBI and 31 demographically matched, non-injured comparison participants. We hypothesized that individuals with TBI would be more likely to offer utilitarian responses to personal dilemmas than non-injured peers. We observed no group differences in the likelihood of offering a utilitarian response across dilemma types (non-moral, impersonal, and personal dilemmas). These results suggest that moral decision-making ability is not uniformly impaired following TBI. We suggest that neuroanatomical and demographic characteristics may be more predictive of a moral decision-making deficit than injury severity alone. These results inform the neurobiology of moral decision-making, have implications for characterizing patterns of spared and impaired cognitive abilities in TBI, and may shed new light on the overrepresentation of individuals with TBI in prison populations.

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CINNAMALDEHYDE PROTECTS AGAINST P. GINGIVALIS INDUCED INTESTINAL EPITHELIAL BARRIER DYSFUNCTION IN IEC-6 CELLS VIA THE PI3K/AKT-MEDIATED NRF2 SIGNALING PATHWAY

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Porphyromonas gingivalis (Pg), a gram-negative oral pathogen, promotes and accelerates periodontitis-associated gut disorders. Intestinal epithelial barrier dysfunction is crucial in the pathogenesis of intestinal and systemic diseases. Altered tetrahydrobiopterin (BH_4), a cofactor for nitric oxide synthases (NOS), and reduced antioxidants have long been known to be associated with gastrointestinal motility disorders. In this study, we sought to elucidate the protective role of cinnamaldehyde (CNM) from *P. gingivalis* (W83) and *Pg*-derived lipopolysaccharide (LPS) induced intestinal epithelial barrier dysfunction via antioxidative mechanisms in IEC-6 cells. IEC-6 (ATCC, CRL-1592) cells were pretreated with or without CNM (50 & 100 µM), in the presence or absence of *P. gingivalis* (strain W83, 10^9 MOI) or *Pg*-LPS (0.1, 1 & 10 µg/mL) between 0-to-48-hour time points by adopting co-culture method respectively. Intestinal barrier function, cytokine secretion and intestinal oxidative stress mRNA gene expressions were analyzed. *P. gingivalis* or *Pg*-LPS, significantly increased ROS, and MDA levels expressing oxidative stress damage. *P. gingivalis* infection or *Pg*-LPS induces inflammatory cytokines via TLR-4 signaling. Furthermore, infection reduced mRNA expression of nuclear factor-erythroid 2-related factor 2 (Nrf2) and superoxide dismutase (SOD) in a time dependent manner. Interestingly, inducible nitric oxide synthase (iNOS) mRNA levels significantly increased with *Pg*-LPS effectively than *Pg* infection itself with increased levels of nitric oxide (NO). BH_4 (cofactor of NOS) biosynthesis enzyme DHFR (salvage pathway) mRNA levels showed a significant decrease while mRNA levels of GSK-3β were elevated. CNM suppressed *Pg*, *Pg*-LPS induced intestinal oxidative stress damage by reducing ROS, MDA and NO production. Furthermore, CNM treatment strengthened intestinal barrier function via increasing the phosphorylation levels of PI3K/Akt/Nrf2, and SOD 1 mRNA expressions. GSK-3β/iNOS mRNA expression were significantly suppressed by CNM treatment. CNM protected against *Pg* induced intestinal epithelial barrier dysfunction via activating the PI3K/Akt-mediated Nrf2 signaling pathway in IEC-6 cells.

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KRUPPEL-LIKE FACTOR 6 MEDIATED REGULATION OF PROLIDASE TRANSCRIPTION

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Prolidase, also known as peptidase D (*PEPD*), is a hydrolase that cleaves dipeptides with a proline or hydroxyproline located at the C-terminus. Prolidase catalyzes the rate-limiting step in collagen production because its substrates are generated mainly during collagen turnover. Prolidase is therefore vital for collagen metabolism, matrix remodeling, and wound healing. Defective wound healing is one of the hallmarks of Prolidase Deficiency, a rare autosomal recessive disorder characterized by ulcerative wounds, bone deformities, and intellectual delays. Prolidase mRNA and activity are increased in scar tissue and wound fluid. Although prolidase plays a significant role in wound healing, its molecular and cellular regulation remains understudied. Our preliminary in silico analysis of the *PEPD* promoter ($PEPD_{pro}$) highlighted key regulatory elements upstream of the transcription start site. We selected Kruppel-like factor 6 (KLF6), a zinc-finger transcription factor associated with vascular injury, wound healing, and collagen metabolism. We amplified the promoter from the human genome and inserted it into a luciferase reporter construct. Our data demonstrate that KLF6 enhances *PEPD* promoter activity in a dose-dependent manner. Additionally, KLF6 is regulated by Transforming Growth Factor β_1 ($TGF\beta_1$), and our data further illustrates that $TGF\beta_1$ drives both *PEPD* promoter activity as well as increases prolidase mRNA levels. Our current and ongoing findings generate new knowledge on the molecular regulation of prolidase and will aid in developing therapeutic approaches to regulate its expression in various physiological and pathological conditions such as wound healing.

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EVALUATING TRUST BETWEEN THE BLACK COMMUNITY AND INSTITUTIONAL PLAYERS OF HEALTHCARE DELIVERY

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Both the historical and current medical injustices and health disparities have eroded the trust between African Americans and the health care entities in charge of their delivery of care. While few studies have evaluated the role of trust in healthcare entities and how they influence healthcare behaviors (e.g., COVID-19 vaccination) and outcome, in the context of a global pandemic in which vaccine hesitation remains high within the Black community, it is paramount to identify factors that contribute to this lack of trust. Although many papers focus on ways of improving the Black community's trust the medical institution, attitudes towards these different entities (e.g., providers, pharmaceutical companies, and researchers) and strategies

to increase trust are not well understood. Using a phenomenological approach, we conducted a semi-structured interview with 30 African Americans who are hesitant about the COVID-19 vaccine to identify reason for mistrust in specific entities and the strategies and challenges to building trust.

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INCREASING THE NUMBER OF MINORITES IN MEDICINE BY IMPROVING THE MEDICAL SCHOOL ADMISSIONS EXPEREINCE

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Studies have shown that Underrepresented Minorities (URMs) students attending Historically Black Colleges and Universities (HBCUs) versus Predominately White Institutions (PWIs) experience different types of barriers to medicine. For example, a common issue amongst HBCUs pre-medical minorities is that despite the beneficial faculty support, the lack of financial resources and exposure to the medical field puts them at a disadvantage when applying to medical school. On the contrary, URM students attending PWIs stated that despite having financial resources and various opportunities for medical exposure, they feel as if they lack culturally component advising and access to supportive faculty. Regardless of these differences, URMs across the board are less likely to matriculate into medical school and require multiple American Medical College Application Service (AMCAS) and American Association of Colleges of Osteopathic Medicine (AACOMAS) application cycles. As medical school administrators seek to increase the number of minority applicants, it is vital to understand how applicants perceive the process, their needs, and the facilitators and barriers they face. It is the goal of organizations such as the Student National Medical Association (SNMA) to come in and fill the gaps where students feel like they are not adequately supported or prepared. Ultimately, with the gaps filled, there can be an increase in the number of URM students matriculating through medical school and a physician population that better mirrors the U.S. population. This study aims to identify application components that are a shared struggle with the goal of providing students with target resources to help increase URM matriculation and decrease application cycles/involuntary gap years. A 22-question survey was created to help analyze the perceptions of current URM medical students on their admissions experience. The survey was distributed to SNMA members across the United States with the goal of identifying areas within the AMCAS/AACOMAS application process that URM students found as a challenge and potential barrier to successful matriculation. Analyzing results will be done through graphs and word clouds. The anticipated results is that a commonality in the medical school admissions experience for URMs will be identified with the goal of organizations like SNMA to facilitate students in said areas to ultimately help to increase the numbers of URM matriculating into medicine. We anticipate that the results will prove that regardless of institution type, there is still a common component of the medical school admission process that is hindering the increase of URM matriculation.

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POLYNEUROPATHY CHARACTERISTICS IN HATTR V142I PATIENTS: A MULTICENTER PERSPECTIVE

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Hereditary Transthyretin Amyloidosis (hATTR) is an inherited disorder in which a misfolded Transthyretin (TTR) protein deposits in different organs and tissues causing dysfunction. One of the most common mutations in the United States is the V142I (Val122Ile) substitution mutation. The allele of this subtype can be found in approximately 3.5% of African American individuals. Current literature states that polyneuropathy is a characteristic of 30% of symptomatic patients. In contrast, clinically we have seen a much higher percentage. This study is an attempt to characterize and quantify the amount of polyneuropathy experienced by these patients. We achieved this by performing more in depth and thorough neurological examinations. In our study we found that around 35% of our patients experienced pain, which is the most used characteristic to classify polyneuropathy by non-neurologists. We also found that around 98% of our patients had some sort of other neuropathy (temperature/pin prick loss, abnormal deep tendon reflexes, vibrational loss, and weakness). In conclusion, in this retrospective study, we have supported our hypothesis that the number of patients with V142I hATTR is underdiagnosed. There were limitations to our study because of the sample size and referral bias so we must continue work on further clarification and classification of this disease.

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EVALUATION OF SERUM BIOMARKERS FOR PROSTATE CANCER USING PROGNOSITIC AND DIAGNOSITC DATA

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Prostate cancer (PC) is the most common cancer among men worldwide and the second and third leading cause of cancer-associated deaths in men in the United Kingdom and United States, respectively. A blood test for prostate-specific antigen (PSA) is commonly used as a screening tool for prostate cancer. Unfortunately, PSA is elevated with other conditions, such as benign prostatic hyperplasia (BPH), and cannot distinguish between low-risk and high-risk cancer (most likely to progress and become metastatic leading to patient death). This results in overtreatment of patients with low-risk prostate cancer and delayed

or ineffective treatment of many patients with high-risk prostate cancer. One of the major clinical challenges in prostate cancer is distinguishing the patients who may benefit from surgery or radiotherapy from patients who should not be treated but rather managed with active surveillance. Thus, there is an urgent unmet need to define new minimally invasive biomarkers that can distinguish men with prostate cancer from those with benign diseases such as BPH. The purpose of this study is to validate eight biomarkers discovered from a previous study for early stratification of high-risk and metastatic prostate cancer from low-risk prostate cancer. In order to evaluate the validity of MK, PVRL4, EPHA2, TFPI-2, hK11, SYND1, ANGPT2, and hK14 as prognostic biomarkers for PC alone or all eight combined, we used the strategy of meta-analysis as diagnostic and/or prognostic biomarkers for PC in public patient datasets. We used online databases and performed bioinformatic analysis to validate the levels of these proteins in patient samples. We found MDK, SDC1, KLK11 and hK14 to be proven as good biomarkers for early detection of metastatic prostate cancer. This result was inconsistent with our expectations that all studied proteins would be pro-metastatic biomarkers, but our results indicated four out of eight proteins are promising.

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MITOCHONDRIAL PROTEIN FUS1 AND SPATIAL MEMORY

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Memory deficits underlie diseases such as late-onset Alzheimer's disease (LOAD). Incidences of LOAD are generally reported to be higher in women than in men, although some findings suggest otherwise. One key element of memory deficits is a dysfunctional excitability of neurons caused by the deregulation of calcium (Ca^{2+}) homeostasis. Our group has found that fusion junction of the ends of a homozygous deletion (Fus1), also known as tumor suppressor candidate 2 (Tusc2), serves as a Ca^{2+} handling protein in isolated immune cells. Fus1 protein preferentially resides in the inner membrane of the mitochondria and assists Ca^{2+} uptake/extrusion via the mitochondrial calcium uniporter (MCU) and mitochondrial sodium-calcium exchanger (mNCX). The loss of *Fus1* increased oxidative stress and disturbed mitochondrial membrane potential and energy production. However, it is not clear how Fus1 functions in neurons and affects memory. Here we examined the role of Fus1 in memory by using mice with a global knock-out (KO) of Fus1. Both Fus1 KO and wild-type (WT) mice at 17 weeks old were subjected to a series of behavioral tests, including Y-maze, novel object recognition (NOR), Morris water maze (MWM), and open-field (OF) tests. Fus1 deficiency impaired short-term spatial memory in males but not in females as assessed with Y-maze test ($p<0.05$). Fus1 deficiency also impaired the long-term spatial memory as assessed with MWM test. Fus1 KO females had increased locomotor activity compared to KO males in OF test ($p<0.05$). Fus1 KO did not affect recognition memory as assessed with NOR. We are also seeing reduced protein levels of MCU and its modulator estrogen receptor a (ERa) in hippocampus, a brain region responsible for memory, in Fus1 KO mice. We did not observe any changes in amyloid b_{1-42} (Ab_{1-42}) levels. Thus, we propose Fus1 plays a pivotal role in spatial memory that may be sex-dependent.

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REGULATION OF CARDIOMYOCYTE MATURATION BY AN RNA SPLICING REGULATOR RBFOX1

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Formation of the adult human heart has two major steps: development (prenatal) and maturation (postnatal). Much is known about heart development, however, the mechanisms regulating heart maturation is still a mystery. Through our lab's previous analysis, RBFOX1 was found to be more highly expressed in adult rodent cardiomyocytes compared to fetal rodent cardiomyocytes. RNA Binding Fox-1 Homolog 1 (RBFOX1) is a protein coding gene that regulates tissue-specific alternative splicing in humans. The objective of our research was to determine if Rbfox1 regulates cardiomyocytes maturation in vivo. We followed two groups of mice (Control and Rbfox1-tg) for 2 months, checking their heart function (at P7, P14, 1m, and 2m) as well as their cardiomyocyte differences at a cellular level (at P14). In our analysis of the P14 cardiomyocytes, we found that the Rbfox1-tg group had significantly longer and thinner cells compared to the control group. Additionally, we found that the Rbfox1-tg group had significantly lower Ejection Fraction and Fractional Shortening at 4 weeks. However, there was not a significant difference between the two groups in the strain data. The preliminary data supports our hypothesis that Rbfox1 regulates cardiomyocyte maturation, but more data will be needed to explain whether this phenomenon is related with cell cycle exit and direct target of Rbfox1 that regulates cell growth. In future experiments, I believe these experiments should be replicated with a larger sample size in order to further support our hypothesis. Also, we should perform a Rbfox1 cardiac specific knockout (Nkx2.5-Cre) in mice to give us a better understanding of its role in maturation regulation.

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NOVEL ASSESSMENT OF THE ROLE OF SURGERY IN RECURRENT DIVERTICULITIS: A PROSPECTIVE, OBSERVATIONAL STUDY OF OBSERVATION VERSUS SURGERY IN RECURRENT DIVERTICULITIS

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Diverticulitis of the sigmoid colon is common in the developed world. Colonic resection is standard practice to care for diverticulitis patients with perforation or peritonitis; however, the role of surgery for treatment of recurrent diverticulitis is poorly defined. Current guidelines suggest that the decision to recommend surgery should be individualized and provide little guidance to care for patients with recurrent diverticulitis. There is a need to obtain more information of which diverticulitis patients benefit more from surgery or observation. We prospectively collected Patient Reported Outcomes (PROs) from patients with recurrent diverticulitis with a year of follow-up to determine if there were any observational differences of patient reported quality of life and/or function for those that elected to undergo surgery or observational management of diverticulitis. Currently, we have reached 90% of our enrollment goal and have 23% of this population complete year-long follow-up. Preliminary data suggests there are responses that diverticulitis patients who elected to have surgery answered more prevalently than patients who elected for observation. This suggests that there are observable baseline differences between those who elect for surgical or observational treatment for recurrent diverticulitis. We plan to finish enrollment and follow-up and perform formal analysis of PROs to help gather information to better guide Colo-rectal surgeons when caring for patients with recurrent diverticulitis.

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KNOWLEDGE ON AND ATTITUDES TOWARD ALZHEIMER'S DISEASE AMONG AFRICAN AMERICANS IN NASHVILLE

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Alzheimer's disease (AD) is a progressive disease that destroys memory and other cognitive functions and AD typically affects individuals who are 65 years and older. There are 5.7 million people who have been diagnosed with Alzheimer's disease. By 2050 Americans with Alzheimer's disease are projected to triple to 16 million. The prevalence of AD is reported to be higher in African Americans than in other racial/ethnic groups and why this is the case remains unknown. We have postulated that contributing factors to the high prevalence in African Americans include lack of knowledge on the nature of the disease which, in turn, may delay adoption of interventions to prevent and/or curb disease progression. Also, African Americans may have limited information (or access to) clinical trials that may be beneficial for the control of AD. To test these notions, we completed a pilot observational study in 2019 whose goal was to raise awareness about AD and thereby empower African Americans to seek early interventions for prevention and/or

management of AD. Participants were members of two local, primarily Black churches in Nashville, Tennessee. Briefly, participants in the IRB-approved study were asked to complete a pre-test to quantify existing knowledge levels and a questionnaire on attitudes towards AD. This was followed by an educational presentation that discussed the biological features of AD. The results revealed adequate knowledge levels of AD and they posted significant improvements in post-test scores relative to pre-test scores ($p < 0.05$; Wilcoxon paired test). The majority of participants (62%) were familiar with clinical trials but felt there were risks in participating in clinical trials. However, it remained unclear how well the findings on knowledge levels determined in our study compared with what has been found in other racial groups globally. This was the focus of my summer research project. The main objective was to compare the outcomes from our completed project with those obtained in similar studies that evaluated knowledge levels on AD (using same questionnaires and surveys) in other racial groups and nationalities.
This project was supported, in part, by NIH Grant number U54 MD007593-10S1.

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DEFINING A PLACE WHERE CHATBOT SYSTEMS MAY SERVE IN THE HEALTHCARE NEEDS OF AYA CANCER SURVIVORS

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Adolescent and Young Adult (AYA) cancer survivors (age 15-39 years) are an underserved population with unique needs that include mental health difficulties which may be experienced for decades after successful cancer treatment. Many AYAs report their needs not being met for one or more services including mental health counseling, with AYA cancer survivors reporting poorer mental health than AYAs without cancer. With recent advancements in technology, and increased use among AYAs, new opportunities to provide AYA's with support exist that may fill a much-needed niche in the field of mental health care for this population. Artificial Intelligence (AI) based conversational agents, or Chatbots, enable users to communicate and interact with software that use AI-based tools. Chatbots may be used to increase AYAs' access to mental health resources and interventions. Despite promising findings in other patient populations, little research has explored how chatbots may benefit AYA cancer survivors. Our project focused on conducting a review of current literature, highlighting the benefits of chatbots on mental healthcare, as well as the current limitations and areas of future improvement. The results of our review show evidence that chatbots are generally acceptable to patients. Preliminary evidence suggests that they may be particularly beneficial in some contexts, including depression and anxiety reduction. Limitations of research? Future work needs to incorporate longitudinal assessment to determine if effects persist, and to repeat the studies with larger populations and with greater diversity in mind. Findings support a push for greater research and funding into what should be considered a promising field that may benefit AYAs in need of mental health care. This work will inform future efforts to build chatbot-based interventions that hold great potential to increase access to mental health resources for this vulnerable population.

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INTERDISCIPLINARY CAPACITY BUILDING BETWEEN URBAN AND RURAL ACADEMIC PROGRAMS: A PUBLIC HEALTH AND DATA SCIENCE COLLABORATION

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The Meharry Master of Science in Public Health program and the University of the South (Sewanee) developed an institutional partnership training urban and rural students in public health and data science. During this Data Science training, the students were taught how to use RStudio, which is an integrated development environment. It allows users to code using R—a programming language for statistical computing and graphics. Using these coding skills, students approached a pressing public health concern. Specifically, some counties in Tennessee are highly underserved due to poor performance by current healthcare facilities such as medical clinics, hospitals, and Federally Qualified Health Centers (FQHCs). To approach this problem, the students aggregated health statistics, demographics, and public health-related information for each county in TN using a variety of credible sources. With this information, students created a database which served as the foundation for their final application. This application gives users a visual representation of the vast Tennessee health data of each of the 95 counties using maps, charts, and other figures. The application contains accurate and up to date public health information such as local treatment services, prevalence of diseases and conditions, FQHCs for residents without health insurance, and other information which will guide them to the care that they are seeking. Utilizing the skills learned via the Data Science workshops students seek to analyze the Meharry COVID-19 vaccine data. Students will then create a similar interactive web application consisting of vaccination sites, vaccination rates, and information regarding the population being served.

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MECHANISM OF ZAP70 DOWNREGULATION IN RUXOLITINIB-TREATED PATIENTS

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Myeloproliferative neoplasms (essential thrombocytosis, polycythemia vera, and myelofibrosis) have been identified to have driver mutations in the JAK2, CALR, and MPL genes in hematopoietic stem cells. Some cases of myeloproliferative neoplasms further developed into acute myeloid leukemia (AML). In patients with an intermediate or high risk of myelofibrosis, Ruxolitinib has been indicated as a drug therapy to prevent the progression of AML. Recent work from Shen & Krishnan et al. has identified platelet differential expression seen in patients treated with Ruxolitinib (RUX). ZAP70 was found to be downregulated two-fold in patients who have been treated with RUX when compared to untreated MF patients. Given the recent research suggesting the immune system's response to cancer, it seemed natural to determine the role of the immune system in these previously identified myeloproliferative neoplasms which are essentially blood cancers. We hypothesized that there was a mechanism of action underlying the downregulation of ZAP70 in RUX-treated patients. ZAP70 is responsible for T-cell receptor stimulation

and signaling. Activated ZAP70 leads to a series of phosphorylations involving the Ras, Raf, MAP/ERK pathway leading to the IL-2 transcription. The JAK1 pathway is responsible for the transcription of IL-2, IL-6, and TNF-alpha which are all proinflammatory cytokines. However, when JAK1 is inhibited, as done by RUX, no IL-2 will be transcribed which leads to the lack of activation of IL-2 receptors in which ZAP70 plays a role in the JAK3 pathway. So essentially RUX blocks JAK1-3 because the products of the JAK1 pathway are supposed to activate the JAK3 pathway. A similar mechanism is proposed to cause the downregulation of similar immune components such as IFI6, TRIMP69, and RanBP2L1. Future work will look at the in-depth downregulation of listed genes. By understanding the mechanistic effects of RUX we can predict possible drug resistance as well as other drug interactions and side effects that patients may be experiencing.

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THE ROLE OF THE RESPIRATORY MICROBIOME IN THE DEVELOPMENT OF CHILDHOOD ASTHMA

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The advent of next generation sequencing (NGS) has allowed for comprehensive characterization of both culturable and unculturable microorganisms living within a particular microbial ecosystem of the human microbiome. Over the last decade, numerous published studies have demonstrated the gut microbiome is an important factor in the development of childhood asthma, the most common chronic pediatric lung disease. However, the role that the respiratory microbiome plays in childhood asthma development is unknown. Our objective was to perform a systematic review of original studies examining the association of the respiratory microbiome with the development of childhood asthma. We searched PubMed up to June 30, 2021, for original articles using NGS to characterize the upper or lower respiratory tract microbiome. Each eligible article examined pediatric asthma phenotypes as the outcome. Two reviewers independently searched the database using structured criteria based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The number of studies examining the role of the respiratory microbiome on childhood asthma has substantially increased over time. Twenty articles met our eligibility criteria and were thus included in the final review; all of these had an observational study design and used 16S rRNA sequencing for microbiome characterization. Twelve (60%) of these showed that a higher abundance of *Moraxella* or *Streptococcus* increases the risk of asthma development. Even when separating our populations into healthy and high-risk groups, similar associations were found. The 3 (15%) studies that examined *Lactobacillus* showed that a higher abundance of this taxa decreases the risk of asthma development. Our results suggest detrimental effects of *Moraxella* and *Streptococcus,* and a beneficial effect of *Lactobacillus*, on childhood asthma onset. The underlying mechanisms behind these associations are unknown, but our findings suggest that modification of the respiratory microbiome could be a potential intervention for the primary prevention of childhood asthma.

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SOLVING AN UNSOLVABLE PROTEIN STRUCTURE TO TREAT ACNE AND ORTHOPEDIC INFECTIONS

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The dominant microbe found on sebaceous human skin can cause numerous diseases. This microbe is *Cutibacterium acnes* (*C. acnes*), a gram-positive, biofilm-producing organism that can be healthy or pathogenic. *C. acnes* causes a significant healthcare burden. For instance, >85% of adolescents suffer from acne vulgaris and *C. acnes* orthopedic infections are estimated to cost $250 million per year in the USA by 2030. *C. acnes* skin colonization requires the expression of RoxP, a protein entirely unique to this organism. How this protein's function relates to its structure is unknown because RoxP's structure has not been determined. The McCoy lab has previously collected x-ray diffraction data on RoxP, but the structure could not be solved using available methods, like molecular replacement (MR) using predictions of the RoxP structure. **We hypothesized that exhaustively assessing components of protein structure predictions will identify MR solutions that can be used to solve crystal structures.** My project tested this hypothesis by evaluating model proteins that have been previously solved. Validation of this approach through my work will support using this strategy to solve our RoxP data sets. We are confident that this approach will help determine the structure of RoxP and many other protein structures, and thus help to improve treatment of numerous human diseases.

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MEDICAL STUDENTS KNOWLEDGE OF ADVERSE CHILDHOOD EXPERIENCES

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The incidence and impacts of Adverse Childhood Experiences (ACEs) in the general population have been well documented, however, more recent studies have highlighted an increased incidence of ACEs in African American and multiracial children. Since, these experiences can be linked to higher chronic disease burdens and premature mortality, the question arises on how to best screen, educate and mitigate ACEs to improve health in African American, multiracial and underserved communities. This study was designed to assess the knowledge of adverse childhood experiences in year-one medical students at an HBCU. After assessing this knowledge, we evaluated the effectiveness of an ACEs educational program intervention. The study entailed dispersion of a pre-program ACEs knowledge survey, the implementation of a trauma-informed curriculum to augment the hypothesized knowledge deficit, and finally a post-program survey assessing the effect of our intervention. Results demonstrated a significant knowledge deficit in year-one medical students but also showed that a trauma-informed curriculum could enhance knowledge survey scores by over 50%. The study adds to the growing body of literature emphasizing the need to include programing in the social determinants of health as a part of every medical school's curricula. It especially highlights the importance of including such curricula in medical training at HBCUs whose graduates often work in underserved areas where the need for trauma-informed care is critical and where such care can be especially impacting.

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IDENTIFYING THE MECHANISM BY WHICH UPREGULATED MIDASIN CONTRIBUTES TO THE GROWTH AND METASTASIS OF LETROZOLE RESISTANT BREAST CANCER

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MCF-7 breast cancer cells are hormone dependent. They require estrogen for growth and are cultured in phenol red media, as phenol is estrogenic. They also have low levels of aromatase, which is the enzyme that converts testosterone into estrogen, thus making it difficult to test aromatase inhibitors (specifically letrozole). The Brodie lab created the AC-1 cell line which was derived from MCF-7 cells stably expressing the human aromatase gene. These cells are also estrogen dependent but overexpress aromatase making them sensitive to letrozole. Later, this same lab created an in vivo model to study aromatase inhibitors in which ovariectomized mice were inoculated with the AC-1 cells and stimulated with androstenedione. Androstenedione, a form of testosterone that can be converted to estrogen by the intratumoral aromatase, stimulates tumor growth. After 4 weeks of letrozole treatment, the tumors initially regressed, but after 35 weeks the tumor volume doubled, and letrozole resistance ensued. The tumors were extracted, cultured in vitro and called the LTLT-Ca (long-term letrozole cultured) cell line. Unlike the MCF-7 and AC-1 cells, these cells are estrogen independent which allows them to grow in media without phenol red. Recently, the Tilghman lab identified that a protein, midasin, was upregulated in this cell line. Midasin is a chaperone protein involved in eukaryotic ribosomal assembly. Midasin assists with the transport of the pre-60S subunit from the nucleus to the cytoplasm where it becomes the mature 60S subunit, destined to assist in translation. Malignant cancer cells proliferate quickly and require increased translation and upregulated ribosomal subunit formation leading to increased protein synthesis. This also contributes to one of the hallmarks of cancer such as rapid growth and metastasis. Previous studies have interrogated how changes in the quality and quantity of ribosomes affect translation, but therapeutic targeting has not been accomplished.

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THE MITIGATING EFFECTS OF CARDAMONIN VIA PD-1/PD-L1 CHECKPOINT IN TRIPLE NEGATIVE BREAST CANCER CELLS

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Triple-negative breast cancer (TNBC) is not only the most common type of cancer in women, but also the second leading cause of death. Unlike other forms of breast cancer, TNBC does not express estrogen,

progesterone, or HER2 receptors. These cancer cells instead choose to employ mechanisms to escape the immune system, including upregulating the expression of PD-L1. While a synthetic drug has already shown to both inhibit PD-L1 activity and stimulate killing effects in TNBC cells, we sought out to determine if Cardamonin, an aromatic enone within the flavonoid family, would lead to a decrease in the expression of PD-L1 in TNBC cell lines. We initially assessed cardamonin's effect on the cell viability of MDA-MB-231 and MDA-MD-468. Afterwards, we treated each cell line with various concentrations of cardamonin and measured PD-L1 concentrations via ELISA assays and RT-PCR with and without IFN-y stimulation. In the MDA-MB-231 cells, the PD-L1 concentration decreased with increasing concentrations of cardamonin. When studying the effects of cardamonin in the MDA-MB-468 line, we found a linear relationship between cardamonin concentration and PD-L1 expression. This phenomenon may hint at differences in the microenvironment between African Americans and non-African Americans. We also found that the post-translational glycosylation of PD-L1 may have prevented the antibodies in the ELISA assays from effectively binding to its polypeptide antigens, which may have contributed to the observed low concentrations of PD-L1.

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RACIAL DISPARITIES MAY BE LEADING TO ENHANCED IMMUNITY AND INCREASED TRANSPLANT REJECTION IN AFRICAN AMERICAN HEART TRANSPLANT PATIENTS

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African American heart transplant recipients have the highest rates of post-transplant mortality among all racial ethnic groups. While the direct mechanism behind this phenomenon is unknown, it is thought to be multi-faceted. Socioeconomic status, graft quality, performance of transplantation facility, and individual HLA antigen mismatching have all been indicated as contributing factors to this disparity. However, one potential contributor which is largely unexplored is the role of race related stress in causing enhanced immune responses in African American transplant recipients which may be leading to increased rates of organ rejection and higher rates of post-transplant mortality. Our project aimed to review the evidence supporting this relationship. Data analysis was conducted on the Genomic Research Alliance for Transplantation (GRAfT) consortium, a 500 patient cohort of heart and lung transplant patients who were followed and given blood tests over the course of their post-transplant treatment, for indicators of enhanced immune responses in the African American compared to their white counter parts. We hypothesized that due to higher stress levels and enhanced immune responses the African American patients would have higher white blood cell counts (WBC). We found that the WBC averages for white patient were actually higher within the first week but began to drop after the first day. The African American patients continued to increase from day 1, rose above the white patient averages by week 1, and did not begin to drop until after to week 2. Readings from both races stabilized to similar levels by the first month. The data was consistent with the hypothesis. Further testing is needed to confirm stress to be a key factor in this trend. Cortisol levels and levels of particular cytokines such as IL-4 and IL-6 will be needed complete the link between stress and enhanced immune responses.

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UNDERSTANDING MIRNA-BASED CARGO OF EVS AND THEIR INFLUENCE ON GENE REGULATION.

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While lot of clinical trials are looking at the role of MSC in cell-based therapy, there are only a few clinical trials in Phase I and II which explore the role of EVs as a cell-free therapy. This is due to the lack of extensive knowledge about the miRNA-based cargo of EVs and how they influence gene regulation at the post-transcriptional level. and Mesenchymal stem cells (MSC) based cell therapies have gained a great deal of interest and attention in medical treatments over the past several years due to their ability to exert therapeutic effects through direct cell contact as well as their paracrine action. In this research we will be focusing on profiling the miRNA-based cargo from MSC-derived EVs and then understand the regulation of network genes by these miRNAs using "in silico" approaches. The research started by (i) Identifying the microRNAs in among three different sources of MSCs- Adipose tissue (AD), Bone Marrow (BM) and Umbilical cord (UC) . (ii) We compared the similarity and differences among the miRNAs found among different sources using ***Venny***. (iii) Using "in silico" approaches the study identified novel miRNA targets for genes related to apoptosis, inflammation, and mitochondrial biogenesis (iii) Gene Ontology (GO) Analysis was used to identify biological pathways affected. In conclusion we found that there was very limited overlap between all three MSC sources in relation to the miRNA secreted by them and the pathways that they affected. The pathways that were mainly affected in all three sources were anti-inflammatory, anti-apoptosis, and neurodegenerative disease.

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INTRACRANIAL MONITORING REINFORCES THE LOBAR MIMICRY OF INSULAR EPILEPSY

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Insular epilepsy is a well-known mimic of frontal, temporal and parietal epilepsy. Its diagnosis and treatment can be challenging due to the insula's position in the cerebral central core near branches of the middle cerebral artery and the basal ganglia. We present three patients with semiology suggestive of lobar epilepsy who underwent insular resection after confirmatory intracranial electroencephalography (EEG). We retrospectively reviewed three patients who underwent insular resection for epilepsy after confirmation with an intracranial EEG study. Imaging including magnetic resonance imaging (MRI), scalp EEG, neuropsychological testing, intracranial EEG, and surgical data were collected. In the three cases patients

presented with semiologies including hypermotor and vocalizations seizures (frontal lobe), and scalp pain seizures (parietal lobe). All patients were non-localizable based on non-invasive studies and subsequently received a combined intracranial depth and surface electrode study. A large grid electrode was used for extensive coverage of the frontal, temporal, and parietal lobes in order to definitively rule-out seizure onset in these locations. The grid was also used for stimulation mapping of sensory, motor, and language function and for seizure induction. Insular depth electrodes were placed in oblique and parasagittal trajectories for maximum coverage of the insula. Seizure onset was highly focal in the insula with spread to an adjacent cortical dysplasia in two cases. The depth electrodes were left in place for guidance during resection, allowing the surgeon to identify the seizure focus and prevent encroachment on the basal ganglia medially. Depth electrode-guided surgery was performed in all cases with no associated morbidity and with seizure freedom on short-term follow-up. Insular epilepsy may present with semiology indicating seizure onset in other lobes. In all cases, the combined surface and depth study localized onset in the insula and ruled out alternative hypotheses. Stimulation mapping also helped to confirm seizure onset area. Depth electrode-guided insular resection is a safe and effective method to optimize resection of the seizure focus and prevent resection of the adjacent basal ganglia.

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UNDERSTANDING THE PHARMACOGENOMICS OF VORICONAZOLE IN REGARD TO SKIN CANCER RISK

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Studies suggest that Voriconazole is associated with an increased risk for cutaneous squamous cell carcinoma (SCC) development in LTRs. To better understand voriconazole metabolism's role in skin cancers we are met with determining how variation in metabolism of voriconazole as measured by metabolizer status of CYP2C19 is associated with the total number of skin cancers a patient develops. The mechanism of voriconazole associated cutaneous malignant neoplasm involves Voriconazole N-oxide (VNO). Voriconazole is primarily metabolized into VNO by cytochrome P450 enzyme 2C19 (CYP2C19) with assistance from CYP2C9 and CYP3A4. Poor metabolizers, patients that lack CYP2C19 activity, have 3 to 4 times higher voriconazole plasma concentrations and greater voriconazole to VNO ratios. The ultrarapid metabolizers, patients with an increased CYP2C19 activity result in lower serum concentrations of voriconazole and a higher circulating concentration of VNO. We used data from Vanderbilt's de-identified research database, the Synthetic Derivative (SD). We identified 842 adult patients with voriconazole exposure and existing genetic data. We measured the association between metabolizer status and the mean number of skin cancers using ANOVA, as well as a generalized linear model to adjust for important covariates such as age and immunosuppression. Patients who were rapid metabolizers developed more skin cancers than those who were normal or poor metabolizers, as well as those missing metabolizer statuses ($p < 0.001$). There is growing literature that highlights the mechanism of voriconazole metabolism and the risk it poses for skin cancer. Prelim results suggest variation in voriconazole metabolism does appear to impact the number of skin cancers a patient will develop. In conclusion, this research has shown that by understanding the pharmacogenetics of voriconazole metabolism, we can personalize treatment for patients at high risk for skin cancer and potentially develop better means of prophylaxis.

This research project was funded by the Fifth Annual Vanderbilt-Meharry James Puckette Carter Summer Scholarship Program. This project has been approved by VUMC's IRB with a non-human subjects' designation, IRB 200335.

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SOCIAL INCLUSION NARRATIVES IN BORDERLINE PERSONALITY DISORDER

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Borderline personality disorder is a severe mental illness characterized by a pattern of instability in emotion regulation. Dysfunctional response to unpleasant stimuli, especially in terms of adverse affect reactivity, has been the main focus of research in BPD over the past several decades. Affective hyperactivity is a core feature of borderline personality disorder, yet little is known about the reactivity to positive affect. In this study, we aim to examine the positive/inclusion narratives of people with a borderline personality disorder to see how they differ from the narratives of people without psychopathology (healthy controls, HC). We aim to develop standardized inclusion scripts, in particular, those of interpersonal relationships to test the impact of evoked positive emotion in individuals with BPD compared to healthy controls. Using Structured Interviews, we collected stories of positive/inclusion social experiences and examined individual responses. Participants completed self-reports in order to collect emotion using the positive and negative affect scale (PANAS) before and after each block. Preliminary results showed that positive affect on average was higher in the initial group of participants at baseline of HC compared to BPD. Negative affect on average was lower in HC vs BPD participants, and we were able to demonstrate that inclusion story collection is feasible and early results are consistent with the hypothesis. When we collect the full dataset for this project, we plan to use a 2x2 ANOVA test to examine group x condition differences in evoked emotion, time to complete storytelling, and word use pattern.

This work was funded in part by the Yale Department of Psychiatry, The Yale School of Medicine, and the Yale Center for Clinical Investigation (YCCI).

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ADDITION OF ADVOCACY PROGRAMS IN ADOLESCENT OBESITY IN METRO NASHVILLE PUBLIC SCHOOLS

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Childhood obesity has been a growing public health concern in the United States. Long-term impacts of obesity during childhood and adolescence can lead to psychological, physical, and mental health morbidity and early mortality. Numerous studies have concluded that prevention of risk factors and reduction of unhealthy behavioral patterns can slow this trend and minimize the resulting adverse effects. This study is designed to formulate and promote adoption of a policy aimed at improving health behaviors within the Metro Nashville Public School system (MNPS). By facilitating partnerships between MNPS health coordinators and advocacy groups such as the National Football League's Play 60 and The Diary Alliance, we will promote development and application of programs to educate members of the public-school

systems, including students and their families, to improve their overall health outcomes. These policies may range from providing nutritional guidance, training in food safety and simple food preparation techniques, and fostering adequate levels of physical activity for all participants. The overall end point of this project is to show improvement in weight status and reduction of risk for chronic diseases associated with obesity in the setting of a large metropolitan school district. This will be accomplished by implementing policies and programs designed to be informative and achieve a positive behavioral change in the public-school students and their families. Conclusion would be creation of policy.

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ELUCIDATING THE ROLE OF PHEP IN *STAPHYLOCOCCUS AUREUS* NUTRIENT METABOLISM

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Staphylococcus aureus is a bacterium involved in many infections in different organ systems including invasive bone infection: osteomyelitis. During osteomyelitis *S. aureus* utilizes specific metabolic pathways and nutrient acquisition strategies, some of which remain to be distinguished. PheP (a putative gamma aminobutyrate permease) was found to be essential for growth in *S. aureus* in the Cassat lab post-traumatic osteomyelitis murine model. In contrast, strains with *pheP* inactivated were able to be grown in nutrient media. PheP is suggested to have a role in transport of phenylalanine; however, the protein structure is homologous with lysine and proline transporters in other bacterial species. The role of PheP in *S. aureus* nutrient metabolism will be investigated with microbiological techniques. Classically, the *pheP*::Tn erm^R strain yielded smaller growth on TSA + erythromycin, thus morphology was compared on other nutrient agar, and I found that colonies on other nutrient agar were similar in size between the *pheP* and WT strain. Additionally, I was interested in growing the *pheP* strain in chemically defined media without the amino acids the protein has been implicated to transport. Thus, I constructed media without lysine and phenylalanine and found that the WT strain developed a lag phase like the *pheP* strain. Previously, a BioLog phenotypic microbial microarray was used to identify compounds that inhibited *pheP* growth compared to WT. To further investigate these compounds, I utilized zones of inhibition filter paper assays to identify bactericidal concentrations for further studies. Given these findings the role of PheP in *Staphylococcus aureus* requires further investigation.

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EFFICACY OF NEPHRON-PROGENITOR CELL ADMINISTRATION IN MICE WITH ACUTE KIDNEY INJURY

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Acute kidney injury is one of the most prevalent forms of disease on the global scale with increasing rates of mortality. Treatment options for kidney disease are mostly limited to kidney transplantation and

maintenance dialysis. Mounting evidence suggests kidney regenerative therapy could serve as a promising alternative. It is hypothesized that induced nephron-progenitor cell administration in mice following AKI will result in a marked improvement in recovery. Nephron-progenitor cells are exclusively present during the early phases of embryological development, functioning as the cell of origin for epithelial differentiation in the developing kidney. Through regeneration new nephrons could be generated that will improve kidney filtration capacity. The study was organized into three experimental cohorts structured as follows: I/R + PBS (n=3) and I/R + iNPs (n=3). HK2 cells were reprogrammed into iNPs via *piggyBac* transposons that express the transcription factors *SIX1*, *EYA1*, and *SNAI2*. AKI was induced by unilateral nephrectomy with ischemic reperfusion. Twenty-four hours following procedure, an iNP injection was administered in half of the cohort with the remaining receiving a saline injection as a control. Markers of kidney function were measured through routine blood draws and collections of urine, respectively. Prior to experimental cohort sacrifice at the end of two weeks, FITC-sinistrin injection was used to calculate transdermal GFR. An organ harvest was subsequently conducted for evaluation of iNP integration and differentiation through human nuclear antigen expression. It is anticipated that iNP cellular differentiation will increase the potential for nephron regeneration in otherwise irreversibly damaged kidneys and contribute to a better understanding of both the regenerative nature and cellular basis of the kidney.

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ROLE OF ENTERIC NEURON AND ENTERIC GLIA IN INFLAMMATORY SIGNALING PATHWAYS: A PILOT

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Background/Objectives: Periodontal disease (PD), a chronic inflammatory gum disease, is one of the most common oral health complications in obese and diabetic patients that may involve increased inflammation and oxidative stress. Data from our laboratory indicate that periodontal infection impaired neuronal nitric oxide synthase (nNOS) mediated gut motility. The Enteric Nervous System is comprised of enteric glia and neuronal cells that control various processes in the gut, including motility, secretion, local immunity, and inflammation. The purpose of this pilot study is to investigate transcriptomes that exist in enteric neurons vs. enteric glia and identify the signaling connection between oral and gut function. Experimental Methods: Primary enteric neuronal crust (pENC's) cells were isolated from adult female mice [9- to 10-week-old C57BL/6J (WT, n=4)] intestine. The cells were stained for glial and neuronal cell markers and sorted using a flow cytometer cell sorter (BD biosciences). The sorted cells were stored at -80 °C and mRNA enrichment, cDNA preparation and sequencing studies were performed at the VANTAGE Core (Vanderbilt University). The DAVID Bioinformatics Database was utilized to analyze the KEGG pathways and Gene Ontology Biological Process terms associated with enteric glial and neuronal cells with the support of the Meharry Bioinformatics core. Results: Our transcriptome analysis from adult female mice pENCs showed 1027 significantly differentially expressed transcripts in enteric neuronal vs. enteric glia cells. In addition, we found 732 transcripts are exclusively present in the enteric neuronal cells. Finally, our data indicate that 459 transcripts were present only in enteric glia. Among these, 12 transcripts show indications to promote inflammatory responses in the literature. Of the 12 inflammatory transcripts, 9 transcripts are exclusively present in enteric neuronal, whereas 3 are exclusively present in enteric glial cells. Conclusions: Our data indicates noticeable capacity in the inflammatory response seen in inflammatory diseases including periodontal disease.

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UNDERUTILIZATION OF ANTIVIRAL THERAPY AMONG RESECTION PATIENTS WITH HEPATOCELLULAR CARCINOMA

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2020 saw the largest single year drop in cancer mortality. Despite the overall drop, Hepatocellular Carcinoma rates are rapidly increasing. The 3% annual increase makes it the fastest growing cancer. HCC is the fourth most common cause of cancer-related death worldwide with an increase of 63% in total death from 1990 to 2013. Viral hepatitis remains the leading cause of hepatocellular carcinoma (HCC) worldwide. Antiviral therapy can improve overall survival (OS) and recurrence free survival (RFS) in HCC, but the proportion of patients undergoing resection who receive the treatment is unclear. The goal of this study is to examine the utilization of antiviral therapy, as well as its impact on OS and RFS among patients who have undergone hepatic resection for viral hepatitis (hepatitis B virus [HBV] or hepatitis C virus [HCV]) related HCC. We performed a retrospective multicenter cohort study of HBV and HCV-related HCC patients who underwent hepatic resection between 1995 and 2020 from 9 centers in US and Asia. HCC was diagnosed based on AASLD criteria. We analyzed baseline characteristics and long-term survival of 341 patients with viral hepatitis-related HCC. We found that Antiviral therapy was associated with a significantly better OS and RFS among resection patients with HCV-related HCC, but not HBV-related HCC. We also found that only two thirds of HCC cases received antiviral therapy. Urgent efforts are required to improve linkage to care and compliance to antiviral therapy.

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COMPARISON OF TWO ULTRASOUND-BASED METHODS FOR ASSESSMENT OF DIAPHRAGM MUSCLE FUNCTION

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The diaphragm is the most important muscle involved with respiration and maintaining airway patency. The most specific measure of diaphragm function is assessing transdiaphragmatic pressure, which is the difference between the esophageal and gastric pressure. This method requires gastric and esophageal probes which are invasive and limit the clinical application of the method. Ultrasonography has become popular due to its non-invasiveness and the "ABCDE" method assesses the diaphragm thickening upon contraction. The diaphragm thickening ratio shows limited relationship with trans-diaphragmatic pressure. Ultrasonography using shear wave elastography allows measurement of tissue stiffness and thus likely reflects transdiaphragmatic pressure. The purpose of this study was to assess the utility of ultrasound methods to discriminate across motor behaviors with different levels of diaphragm force. The SWE method

and "ABCDE" thickening fraction were both performed on volunteers with no pre-existing respiratory conditions. Images were obtained during different breathing maneuvers. The diaphragm muscle thickness was measured as was shear wave velocity. 8 volunteers were evaluated under both ultrasound methods. The average thickness amongst volunteers for end-expiration, end inspiration, max inspiration, and Valsalva were 2.8 mm, 3.2 mm, 4 mm, and 4.3 mm, respectively. Median shear wave velocities were 3.4 m/s, 3.5 m/s, 4 m/s, and 4.7 m/s, respectively. The coefficient of variation was xx and yy for the thickness ratio and shear wave velocity, respectively. The p value for the mean-mean was .0079. The p value for the mean difference was .7963. There is a significant difference in diaphragm thickness and shear wave velocity across breathing maneuvers of increasing force. There was no evidence that the two methods are substantially different. Further evaluation of the utility of these methods using larger sample sizes and different conditions associated with diaphragm weakness is needed.

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ORAL HEALTH STATUS OF SUBJECTS TESTING FOR COVID-19

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The novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), causes severe morbidity and mortality worldwide. People infected with COVID-19 have pneumonia-like symptoms including fever, cough, myalgia or fatigue, and complicated dyspnea. Patients having underlying health complications such as diabetes, cancer, cardiovascular diseases, and hypertension are more susceptible in developing COVID-19. In this descriptive study, we gathered information regarding COVID-19 symptoms, oral health status and the presence of comorbidities to determine if a relationship exists among these variables. The objective is to investigate a correlation between COVID-19 symptoms, present medical conditions and self reported oral health status. The study was approved by the institutional review board (IRB #20-05-998). Five-hundred and ten (n= 510) patients (ages 1-91) of various ethnic backgrounds approached at COVID-19 testing sites in Nashville, TN were randomly selected for this study A standardized questionnaire regarding present COVID-19 symptoms, oral health status and history of systemic disease has been instrumented. A frequency analysis was used to assess oral health status for subjects tested for COVID-19 symptoms. In addition, Chi-square tests were performed to determine a subset of symptoms and medical conditions significantly associated with oral health ($p < .05$), respectively. ***Results:*** Our data indicates there is a significant variation in those that reported gum bleeding while brushing and experiencing the common COVID-19 symptoms —loss of taste/loss of smell ($p = 0.045$) and chills ($p = 0.009$). There is also statistical significance between those that reported tooth sensitivity and hypertension ($p=0.004$). The study results suggested that certain testing participants with COVID-19 symptoms had oral challenges in oral inflammation and potential caries. The data collected from this self reported oral status with viral symptoms and systemic diseases suggest that there is a relationship present, although there is not enough evidence to support the causal relationship between these variables.

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DISTANT RELATEDNESS AND PHENOTYPIC EVALUATION TO INVESTIGATE UNDERDIAGNOSIS OF PICK'S DISEASE

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Pick's Disease (PcD), a subtype of Frontotemporal dementia, results in gradual but progressive loss of thinking, language, and problem solving. Clinical diagnosis fails to differentiate PcD from Alzheimer disease and progressive dementia. PcD is estimated to affect 1 in 100,000 people but underdiagnosis could be possible. PcD has been known to segregate within families and exhibit an autosomal dominant mendelian pattern of inheritance. Identity-by-descent (IBD) segments are sections of the genome shared by two or more individuals that are identical because they were inherited without recombination from the same common ancestor. The objective of our research was to demonstrate that individuals with genetic risk factors for PcD are instead diagnosed with Alzheimer's or dementia. IBD information was leveraged to identify relatives of PcD patients and evaluate electronic health record data for potential missed PcD cases. We found 100 individuals who shared IBD segments with PcD patients and symptoms of PcD. Further investigation is needed to determine if pathogenic genetic variants can be linked between the identified PcD patients and potential PcD relatives. These results are consistent with the hypothesis that the combination of electronic health record review and genetic data may be useful in identifying misdiagnosed cases of rare diseases.

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THE IMPACT OF TARGETED OUTREACH ON MASSHEALTH ACCOUNTABLE CARE PATIENTS WITH OPIOID USE DISORDERS

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The Lynn Community Health Center Medication for Opioid Use Disorder (MOUD) treatment is funded primarily through grants. The grants often stipulate a patient retention rate that is virtually unattainable in such a volatile patient population. Patients who are retained in MOUD treatment are less likely to die of an overdose. Thus, it is in a provider's best interest to keep patients engaged in care. In order to increase patient retention, we aimed to analyze the effect of targeted outreach on returning patients who had been lost to care. This study found that using targeted outreach on patients without an active prescription or scheduled appointment had a moderate effect of returning patients to care. However, the limited sample size and time

constraint limited the power of the study. This study looked at only short-term outcomes of outreach and did not include analysis of populations outside of MassHealth Accountable Care-insured patients.

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THE MOLECULAR IMPACT OF FOXA1 DYSREGULATION IN PROSTATE CANCER MALIGNANCIES

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Prostate cancer (PCa) is one of the most common types of cancers diagnosed in American men. Moreover, PCa malignancy disproportionally strikes more on African American (AA) men than any other ethnic groups including Caucasian American (CA) men. Forkhead Box A1 (FOXA1) is frequently mutated in hormone receptor-driven cancers including PCa. FOXA1 mutation rates in AA PCa specimens are 3-fold higher than that in CA PCa. By annotating the FOXA1 mutation landscape two hotspots were defined in AA PCa patients located in the forkhead domain: D226N and R219C. FOXA1 expression and functions are regulated by lysine [K]-specific demethylase 5B (KDM5B). KDM5B contributes to the activation of signaling pathways that promote cancer progression. Here in this project, we will focus on the mechanistic role of FOXA1 dysregulation and its interaction with KDM5B and AR on PCa progression in AA vs CA PCa cells. Therefore, we hypothesize that the dysregulation of FOXA1 plays an essential role in the progression of PCa by altering chromatin remodeling and AR interaction, and FOXA1 mutation promotes more aggressive malignancies in AA PCa cells. In order to investigate the biological function and regulation of FOXA1 in PCa cells we first need to knockout (KO) the endogenous expression using CRISPR technology and then knockin (KI) the unique mutants R219C and D226N. These *in vitro* studies of FOXA1 mutations found in AA PCa will be critical to determine the biological functions of these mutants for PCa progression. The findings from this study will provide valuable insights into the contributions of the FOXA1 regulation and will add to our knowledge base for the potential development of a novel therapeutic strategy to reduce PCa disparities between AA and CA populations.

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REDUCING DIAGNOSTIC ERROR OF RARE DISEASES IN ETHNIC MINORITIES

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Rare diseases are especially prone to diagnostic error – delayed diagnosis, missed diagnosis or wrong diagnosis – by physicians, resulting in potential harm to the patient. While rare diseases can affect people

of any race or ethnicity, many conditions are more common in minority populations due to genetic, sociocultural, or geographic factors. While each rare disease presents a specific set of diagnostic and therapeutic challenges, minority patients face compounding inequities due, in part, to higher rates of diagnostic errors, underrepresentation in the medical literature, and difficulty accessing the right specialist. Thus, minority patients that are most vulnerable for certain rare diseases experience significant health inequities. The objective of our research is to address these disparities by identifying underrecognized and rare diseases that disproportionately afflict minority populations and examining the processes or cases that led to diagnostic error. We identified X rare diseases disproportionately affecting people living in the US of African descent. Broadly, identified processes or cases that led to diagnostic error include X, Y and Z. This information will be leveraged to create educational curriculum about this neglected area of study to assist both patients and providers in the diagnostic process, thereby reducing diagnostic error and improving the health status of minorities experiencing a rare disease.

This project was supported by the FY21 Stanford CARE (Center for Asian Research and Education) Seed grant, the Sean N. Parker Center for Allergy and Asthma Research at Stanford University, and the Stanford University Presence Center.

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THE MECHANISM OF CELLULAR APOBEC3G AGAINST HUMAN IMMUNODEFICIENCY VIRUS TYPE-1 INFECTION

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Human apolipoprotein B mRNA-editing enzyme, catalytic polypeptide-like 3G (APOBEC3G, A3G), is a host restriction factor that plays a vital role in antiviral innate immunity. In terms of human immunodeficiency virus type 1 (HIV-1) infection, it restricts replication due to its antiviral effects inducing lethal G to A hypermutations in the viral genome and inhibition of reverse transcriptase. Evidence supports the idea that A3G is packaged into HIV-1 virions and introduced to the target cell before exerting its antiviral effects. In this study, however, we are revealing a novel mechanism that cellular A3G immediately takes antiviral effect during early HIV-1 infection. Human A3G knockout T-cells (Δ3G), were used to investigate the effects of cellular A3G during initial infection. An enveloped deficient pseudo-HIV virus was employed to ensure one infection round. Lentiviral plasmids expressing A3G were transfected in the Δ3G cell line to restore endogenous expression. Preliminary data showed that the Δ3G cell line was more susceptible to HIV-1 infection than its parental A3G expressing cell line in a viral replication system suggesting that cellular A3G plays a role in inhibiting HIV early replication. To confirm the novel function of A3G, we transfected the A3G expressing construct into Δ3G cell line, which will be used in a complementation test. We are the first to show that cellular A3G restricts incoming HIV infection. This study will lay a foundation for revealing a novel antiviral mechanism of
A3G. It will shed light on future HIV gene therapy studies.

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SLC10A2 AS A NOVEL TARGET FOR MEMORY IMPAIRMENTS IN MICE LACKING MITOCHONDRIAL CALCIUM PROTEIN FUS1

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Alzheimer's disease (AD) is the most common cause of dementia and as of today there is no cure. While treatments have been developed that help slow its progression, current research is focused on finding solutions that could help prevent the disease before it has a chance to manifest. SLC10A2, a bile acid transporter that has shown relevance in AD progression in African Americans, is an example that indicates that the solution may be found in tailored medicine. Research into Fus1, a mitochondrial calcium protein, shows that its downregulation produces disruptions in mitochondrial homeostasis that result in conditions that exacerbate long- and short-term memory deficits. Using behavioral tests for memory impairment, the Shanker and Shimamoto lab has ascertained that mice lacking Fus1 (KO) consistently perform poorer than their counterparts with Fus1 (WT), creating a model that mimics AD. Our next steps were to determine if SLC10A2 could be detected in these mice and how sex factors into our findings. We completed a Bradford assay in order to determine the protein concentration of WT and KO Fus1 mouse brain lysates and followed up with a mitochondrial isolation of WT and KO Fus1 mouse brain tissue samples. We used the Bradford assay values to conduct Western blots for SLC10A2, mitochondrial calcium uniporter, and ER-alpha. Our results showed that SLC10A2 was detected across Fus1 mice and was decreased in KO females and increased in KO males. This could indicate that any neuroprotective benefits SLC10A2 could have might not be equally effective across genders. Similar results in human AD brain tissue samples could provide further information. Additional research into SLC10A2 levels in African Americans vs age-matched Caucasian AD brain tissues could strengthen the case for specific treatments in tackling this disease and help address current health disparities.

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PERI-PROSTATIC LYMPH NODE (LN) DETECTION BY DCFPyL PSMA PET-CT IN PATIENTS WITH NEWLY DIAGNOSED HIGH RISK, PROSTATE CANCER, NOT DETECTED ON CONVENTIONAL IMAGING

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Periprostatic lymph nodes are small lymph nodes identified infrequently near the prostate in radical prostatectomy specimens. They are often located in the region of the posterior base and may be too small to detect grossly. Metastases isolated to periprostatic lymph nodes should be considered N1, but isn't currently considered in prostate cancer staging. Patients with metastasis to periprostatic lymph nodes tend

to have prostate cancer of a higher grade and stage, a larger tumor volume, higher Gleason score, higher recurrence rate, shorter time to recurrence, and worse pathological features. Patients with metastasis to periprostatic lymph nodes also showed a significantly higher metastatic rate compared to patients with metastasis to pelvic lymph nodes. There is no current preoperative imaging recommended for the detection of periprostatic lymph node metastasis. Prostate specific membrane antigens (PSMA) are transmembrane proteins that are overexpressed on prostate cancer cells and can be used as a target molecule for PET scans to detect prostate cancer and possible metastases. PSMA PET-CT was recently FDA approved in the US for patients with prostate cancer as baseline staging initially or identify sites of recurrence after therapy. PSMA PET has a very high specificity and PPV in detecting pelvic lymph node metastasis and may prove histological confirmation unnecessary. Recently DCFPyL PSMA PET-CT (trade name PYLARIFY) has shown a specificity that is significantly higher than conventional imaging (97.9% vs 65.1), a PPV value nearly triple that of conventional imaging (86.7% vs 28.3%) and similar sensitivity to conventional imaging. Staging via PSMA PET also showed a higher sensitivity compared to MRI in identifying histological pelvic lymph node metastasis, men with negative PSMA PET/CT had a lower risk of lymph node metastases compared to MRI (Petersen & Zacho).

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UTILITY OF HEALTH COACH TRAINING FROM THE LENS OF CLINICAL CLERKSHIPS

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Meharry Medical College (MMC) and Vanderbilt University Medical Center partnered to create the Meharry-Vanderbilt Health Coaching (HC) Program in 2018 as part of first-year medical student curriculum. The objective of our cross-sectional research was to identify students' perception of the helpfulness of HC training, frequency of HC skills used, preparedness to use HC skills, and the most and least important HC skills in the context of clerkships. We also assessed differences between helpfulness, use frequency and preparedness ratings by the following: clerkship; interest in primary care, specialty care, or undecided; and one versus multiple clerkships. The survey was given via REDCap to the Class of 2023 by email and 10 minutes of dedicated class time was allotted to complete it. The survey included demographics, 48 11-point numerical rating scales (NRSs) assessing helpfulness, use frequency and preparedness for each skill. Although 82.9% responded, those with clear response bias were removed. Descriptive statistics showed that 97.92% of 48 NRSs were $\geq$ 5. Active listening, asking-open ended questions to obtain information or the patient's perspective, and demonstrating empathy were rated most important. Least important was leading a mindful moment. One-way ANOVAs with post-hoc independent t-tests showed no differences between one versus multiple clerkships ($p > 0.05$ one-tailed). Five of 18 skills showed differences in use frequency across clerkships ($p \leq 0.025$, two-tailed), while 15 showed no differences. Preparedness for two skills showed differences ($p \leq 0.025$, two-tailed), depending on care interest. Though the use frequency of 5 skills is dependent on clerkship. Most HC skills have broad applicability. The patient-centered communication skills of HC training were helpful for clerkships and align with residency directors' ranking of the most important communication skills. Further research is needed to explore the generalizability of the findings beyond the Class of 2023.

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ANNEXIN A6 EXPRESSION IN ANNEXIN-LOW TRIPLE NEGATIVE BREAST CANCER BASAL CELLS POST TKI TREATMENT

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Triple Negative Breast Cancer (TNBC) is not only an aggressive cancer, it is a cancer that predominantly affects black women. Breast cancer is typically treated with hormonal therapies, however, TNBC lacks the hormonal receptors targeted for these treatments. To replace hormonal therapies, Tyrosine Kinase Inhibitors (TKIs) can be utilized as treatment. However, Annexin-A6 (AnxA6) low cells have been known to produce high levels of AnxA6, which leads to the development of resistance to certain TKIs. The goal of this research is to determine which TKIs have the highest production of AnxA6 after treatment. In order to determine this, MDA-468 cells, a type of TNBC basal cell, was treated with 10 different TKIs. Gel electrophoresis was done before and after 72 hours to determine the amount of AnxA6 produced after treatment compared to before treatment. Analysis of the gel determined that an excess of AnxA6 was produced in all 10 drugs, indicating that resistance will occur. In conclusion, this specific basal cell shows that it has high chances of becoming resistant.

This project was funded by Meharry Medical College.

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CAN REMINDER EMAILS INCREASE PRE-PLACEMENT EVALUATION COMPLIANCE AMONG INCOMING FIRST YEAR DENTAL STUDENTS?

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Healthcare professionals (HCPs) have an increased risk of Vaccine-Preventable Diseases compared to the general population. The Advisory Committee on Immunization Practices (ACIP) recommends HCPs get vaccinated against Hepatitis B, Influenza, MMR, Varicella, Tetanus, Diphtheria, Pertussis, and Meningococcal infections. HCP students are also advised to follow these recommendations, therefore more HCPs schools are requiring incoming students to get vaccinated prior to arrival on campus. However, HCPs continue to not meet targeted ACIP vaccination recommendations and acceptable forms of evidence of immunity. One approach for increasing pre-placement compliance for HCPs involves the creation of a reminder system. Hypotheses: 1. The majority of incoming Meharry Medical College dental students will not have submitted their health documentation before the submission deadline of May 30, 2021. 2. Sending a reminder email will increase the number of dental students with completed health records. Outcome: proportion of incoming dental students that are compliant with pre-placement evaluation requirements as shown by completed health records. Methods: Data will be extracted from submitted health records (hard copy/paper) from the incoming class of dental students at Meharry Medical College (n=60). Students with incomplete health records, as of June 10, 2021, will be identified and the status of each health record

document will be recorded in an Excel spreadsheet. Intervention: A one-time personalized reminder email will be created that addresses each student's specific health documentation needs. Data Analysis: Data will be collected at baseline and 2 months later. Numeric data will be summarized as mean and standard deviation (SD). Categorical data will be presented as frequencies and percentages. Pearson's chi-square (or Fisher's exact test) will be used to compare baseline data to post-intervention data. Results: Pending. Conclusion: Findings from this study will inform the development of effective interventions that will improve pre-placement compliance among dental students at Meharry Medical College.

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A REVIEW OF IDIOPATHIC TOE WALKING: NATURAL HISTORY AND TREATMENT MODALITIES

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Background: Idiopathic toe walking (ITW) is a diagnosis of exclusion identified when there is no underlying etiology for consistent bilateral gait predominantly on the forefoot, with little to no heel strike. While there has been success employing a variety of treatment measures, there remains to be a consistent treatment choice that physicians can recommend to patients and their families. The aim of this review is to examine the natural history of ITW and management options available to provide more consistency to parents when treating this condition. **Methods**: PubMed was searched to find eligible studies that included pediatric toe walkers with no underlying neurological deficits. Outcome measures including parental report of toe walking, gait analysis classification, kinetics/kinematics were evaluated in comparison of multiple treatment modalities. Stanford University School of Medicine Motion Analysis Lab was consulted to provide normal ankle ROM values for comparison. **Results**: From the reviewed literature, 65% of patients spontaneously cease toe walking when they are not treated. With each conservative treatment measure, nearly 65% of patients from evaluated studies improved in toe walking while the remainder continued to toe walk despite treatment. Surgical treatment of ITW provided the most consistent improvement of ITW with 100% of patients in the reviewed studies showing significant improvement in time spent toe walking, kinematics allowing for normal gait, and parental satisfaction. **Discussion/Conclusion** The results show that there are various conservative treatment measures that exist but there is not enough consistency with improvement to advocate for these management options. From the existing data surgical treatment, specifically tendo-Achilles lengthening or gastrocnemius/soleus shortening can be advocated for due to its consistency with improvement in toe walkers. More extensive long term follow up is needed regarding idiopathic toe walkers to ensure validity of treatment choices.

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A NOVEL, DE NOVO VARIANT IN POGZ CAUSES WHITE-SUTTON SYNDROME

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White-Sutton Syndrome (WHSUS) is typically characterized by a wide spectrum of intellectual disability and global developmental delay with or without autism spectrum disorder. Congenital diaphragmatic hernia (CDH) has also been described in 4 individuals. WHSUS can be caused by heterozygous missense, nonsense, and frameshift variants in *POGZ*. We present a 4-year-old female with common phenotypic features of WHSUS, including CDH. She is the fifth case of CDH in individuals presenting with WHSUS. She presented to the Undiagnosed Disease Network (UDN) with a non-diagnostic clinical trio exome sequencing. Re-analysis of her exome sequencing data within the UDN revealed a heterozygous, de novo, intronic variant in *POGZ* (NM_005245000,c.2546-20T>A). RNA sequencing in fibroblasts from the patient revealed an intronic variant that leads to skipping of exon 18. This causes a frameshift and predicted premature stop codon in the last exon of *POGZ*. The levels of POGZ expression in fibroblasts from the patient are equivalent to controls suggesting that the mutant transcript escapes NMD. Overall, this case is first case of WHSUS caused by a *de novo*, intronic variant that is not near a canonical splice within *POGZ*. These findings emphasize the value of using RNA sequencing combined with reanalysis of clinical exome sequencing to diagnose WHSUS. Her presentation of CDH along with other previously reported cases demonstrate that WHSUS should be considered in the differential diagnosis for patients with syndromic CDH.

This project was supported by the Undiagnosed Disease Network.

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SEGMENTATION FOR ASSESSMENT OF LUMBAR MUSCLE MASS METRICS USING QUANTITATIVE ANALISYS

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Sarcopenia is the loss of muscle mass that naturally occurs in aging adults. Cancer patients who are treated with radiation therapy can also experience sarcopenia as a side-effect of their tumor's radiation therapy. Previous studies have discovered a correlation between radiation-induced sarcopenia and decreased survival and quality of life post-radiation therapy. The aim of our research was to show that if we manually segment patient CT scans to train a deep learning system, this system can be used to auto-segment regions of the body to extract quantitative data for lean body mass pre and post radiation treatment. We extracted pre-therapy CT scans from EPIC for 30 cancer patients. Manual segmentation of lean-body mass, subcutaneous fat, and intraabdominal fat at the L3 region of the spine was done using Velocity software. Auto-segmentation of these same regions will be done with an AI model. We anticipate that about 30 manual segmentations will be sufficient to train the AI model for auto-segmentation. Assessment of changes in lean-body mass and adiposity at the L3 region pre and post therapy will be done via statistical analysis. Future analysis will also compare lean-body mass at the L3 region to lean-body mass at the C3 region for each patient to assess congruence of initial lean-body mass across regions of the body. We predict that these results will be consistent with our hypothesis that these auto-segmentations will allow us to statistically

analyze muscle mass metrics based on CT imaging done before and after radiation therapy in cancer patients. This process will allow for improvement in the individualization of radiation therapy by providing a way to analyze a patient's pre-therapy risk for sarcopenia and related radiation induced toxicities.

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TREATMENT GUIDELINES FOR AFRICAN AMERICAN PATIENTS WITH HYPERTENSION AND APOL-1 VARIANTS

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One in seven African Americans have a mutation in the APOL-1 gene. African American patients who are hypertensive and have a mutation in APOL-1 are at a five to ten times greater risk for developing chronic kidney disease. Currently, there are no guidelines for providers to follow when treating African American patients with hypertension and APOL-1 mutation. The goal of this study is to see how both the patient's and provider's behaviors change around controlling and managing blood pressure after a patient's genetic risk for chronic kidney disease is known. These behaviors were assessed through measuring of blood pressure and answering questionnaires at the patient's first appointment, follow up appointment at three months, and final appointment at six months. The patient's blood is drawn during the first appointment. Patients are randomized into either the interventional group, where they learn their genetic results a few weeks after their blood draw, or in the control group, where patient learn their risk at the end of 6 months. Thus far, seven out of twenty-six patients are at an increased risk for developing chronic kidney. Only three patients have completed their 3-month follow up appointment, in which two patients were assigned to the interventional group. Out of those three patients, one patient in the interventional group reported no changes in behavior and no changes in blood pressure and the other patient reported changes in behavior but no changes in blood pressure. The third patient, in the control group, reported no changes in behavior and a slight increase in blood pressure. By the end of the six months, we anticipate that patients will change their behavior to better manage their blood pressure and there will be an overall decrease in blood pressure.
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NOW YOU SEE "ME": THE UNEXPECTED DISCOVERY OF EPITHELIOID MESOTHELIOMA IN EFFUSIONS WITH MOC31 IMMUNOSTAINING, A POTENTIAL PITFALL FOR MISDIAGNOSIS AS CARCINOMA

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In pathology, MOC31 immunostaining has been widely used to distinguish between mesothelial and epithelial cells. MOC31 is a monoclonal antibody against the Epithelial Cell Adhesion Molecule (EpCAM)

protein, a 40kD glycoprotein present on epithelial cells, whether benign or malignant, but not expressed on mesothelial cells. We seek to investigate the prevalence of strong diffuse positivity of MOC31 staining in epithelioid mesotheliomas (EM). In this study, we searched the electronic medical record/pathology database from Stanford Health Care between 2011 and 2021 for cytology effusion specimens with a diagnosis of positive, suspicious, or atypical from patients with known epithelioid mesothelioma at that same location. Matched controls were also identified. Cases/controls with accessible material were obtained from the archive. The Stanford Clinical (CLIA approved) Immunohistology Laboratory performed immunohistochemical studies on 4 μm-thick sections prepared from formalin-fixed, paraffin embedded cell block material using the Ventana Benchmark Ultra automated staining platform. Slides were incubated with a predilute monoclonal antibody against MOC31 and then scored by a pathologist (A.L.) to assess the fraction of mesothelial cells with positive staining (%), along with the degree of staining, scored as weak, moderate, or strong or scored as variable if weak to strong staining was observed. Of the 17 epithelioid mesothelioma cases identified, 53% showed MOC31 positivity and 18% of the cases showed moderate to strong staining. Most cases showed a small fraction of cells with positive staining, however, rare cases showed diffuse positivity, including a single case with 80-90% strong MOC31 staining. All controls were negative for MOC31. The results are consistent with the hypothesis that strong, diffuse MOC31 immunostaining may be seen on a subset of epithelioid mesotheliomas. The information gained from this research will help pathologists be aware of a potential pitfall in misdiagnosing epithelioid mesothelioma as carcinoma when strong, diffuse MOC31 staining is seen.

This project was supported, in part, by the Department of Pathology at Stanford University School of Medicine.

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AN INITIAL LOOK INTO THE BARRIERS OF LUNG CANCER SCREENING FROM THE PERSPECTIVE OF PROVIDERS AND PATIENTS: A MIXED-METHODS ANALYSIS

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Lung cancer is a leading cause of death and screening is underutilized, thus limiting the treatments available to combat the disease in earlier stages. The importance of creating and evaluating methodology and interventions to improve screening guidelines and approaches is critical in the process of reducing lung cancer mortality. The objective of our research was to perform a qualitative assessment of the barriers and facilitators to increased screening through interviews with providers and patients under the BJC Collaborative. Interviews were conducted via zoom with providers of the 16 sites that had initially received the I-STEP toolkit of educational material of low dose CT (LDCT) to give to patients eligible for lung cancer screening established by the new guidelines, and with patients who have been screened for lung cancer with LDCT at the same sites. 35 interviews were initially conducted through July, 24 providers and 11 patients. We found that within the BJC Collaborative, both specialists and primary care providers felt positive of the updated guidelines to LDCT screening and felt that they had increased in awareness and education of patients in the process. Challenges that faced providers however included a lack in EMR prompts as robust as other cancer screening tools, redundancy in order forms, insurance approvals and prior authorizations, and follow-up management policies not being uniform. Patients described the value of trust and communication with providers, as they felt involved in understanding the value of lung cancer screening and the LDCT procedure.

This project was supported, in part, by BJC Collaborative 202101027.

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LGFMS OF THE BREAST AND AXILLA: A REPORT OF THREE CASES AND ANALYSIS OF MUC4 AS A SENSITIVE AND SPECIFIC DIAGNOSTIC BIOMARKER

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Low-grade fibromyxoid sarcoma (LGFMS) is a distinct sarcoma subtype that typically arises in the deep soft tissue of young adults. Characterized by an overall bland fibrous appearance and alternating areas of collagenous and myxoid proliferation, this neoplasm can be quite difficult to diagnose. Histologically, LGFMS has several similarities with more common mammary spindle cell tumors such as sclerosing epithelioid fibrosarcoma (SEF). This, coupled with the fact that LGFMS rarely develops in the breast or axilla, results in this entity often being overlooked as a part of the differential diagnosis. The object of our research was to determine whether MUC4, a cell surface glycoprotein involved in growth signaling, has the capacity to serve as a diagnostic tool to distinguish LGFMS from other mammary spindle cell lesions. Cases of LGFMS of the breast/axilla were identified using the Stanford University Hospital patient database, and subsequent analysis of cases was performed. Immunohistochemical (IHC) stainings of biopsy specimens were performed to detect the presence of MUC4 and other diagnostic markers. An IHC comparison between the identified LGFMS cases and other known mammary spindle cell neoplasms was conducted using a tissue microarray (TMA). We found that the LGFMS samples had strong cytoplasmic staining for MUC4 while the other tumors had either minimal or absent staining. These results are consistent with the hypothesis that the MUC4 can serve as a diagnostic biomarker for LGFMS in the setting of mammary spindle cell lesions.

This project was supported, in part, by the Stanford-Meharry Summer Research Program.

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POLYETHYLENE GLYCOL TREATMENT ON TRANSECTION SPINAL CORD INJURY SHOWS EFFECT ON NERVE MEMBRANE REPAIR

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Direct injury to the spinal cord can result in damage to the nervous system pathways within the spinal cord, leading to loss of function and sensation at the level of the injury and below. With these traumas, one's axons lose the ability to send and receive the needed messages from the brain to the rest of the body. Polyethylene glycol (PEG) has been widely used as a membrane fusogen that has the ability to rapidly repair nerve membranes that have been mechanically damaged. The objective of our research was to examine if transection injuries to the spinal cord can be susceptible to PEG mediated repair, such as with crush injuries. Spinal cords were harvested from freshly euthanized pigs and a transection was done on the harvested spinal cords and subsequently repaired with and without PEG treatment. Tissues were fixed with formalin and Cy dye was used as a method of labeling the axons to access the results of the PEG treatment. Results will be added soon.

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AFRICAN AMERICAN ENGAGEMENT IN PHYSICAL DISTANCING AND FACE MASK USE DURING COVID-19 PANDEMIC

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Objective: To understand barriers and motivators for engaging in physical distancing and face mask use among African Americans during the early stages of the COVID-19 pandemic. **Methods:** We conducted 62 semi-structured interviews with four sub-populations within the Black community: young adults, underlying medical conditions, essential workers, and parents. Thematic analysis was used to evaluate experiences and reasons why people choose to or choose not to engage in COVID-19 preventive behaviors in these four groups. **Results:** Our qualitative analysis yielded six themes: 1) Definition of preventive behaviors, 2) Views towards preventive behaviors, 3) Experiences with preventive behaviors, 4) Motivators to engage in preventive behaviors, 5) Barriers to engage in preventive behaviors, and 6) Strategies to increase engagement in preventive behaviors. **Conclusion:** Physical distancing and the use of face masks were widely viewed as effective behaviors to protect people against COVID-19. However, factors such as personal beliefs, economic status, or mental health influenced whether participants followed public health guidelines. Each group's unique experience provides useful data to improve community outreach efforts and educational material about preventive behaviors.

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OPTIMIZING ENGAGEMENT OF UNDERREPRESENTED INDIVIDUALS WITH CANCER GENETIC TESTING FOR RARE CANCERS

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NIH ethical, legal, and social implications (ELSI) programs prioritize diversity in human genomics research and to understand genetic sequencing information, return of results and the impact of receiving genetic test results on health-related behaviors and communication. However, there is still a need to increase the diversity of participants and identify specific ELSI concerns. The research of our center will focus on 3 rare cancers that disproportionately affect under-represented populations including African American and rural residents. Our center aims to increase the use of genetic testing and return of results among underrepresented populations with 3 rare and understudied cancers using implementation science methods, qualitative interviews, and a web-based decision aid designed to increase access to genetic testing and return of results within these high-risk populations. We conducted a full literature search in PubMed to identify key ELSI concerns regarding genetic testing for rare cancers, the underrepresentation of populations in genomic research, and key barriers or facilitators to accessing genetic testing. The complied references

were used to create a database of key articles focused on rare cancer types, disparities in minority and rural population and ELSI issues. We were able to identity reoccurring themes and concerns surrounding privacy, communication, and lack of knowledge. These findings will help to improve consent, recruitment, data collection and return of results among rural and minority population that have previously not been included in implementation science studies in genomic medicine

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HOW CLINICIANS CONCEPTUALIZE INTERACTIONS AMONG THE PRESENCE 5 FOR RACIAL JUSTICE PRACTICE DOMAINS

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There's a long history of disparities in the care that Black patients receive. The Presence 5 framework identifies clinician communication practices to enhance the clinician-patient relationship. The Presence 5 for Racial Justice project adapts this framework to focus on anti-racism communication practices to promote health equity with Black patients. While the framework comprises five distinct domains, practices that cross domains may offer even greater value to clinician-patient interaction. The objective of this study is to explore clinician communication practices that employ multiple domains from the Presence 5 for Racial Justice framework. Emergent themes were tracked and analyzed from transcripts of clinician circle discussion groups and community advisory board meetings. Through analysis, we found that rather than five separate entities, all of the domains are interconnected in practical utilization. Although early learners may benefit from learning the discrete practices, more advanced clinicians, who are more comfortable with the practices, may improve their patient interactions by integrating practices from different domains concurrently. Utilizing multiple, interconnected anti-racism communication strategies may be an effective mechanism to build trust, promote racial justice, and engage more Black patients in clinical care. The anti-racism communication strategies are critical for equitable health care and the advancement of inclusive science.

This project was supported by Stanford University.

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AGGREGATIBACTER ACTINOMYCETEMCOMITCANS SEQUESTERS PLASMINOGEN VIA SURFACE GLYCERALDEHYDE PHOSPHATE DEHYDROGENASE

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Objectives: Plasminogen has a fundamental role in infection processes and a specific role in determining the onset and severity of periodontal disease. A critical experiment showed that loss

of plasminogen activation in Tissue plasminogen activator/urokinase plasminogen activator double knock out mice (so that no plasmin is produced) produced periodontal pathology with bone loss, thereby showing that plasmin is "essential in protecting against periodontal disease". **Experimental Methods:** Clinical isolates CU 1000 and IDH-781 of A.a was used in this study. *In situ* plasminogen binding assays as well as Plasminogen overlay far western assays were used as per the standard protocols. A.a cells with pre-bound GAPDH antibodies knocked down in situ detection of plasminogen binding were observed. For Plasminogen overlay *far western* assays, GAPDH-Plasminogen binding was assessed for the ability of plasminogen protein to block A.a GAPDH detection on blots. In contrast a parallel filter incubated with human plasminogen (15 micro-grams/ml) before probing with anti-GAPDH, blocked GAPDH detection. **Results:** We began study by examining GAPDH expression in A.a to identify anti-body preparations that detect GAPDH protein. The data base indicated that one GAPDH protein is encoded in the A.a, showed that a 37 kDa GAPDH is identified in total protein samples from A.a by immunoblot detection alternatively investigations were done in E. coli. Detection of surface GAPDH and surface bound plasminogen was done in A.a cells, signal was seen in rough(virulent) than in smooth (FLP) by immunofluorescence microscopy and cell-pull down assays. **Conclusion:** This study provided evidence that aggregatibacter actinomycetemcomitans re-distributes GAPDH to its exterior cell surface as like yeast and other mammals do. Our biochemical studies indicated that A.a possesses a single predominant plasminogen binding protein.

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BREASTFEEDING AND POSTPARTUM WEIGHT RETENTION AMONG AFRICAN AMERICAN WOMEN IN NASHVILLE, TENNESSEE

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Obesity is a leading cause of poor health outcomes among the U.S. and has a high prevalence amongst the African American communities. African American women have been identified as a priority population at risk and gestational weight gain has been noticed to have a high association with obesity development. Breastfeeding patterns have been found in a majority of studies to have an influence on weight change. In a majority of studies, breastfeeding for less than 3 months has been shown to have little or no influence on weight change. However continuous breastfeeding for more than 6 months has been shown to have a positive association on weight loss. A secondary analysis of data was collected from a prospective breastfeeding promotion study investigating rapid weight gain in Africa American infants. The data analyzed was collected from a study involving the enrollment of 258 women who received four 30-minute breastfeeding sessions and were followed up at birth. Mothers were followed for a total of four times after birth which were marked at 1 month, 3 months, 6 months and 12 months. Calculations from the study were used to determine whether breastfeeding had an association in decreasing postpartum weight retention. Weight change and BMI were not significantly impacted by breastfeeding patterns, education status, income, job status, or marital status. Demographic characteristics have no significant association with postpartum weight retention/loss, nor breastfeeding behavior. There is a need for a more intensified effort on postpartum weight loss and breastfeeding education for all pregnant mothers.

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INVESTIGATING THE ASSOCIATION OF WHITE MATTER BRAIN INJURIES AND FAMILY FACTORS WITH THE DEVELOPMENT OF ADHD IN VERY PRETERM CHILDREN AGE 5 YEARS

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There is a known correlation between white matter brain injuries and deficits within neurodevelopment among infants born very preterm. Follow-up studies have also shown that parents of very preterm children with complex neurological and medical needs also experience higher levels of parenting stress and family dysfunction. However, there is less information known about the association of these white matter injuries and the development of ADHD symptoms and diagnoses in very preterm (VPT) children, or how family factors might also affect these relationships. The objective of this study was to examine the association between white matter brain injuries and the development of ADHD symptoms and the role of family factors. Data associations between prematurity, brain injury, family factors and ADHD symptoms were examined using linear mixed-effect models. We found that the birth of VPT infants with brain injuries was associated with higher rates of ADHD compared to children born full term (FT). There were also higher rates of parenting stress among families with VPT children with brain injuries. Family dysfunction and parenting stress were also found to be highly related to the outcome of ADHD in VPT infants. Furthermore, parental stress and family dysfunction were found to be key correlates of ADHD symptoms in VPT children. These results are consistent with the hypothesis that the presence of these brain injuries would be correlated with higher rates of ADHD symptoms and diagnoses, with increased risk for preterm children with brain injuries who are also exposed to parenting stress and family dysfunction.

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RELATIONSHIP BETWEEN DENTAL CAVITIES AND PROTECTIVE RISK FACTORS AMONG 0-5 YEARS OLD CHILDREN

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The purposes of this study were: (1) to collect and analyze data that help guide decision making for continuous improvement in dental care among children aged 0-5; and (2) to determine protective risk factors that contribute to the prevention of children aged 0-5 contracting dental cavities. Caregivers of children 0-

5 years old were recruited from various locations. More than 200 surveys were instrumented to assess caregiver and child's oral hygiene practices, current dental health, and access to a dental home. The Generalized Linear Model (GLM) with Logit Link and the Partial Least Squares Statistical Analysis: Regression (PLS) Model were used to determine the protective risk factors associated with the prevention of children contracting dental cavities measured in a binary scale (Yes/No). The significant effects of the protective risk factors were determined via IBM Statistical Packages for Social Sciences (SPSS) by the pvalue being less than the 0.05 significance level. The Artificial Neural Network (ANN) is a preferred benchmarking tool used by researchers to recognize patterns as well as effectively classify data. The results showed significant contributions to the adverse oral health outcome (cavities) among children aged 0-5 were found ($p < .05$) in the behavioral protective factors. The study also revealed that children whose teeth were flossed by their parents were three times less likely to develop cavities. In addition, children were least likely to have cavities if their parents used toothpaste and mouthwash, avoided sharing chewed food and refrained from drinking 100% juice. In contrast, children were more likely to obtain cavities if their parents had a lower educational level, rarely cleaned teeth, and often consumed marijuana, cow or goat milk, juice drinks and sugary beverages. In conclusion, this study demonstrated protective risk factors that contribute to the prevention of children aged 0-5 yrs contracting dental cavities.

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SMALL-MOLECULE TARGETING OF THE NPM1/RAD51 REPAIR COMPLEX FOR THE RADIOSENSITIZATION OF NSCLC

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Immune checkpoint consolidation therapy following concurrent chemo-radiation therapy (CRT) has significantly improved survival for patients who present with locally advanced stage III non-small cell lung cancer (NSCLC). However, 25 to 30% of patients will not be eligible to receive durvalumab consolidation therapy because of local-regional tumor progress or CRT-induced toxicity. For those patient who are eligible for durvalumab therapy, an additional 25% experience in-field and local-regional disease progression. Thus, the challenge is to improve the ability of chemo-radiation to achieve local regional control without increasing normal tissue toxicity. Achieving this goal required developing a small molecule DNA Damage Response inhibitor that would increase radiation efficacy. A forward chemical genetics screen coupled with phenotypic structure/function analysis identified 5-((N-benzyl-1H-indol-3-yl) methylene) pyrimidine-2, 4,6(1H,3H,5H) trione as an excellent radiosensitizer (YTR107) as an efficacious radiation sensitizer. YTR107 was found to radiosensitize 7 NSCLC cell lines and associated xenografts and syngeneic tumor models. Pharmacokinetic and pharmacodynamic studies undertaken in mice revealed that YTR107 was rapidly degraded. Thus, the chemical structure of the radiosensitizing compound was now in question: Was it YTR107 or the degradation product? Herein we present data that indicates that YTR107 is the radiation sensitizing molecule. Colony formation assays were used to test the hypothesis that YTR107 and not the degradation product was the radiosensitizing entity. Cell survival curves derived from gamma-irradiated A549 NSCLC cells were quantified and statistical analysis indicated that the degradation product did not radiosensitize cells. These experiments unequivocally identify YTR107 as the radiosensitizing moiety that provides enhanced radiation efficacy.

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COMPARING STING RELATED PATHWAYS TO STING PATHWAY ACTIVATION POST RADIOTHERAPY IN ANDROGEN RESISTANT AND ANDROGEN SENSITIVE CELL LINES

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Immune checkpoint inhibition (ICI) combined with radiotherapy (RT) can provide a synergistic treatment effect, enhancing and sustaining the immune response against a variety of tumors. The optimal combination of ICI + RT for prostate cancer is unknown. STING, a sensor of cytosolic double-stranded DNA (dsDNA), is increased following radiation in a variety of cell lines and triggers the immune response. In melanoma, silencing of androgen receptors (AR) results in increased cytosolic dsDNA and STING activation. AR loss is a crucial step for resistance to conventional androgen deprivation when treating prostate cancer. A link between the STING pathway and AR loss is unknown. Our goal was an investigational inquiry as to whether STING related pathways following radiation showed similar differences between androgen sensitive cell lines and androgen resistant cell lines as seen in the STING pathway following radiation. Androgen-resistant cell lines include 22Rv1, DU145, PC3 and androgen-sensitive cell lines are LNCaP, MDA-PCa-2b. To delve further into why each pathway was looked at, the HR(Homologous Recombination)and NHEJ (Non-homologous End Joining) are the 2 most common ways to repair DNA damage. We looked at mismatch repair because MDA-PCa-2b is known to be deficient in mismatch repair. We looked at Nod-like receptor signaling because it can also trigger the immune response following double stranded DNA accumulation in the cytoplasm. We looked at the p53 pathway because it is intrinsically involved in the DNA damage repair and response. We looked at the expression of the STING pathway in cells. In conclusion, pathways that were immediately relevant to radiation response and the STING pathway did not have any specific mutational patterns or overexpression discrepancies that could account for the difference in STING pathway activation following radiation. The next step of the laboratory will be to knock down androgen receptor and see if loss of androgen receptor in LNCAP and MDA-PCa-2b increase STING activation.

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PLIC-1 RESCUE MECHANISMS OF DEVELOPMENTAL EPILEPTIC ENCEPHALOPATHIES

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The β subunits of the $GABA_A$ receptor are abundantly expressed during the development of the central nervous system and have been linked to Lennox-Gastaut Syndrome (LGS) in humans. The impact of the mutation in the brain and how it can cause a developmental and epileptic phenotype are poorly understood, let alone mechanism-based treatment. Ubiquinlin-1(Plic-1), the ubiquitin-like protein is an adaptor protein between ubiquitin and the proteasome reported to stabilize β_3 subunit encoded by GABRB3. Preliminary work in the lab has shown that the overexpression of, Plic-1, can rescue mutant subunit containing receptors. We have developed a novel mouse model of LGS (*Gabrb3*$^{+/N328D}$) to compare the major defects caused by the mutation from molecular to neurobehavioral levels. With overexpression of the Plic-1, we can determine if molecular and functional phenotypes of the mutant mice can be rescued. Expression of the α_2, β_3, and γ_2 subunits of the $GABA_A$ receptor in both total lysates, cell surface level, and synaptosomes will be determined in mice without or with overexpression of Plic-1. Video monitoring and synchronized EEG recordings will be conducted. The receptor subunits will be assessed via immunoblot within mice to assess differences in gross protein expression and subcellular localization. There was seen reduced expression of this subunit within heterozygous mice compared to wildtype. The expression of β_3 subunits was reduced in both total lysates and synaptosomes in the *Gabrb3*$^{+/N328D}$ and *Gabrb3*$^{+/-}$ mice compared to wild-type littermates. Plic-1 rescued the expression and function of mutant β3 subunit containing receptors in vitro and in Gabrb3$^{+/N328D}$ mice.

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THE ROLE OF HUMAN A-DEFENSIN 5 AS A BIOMARKER IN INFLAMMATORY BOWEL DISEASE

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Approximately 30 percent of inflammatory bowel disease (IBD) patients cannot be accurately diagnosed. As a result, these patients may be prescribed ineffective medical or surgical treatments. The research is focused on improving the diagnosis for patients with the predominantly colonic IBD subtypes of ulcerative colitis (UC) and Crohn's colitis (CC). A systematic literature review to identify potential molecular biomarkers that can be used in IBD subtype diagnostics with accuracy was performed. To gain a better understanding of the global epidemiology of IBD and normal role of Human α-defensin 5 (DEFA5) immunologically, the relevant literature was reviewed using a predetermined protocol and in accordance with the quality of reporting meta-analyses of observational studies. The data show that UC and CC can accurately be distinguished molecularly by examining DEFA5 in biopsies without delay. These observations are under preclinical tests to validate data in support of the safety of the predominantly colonic inflammatory bowel disease diagnosis. If successfully developed, widespread use of DEFA5-bioassay would become a "Gold Standard" diagnostic tool to facilitate more accurate diagnosis and could potentially undergo a quick translational clinical practice in IBD clinic.

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BEHAVIORAL AND PHYSIOLOGICAL ASSOCIATES OF INHIBITORY CONTROL IN CHILDHOOD STUTTERING

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Stuttering occurs in 5-8% of young children, although 80% of these children will eventually recover from stuttering, leaving approximately 1% of the population to continue to stutter or "persist." Psychophysiological factors have been shown to influence stuttering, but these markers are poorly understood regarding the potential role in stuttering persistence and recovery. To date, present findings have demonstrated differences in emotional temperament and behavioral responses in children who stutter (CWS) and children who do not stutter (CWNS). However, there are no replicable objective markers of risk nor a systematic understanding of the neurophysiological mechanisms of emotional contributions to stuttering. Without this knowledge, clinicians and those invested in the prognosis of children who stutter do not have psychophysiological markers of risk for stuttering persistence, which are necessary to develop innovative diagnostic and therapeutic approaches. This research design tests whether physiological measures of emotion are associated with inhibitory control and motor execution during neutral and emotionally arousing conditions. Young children who stutter (CWS) and children who do not stutter (CWNS) performed a Go-NoGo task with emotion induction. In this study, physiological and behavioral measures during neutral and emotionally arousing conditions are assessed. Results indicate that (1) there were no significant differences in RSA between the groups during affective or neutral conditions, (2) there were no significant differences between the groups in Go reaction time during the neutral or negative conditions, and (3) CWS, compared to CWNS, exhibited significantly lower accuracy during the NoGo conditions; however, there was no effect of emotion on NoGo accuracy. The findings may indicate that CWS have decreased inhibitory control but that it is not vulnerable to emotional interference.

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NEEDLESTICK EXPOSURE DOCUMENTATION IN VETERAN AFFAIRS TENNESSEE VALLEY HEALTHCARE SYSTEM IN NASHVILLE AND MURFREESBORO

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Occupational exposure to bloodborne pathogens is a serious risk for healthcare workers. Needlestick injuries pose a substantial risk for transmitting infectious diseases. The three common pathogens associated with needlestick injuries are hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). Most needlestick incidents are never reported which can partly be attributed to barriers for efficient reporting in a healthcare setting. Once a needlestick injury occurs, it is paramount that healthcare workers receive prompt evaluation. This evaluation involves reviewing the source patient's bloodwork. Medical residents and medical students who sustain a needlestick injury while rotating in the Veteran Affairs (VA) Tennessee Valley Healthcare System (TVHS) must return to their institutions to receive evaluation. The source patient must be consented for lab work and there must be a release of information prior to the lab work being sent. This can affect proper treatment due to delays in transmitting the source patient's lab work between two different institutions. The objective of this research was to facilitate the documentation of needlestick injuries for improved transmission of source patient's lab work to the trainees' institutions. The study will take place at the VA in Nashville and Murfreesboro. We will work with Information Technology and Privacy at the VA to construct a template in the Computerized Patient Record System (CPRS) that consolidates the source patient's release of information and informed consent into a single template which can facilitate the relay of information. The primary outcome to be evaluated is the improved transmission of source patient's lab work from the VA to the trainee's universities within 24 hours of a needlestick injury.

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DIABETIC KETOACIDOSIS WITH HYPOKALEMIA IN THE SETTING OF CRUSH INJURIES FROM MULTIPLE DOG BITES IN HOME ENVIRONMENT

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Trauma is a precipitating cause of diabetic ketoacidosis in type 1 diabetics, but is much less common in presentation in type 2 diabetics. However, in this case report, when a type 2 diabetic was presented to the trauma bay of the emergency department for evaluation and management of severe dog bites from a pitbull breed canine in her backyard; diabetic ketoacidosis with a blood glucose of 650, serum acetone, an anion gap of 19, a pH of 7.08 and rhabdomyolysis with a creatine kinase of 1075 U/L were incidentally found in the blood work during evaluation and management of the dog bites. This further complicated management for this patient due to the fact that diabetic ketoacidosis causes metabolic and electrolyte dysregulations that can complicate treatment; potassium in diabetic ketoacidosis often causes pseudo-hyperkalemia or pseudo-eukalemia due to intracellular potassium rushing out of the cells from increase in acid in the blood. Insulin results in rush of potassium back into cells, resulting in hypokalemia requiring management with potassium replenishment. A dilemma here is whether to administer potassium for diabetic ketoacidosis, because of potential risk of rhabdomyolysis from the animal bite crush injuries that could result in potassium rushing out of the damaged muscle cells resulting in hyperkalemia that could result in side effects such as arrythmias in the patient. After administering IV fluids, pain medication, IV potassium and irrigating the wounds with sterilized water and Betadine before applying wet to dry dressing, the patient was transferred by helicopter to a tertiary hospital for vascular surgery due to immediate risk of loss of life and limb. Insulin was held before transfer to due to potassium being in the process of being repleted and the accepting physician was notified to give insulin upon arrival to the tertiary health care center.

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EFFECTIVENESS OF COMMUNITY-BASED, TARGETED VACCINATION SITES

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COVID-19 is an infectious respiratory disease caused by a newly discovered coronavirus. Nashville, TN has over 100,000 reported cases and 944 deaths from COVID-19. At the pandemic's height thousands of new cases were being diagnosed daily, however with the emergency use authorization of a vaccine for COVID-19 numbers have decreased. Administration of this vaccine is the most effective way to prevent contracting and spreading the virus. The objective of our research is to evaluate whether selected vaccination locations were effective to maximize vaccination rates, slowing the spread of COVID-19. Comparisons were made between the efficacy of smaller scale, temporary, community-based vaccination sites and fixed location, longer-term mass vaccination sites to vaccinate minority and vulnerable populations. Analysis was made through statistical analysis of patient vaccination records and a survey administered to those who received their COVID-19 vaccine at both types of sites. We found that vaccination of black and multiracial persons was higher at smaller scale, temporary, community-based vaccination sites. Those who are hesitant to receive the vaccine are more willing to do so when the event is hosted in their neighborhood, at a location they are familiar with and most importantly trust. Results have prompted the Metro Public Health Department to expand their community outreach vaccination program, creating a second team of nurses to create more Community-based, targeted vaccination sites in hopes of continuing to increase COVID-19 vaccination rates throughout Nashville, especially in minority/vulnerable populations. Analysis of the entirety of the data including surveys will continue to form additional conclusions.

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CHEMOPROTECTIVE EFFECTS OF SULFORAPHANE: A SYSTEMATIC REVIEW OF PRECLINICAL STUDIES

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Colon cancer is the third most diagnosed cancer that affect males and females alike in the United States. There have been many studies that link colon cancer to dietary habits. A diet that is high in red meat, low in fiber, fruits and vegetables have been linked to colon cancer. Nonetheless, recent research has

demonstrated that the inclusion of cruciferous vegetables into one's diet has chemoprotective effects in in vivo animals' studies due to the presence of sulforaphane. Sulforaphane, an isothiocyanate that is formed from the hydrolysis of glucoraphanin contained in cruciferous vegetables, possesses a wide variety of chemoprotective properties. Chemoprotective mechanisms of sulforaphane include antioxidant, anti-inflammatory, histone deacetylase inhibition, and cytoprotective phase 2 detoxification properties. Sulforaphane is a promising agent for cancer prevention and treatment, but there are few clinical trials in animals to date. A summary and evaluation of the body of preclinical research can provide guidance for future translational research. The goals of this study are to systematically review the preclinical literature evaluating the chemoprotective properties of sulforaphane in colon cancer, and to produce a summary of the available evidence that informs the future research agenda for translational applications. The systematic review included randomized control trials from five articles that focused on in vivo animal studies. The results that were extracted and analyzed demonstrated that sulforaphane was an effective treatment strategy in reducing colon cancer through a variety of biomarkers. Further research needs to be conducted in order ascertain the maximum efficacy of sulforaphane in chemoprevention of colon cancer. Furthermore, sulforaphane can be the focus in a nutritional plan of approach to colon cancer prevention in the future.

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HUMAN iEEG CHARACTERIZATION OF THREAT AND ANXIETY RELATIONSHIPS ACROSS AMYGDALA, HIPPOCAMPUS, AND FRONTAL CORTEX IN EPILEPSY PATIENTS

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It is common for epilepsy patients to experience psychiatric co-morbidities such as anxiety and depression (Ann of Gen Psychiatry 6:28,) which independently affect the quality of life. Targeting the location and onset of negatively associated emotions could provide treatment strategy to epileptics at-risk. Using, intracranial encephalography (iEEG) recordings amygdala-hippocampus-prefrontal cortical brain rhythms have recently been used to define subjective mood states in patients with epilepsy. Identification of specific brain activity patterns may be exploited as targets for electrical stimulation to alter persistent negative emotional states. In this pilot study, we aimed to identify specific brain rhythms across different neural substrates that correspond to anxiety and threat-related behaviors across the threat imminence continuum. We conducted a pilot study using intracranial electrophysiology in epilepsy patients undergoing intracranial EEG (iEEG) for seizure onset localization to understand continuous spatial threat avoidance using in n=9 subjects. Subjects played a spatial avoidance game previously linked to state and trait anxiety (Wise & Dolan, 2020) with simultaneous recording of neural oscillations in the hippocampus, amygdala, and frontal circuits. Up to n=269 trials of continuous threat avoidance behavior in each subject (n=9) were acquired during iEEG monitoring. All subjects performed above chance level in threat avoidance. Preliminary analysis showed evoked potentials in the hippocampus linked to aversive game events. Subsequent analysis will be based on coherence between band-specific electrophysiological signals in a pairwise fashion between the hippocampus, amygdala, and several frontal cortical regions (orbitofrontal, medial prefrontal, cingulate, and insula). These findings suggest that eliciting aversive experiences via repeated spatial avoidance behavior is feasible in iEEG subjects, permitting invasive recordings of trans-diagnostic negative

emotion constructs in mental health. Understanding the network electrophysiology of threat processing using these approaches may yield insight into anxiety- and mood co-morbidity in epilepsy, subsequently, providing stimulation targets to alter negative emotions.

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IN VITRO AND *IN VIVO* STUDIES SHOW A UNIQUE PROFILE OF THE SMALL TBTIMS IN *TRYPANOSOMA BRUCEI*

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Trypanosoma brucei causes a deadly disease known as African trypanosomiasis that affect rural population in Sub-Saharan Africa. *T. brucei* contains a single mitochondrion that needs to import thousands of proteins for its function, making mitochondrial protein import essential. However, the translocase of the mitochondrial outer and inner membranes (Tom and Tims) in *T. brucei* are significantly divergent. *T. brucei* possesses 6 homologues of the Tims (TbTim9, TbTim10, TbTim11, TbTim12, TbTim13, and TbTim8/13) with a characteristic secondary structure, but except for TbTim9 and TbTim10, others are unique to *T. brucei*. Therefore, it is necessary to understand how these TbTims interact with each other. Previous studies show that, all the TbTims are present in the single TbTIM complex and critical for the stability of this complex. Here, we analyze the interactions pattern of TbTims by yeast two hybrid (Y2-H) analysis. All TbTims are expressed in yeast and show direct interaction with each other, however, stronger interactions were found between TbTim8/13 with TbTim9 and TbTim10. To determine the structural domain(s) necessary for their interaction, the small TbTims were split into their N-terminal and C-terminal helices to use for Y2-H analysis in all sorts of combinations. We found that both helices of TbTim9, TbTim10, and TbTim8/13 are involved in interaction among themselves and with TbTim11, TbTim12, and TbTim13, indicating a central role of the former 3 TbTims. Furthermore, we observed that overexpression of TbTim10 in *T. brucei* could complement the deficit of TbTim11, TbTim12, and TbTim13, suggesting these are iso-functional. However, TbTim10 overexpression could not complement the effect of TbTim9 and TbTim8/13 knockdown on TbTIM complex integrity, because TbTim10 stability depends on TbTim9 and TbTim8/13. Altogether, our *in vitro* and *in vivo* data suggest that TbTim9, TbTim10, and TbTim8/13 are the core of the small TbTim complex and other TbTims have auxiliary functions.

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PERIODONTAL DISEASE: VIRULENCE FACTORS OF THE RED COMPLEX AND THEIR EFFECTS ON THE GUT

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OBJECTIVES: Periodontal disease (PD) is oral pathogenic-based; failure to control the disease could contribute abnormalities in the gut homeostasis. The aim of this study is to examine the trends of PD from previous literature and analyze the mechanisms by which the main virulence factors of the red complex contribute to pathogenesis in the gut. **EXPERIMENTAL METHODS:** Thirty-six 36 publications identified in the *PubMed* using selective key words between the period of 2015-2020 were reviewed for their relevance. Articles were categorized based on the differing characteristics of the red complex bacteria as well as their relation to PD, primarily by their virulence factors. **RESULTS:** The virulence factors of major periodontal pathogen, *P. gingivalis, however,* are most damaging to epithelial cells lining of the gut. *P. gingivalis* uses its virulence factors to invade immune and epithelial tissues, as well as to escape detection by defense mechanisms of the immune system. Gingipains, one of the main virulence factors of *P. gingivalis (*along with LPS), are responsible for roughly 85% of the total proteolytic activity in different strains of the bacteria. *P. gingivalis* uses gingipains to inhibit innate immune responses to accommodate its growth and proliferation. Gingipains activate the complement system, consequently inducing cell lysis. LPS, from *P. gingivalis* binds to the TLR4, and this signaling pathway (involved in oxidative stress) activates MYD88, to further activate the MAPK and NF-κB pathways and additional downstream effects. NF-κB is responsible for expressing pro-inflammatory factors through its inhibition of Nrf2, effectively eliciting oxidative stress. Additionally, AP-1 mediates iNOS, which enhances NO levels, impairing gastric motility. **CONCLUSION:** The oral microbiome largely influences the health of the gut, and the rest of the body. Maintaining optimal oral health along with any needed periodontal therapy is key for the mitigation of oral-bacterial induced gut homeostasis.

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MITOCHONDRIAL DNA CONTENT IN EXOSOMES SECRETED FROM HUMAN GLOMERULAR PODOCYTES EXPRESSING APOL1 RISK VARIANT G2 IN HIGH GLUCOSE MILIEU IS REGULATED BY ANGIOTENSIN-CONVERTING ENZYME 2.

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Previous studies have shown that risk variants of Apolipoprotein L1 (APOL1 RVs) can induce mitochondrial dysfunction, however these mechanisms are poorly understood. Moreover, extracellular vesicles, specifically exosomes, have been implicated in the pathogenesis of kidney disease due to their ability to exchange biomolecules between cells and reprogram the biological activity of the recipient cells. Of these biomolecules, cytosolic DNA of mitochondrial origin (mtDNA) can be released in exosomes and, when taken up by recipient cells, can activate specific cytosolic DNA-sensing pathways. Based on these observations, we hypothesize that APOL1-mediated mitochondrial dysfunction, especially in the context of hyperglycemia, may increase the mtDNA content in exosomes released from kidney glomerular podocytes. Exosomes were collected from the culture media of human conditionally-immortalized glomerular podocytes transduced with APOL1 gene variants under control of a doxycycline-inducible promoter. To acquire biological characteristics of the kidney glomerular podocytes, the cells were differentiated for 2 weeks then treated with doxycycline to induce the expression of APOL1 RV G2 or exposed to glucose at concentrations similar to those found in hyperglycemic patients. The amount and size of exosomes released by these differentiated podocytes were quantified using nanoparticle tracking

analysis, and exosomal mtDNA content was analyzed by qPCR. We have shown that while the expression of APOL1 G2 does not have a significant effect, high glucose greatly impacted the amount of released exosomes and their mtDNA content. In addition, the amount of mtDNA encapsidated in exosomes was significantly reduced in podocytes overexpressing angiotensin-converting enzyme 2 (ACE2) receptor, suggesting a protective role of ACE2 against glucose-induced mitochondrial dysfunction and release of mtDNA into the cytosol.

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DEVELOPMENT OF AN IN VITRO ASSAY TO DETERMINE CELLULAR EXPRESSIONS OF POLYMERIC IMMUNOGLOBULIN RECEPTOR IN MICE

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Emerging evidence suggests that loss of secretory IgA (sIgA) in small airways contributes to chronic obstructive pulmonary disease (COPD) progression. Data suggests that loss of sIgA could be a result of the reduction in polymeric immunoglobulin receptor (pIgR)-expressing cells. However, the cells expressing pIgR have not been investigated in a mouse model. Based on our data, we hypothesized that the loss of SIgA in small airways is a result of reduced amounts of secretory cells expressing pIgR. We examined the effects of ciliated and secretory cell-specific deletions of pIgR in primary murine tracheal epithelial cells (MTECs) on the global pool of pIgR and secretory IgA (sIgA) transcytosis. pIgR expression was determined by immunostaining and western blotting, and sIgA was measured by ELISA. FoxJ1.Cre/pIgR$^{fl/fl}$ (pIgR$^{\Delta ciliated}$) will have similar amounts of pIgR expression during immunostaining and western blot and similar amounts of sIgA during transcytosis as WT Mice. Whereas Scgb1a1.Cre/ pIgR$^{fl/fl}$ (pIgR$^{\Delta secretory}$) mice will have reduced amounts of pIgR expression during immunostaining and western blot as well sIgA during transcytosis compared to WT mice.

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TRYPANOSOMA CRUZI MODULATES EXPRESSION OF piRNAs AND THEIR TARGET GENES IN PRIMARY HUMAN CARDIAC FIBROBLASTS DURING THE EARLY PHASE OF INFECTION

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Trypanosoma cruzi, the causative agent of Chagas Disease, causes severe morbidity and mortality worldwide. Though originally endemic to Central and South America, it is now present in most industrialized countries due to modern globalization and international travel. About 40% of infected individuals will develop cardiovascular, neurological, and/or gastrointestinal pathologies. Cardiomyopathies induced by chronic parasite infection include hypertrophy and fibrosis, accompanied by significant changes in the extracellular matrix (ECM) deposition and composition. Accumulating evidence suggests that the parasite induces alterations in host gene expression profiles in order to facilitate infection and pathogenesis. The role of regulatory gene expression machinery during *T. cruzi* infection has yet to be elucidated. In this study, we aim to understand the role of a class of small noncoding RNA molecules, piwi-interacting RNAs (piRNAs) during the early phase of *T. cruzi* infection in primary human cardiac fibroblasts (HCF). RNA purified from parasite challenged HCF were subjected to RNA-sequencing. We utilized bioinformatics tools such as NOISeq to analyze the piRNA expression profile and miRanda/RNA22 to predict piRNA target genes. We found about 26,496,863 clean reads (92.72%) which mapped to the human reference genome. During parasite challenge, about 441 unique piRNAs were differentially expressed. *In silico* analysis predicted that several piRNAs, including hsa_piR_019949 and npir_1530 mapped to genes of interest, such as DDR2, TLR2, and SMAD2, respectively. We used RT-qPCR to validate the expression of piRNAs and their downstream targets. We show that hsa_piR_019949, npir_1530, DDR2, and TLR2 were dysregulated over the course of infection ($p < 0.05$). Our findings are the first to implicate piRNAs as novel regulators of inflammatory and ECM components during *T. cruzi* infection.

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DEEPER MEANING: UNDERSTANDING HOW TO CHANGE FAMILY HEALTHY FOOD HABITS

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The Food for Thought study addresses food security by enhancing parent-child skills building and grocery delivery to active behavior change. It is a randomized controlled trial where all 120 families receive recipes and grocery delivery, and the intervention group also receives weekly skills-building health coaching to improve family health. My project will add a qualitative component to assess the family process, culture, and sustainability of healthy behaviors. The questions will help measure the effectiveness and sustainability of the study by evaluating if the participants have adapted healthy behavior habits. We accessed the participants' behavioral patterns through the design and implementation of qualitative research questions. The questions are designed to answer how the integration of healthy alternative meals and bite-sized recipe videos affects behavior and nutrition change for parents and children. Brief semi-structured interviews were conducted with families currently enrolled in the Food for Thought study. This subcomponent of the study was recently initiated. Our very early findings indicate these themes. 1. Incorporating children, 2. Building cooking skills, and 3. Ease of offering children different types of food choices. Data collection will continue

for the next three months. Once data collection is complete, we will identify themes and conduct a full qualitative analysis.

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DEVELOPING A SENSITIVE ASSAY FOR CD73 THAT IS TRANSLATABLE FOR EXOSOMES AND EVENTUALLY PLASMA WHILE DEMONSTRATING SPECIFIC CHARACTERISTICS OF CD73 WITH CANCER CELL LINES

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The progression of cancers and tumor growth is facilitated by immunosuppression and the inhibition of normal cell checkpoints and specific cell markers. CD73, a GPI-linked dimeric protein on cell surfaces, is found in exosomes and extracellular vesicles from many cancer cell lines. CD73 produces large amounts of adenosine which is a cancer-linked immunosuppressant that facilitates cancer progression and tumor growth. The activity of CD73 is essential in determining the survival of the cancer and even metastases. The objective of our research was to develop a sensitive assay that efficiently and effectively determines the enzymatic activity of CD73 that can be used for exosomes and eventually plasma. We first demonstrated and proved the presence and activity of CD73 in many prominent cancer cell lines such as CaCo-2 and DiFi by Western blots and protein quantification. We also created a standard curve for CD73 amounts to find the average amount of this protein in lysates of DiFi cells. Confocal imaging of CD73 and DiFi cells further proved the presence and specific location of this protein in prominent cancer cell lines. We performed an assay with CD73 and used adenosine and AMP to determine its specific enzymatic activity. Statistical analysis showed the specific activity of CD73 in different protein amounts. These results were consistent with the expected location, identification, enzymatic activity, and standard activity in conjunction with adenosine.

This project was supported in full by the Robert J. Coffey lab funds.

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CAN A HISTORY OF ADVERSE CHILDHOOD EVENTS ALTER SYMPATHETIC & PARASYMPATHETIC REACTIVITY TO ACUTE STRESS? HEALTHY MIDDLE-AGED & OLDER ADULTS DEMONSTRATE PATTERNS OF PHYSIOLOGICAL RESLIENCE

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Can adverse childhood events alter the reactivity of the human stress axis? Current literature has associated early childhood adversity to long-term dysregulation of the physiological stress-response. The objective of our research was to analyze heart rate variability & skin conductance, measures of parasympathetic & sympathetic respectively, to determine autonomic nervous system baseline levels & reactivity. An additional exploratory aim examined the relationship between emotional intensity of disclosures & autonomic reactivity as a function of early life adversity. During this observational study, couples ages 25 & older completed a 5-min baseline, a battery of questionnaires, & individual disclosures of upsetting events. HF-HRV, HR, and SC were recorded continuously to provide measures of reactivity and recovery. CTQ sum scores were compiled based on participant responses to the Childhood Trauma Questionnaire. Upsetting memories were coded by independent rater for whether there was a focus on traumatic childhood events. We found that adults with extensive history of childhood physical abuse had lower SC levels, while no overall differences were noted in baseline HRV. No differences were observed in either parasympathetic or sympathetic reactivity between individuals with & without a history of childhood trauma during acute stress. These results were consistent partially for the first hypothesis and displayed increased baseline sympathetic data in non-dominant wrists. The results were inconsistent with our second hypothesis due to no changes in either SNS or PNS reactivity levels. The sample did not include individuals with pre-existing health comorbidities, which may be indicative that healthy individuals with a history of childhood adversity do not display adverse alterations of their stress axes. Due to the extensive exclusion criteria, the sample population's data was representative of only a small subset of the community demographic, which calls for addition research with a more diverse sample for better generalizability of findings.

This project was supported by the National Institute of Aging (R00 AG05667, PI: Wilson; R01 AG057032, PI: Kiecolt-Glaser. Briana Rollins was supported through the Meharry School of Medicine Center of Excellence.

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EVALUATING DISPARITIES IN THE AVAILABILITY OF EMERGENT HAND CARE, TELEHEALTH, AND TELEMEDICINE SERVICES IN TENNESSEE

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In 2018, 130 million ED encounters were reported nationally. During the early coronavirus disease 2019 (COVID-19) pandemic period, a decrease in ED volumes by 49% was observed, and more serious cases constituted a greater proportion of the presenting cases. Approximately 5% of hand injuries require acute management, disparately in rural areas. Many individuals are therefore transferred to hospitals with acute hand care. Telemedicine and telehealth are gaining interest as methods of providing care and may reduce the rate of transfers. This study assesses disparities in emergent hand care and the use of telemedicine and telehealth in Tennessee hospitals. A list of hospitals was obtained from the Tennessee Hospital Association; the hospitals were surveyed on their management of hand trauma and use of telemedicine and telehealth for hand surgery and other specialties. 2019 census data provided demographic information on Tennessee counties, then coded as metropolitan, micropolitan, or other based on population size. Chi-squared and independent t-tests were performed. Hospitals in metropolitan counties were more likely to accept hand trauma (P= .018) and to have a hand specialist on staff (P=.034), but not to provide 24/7 hand coverage (P= .249). Hospitals in counties with a greater white population are less likely to manage hand trauma (P= .002), have a specialist (P< .001), and to have 24/7 coverage (P= .012). Hospitals in counties with a median income greater than the Tennessee county average were more likely to have a specialist (P= .038), but not

to manage hand trauma (*P*= .291) or to have 24/7 coverage (*P*= .239). Insufficient telemedicine and telehealth programs (n=1) were present for analysis. A disparity in hand care exists predominately in non-metropolitan counties with increased white populations. Implementation of telemedicine and telehealth programs are an underutilized program which may reduce the disparity in hand care access in Tennessee hospitals and reduce the number of unnecessary hospital transfers.

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A PRECONCEPTION PATERNAL FISH OIL DIET INFLUENCES E-CADHERIN AND BETA-CATENIN ACTIVITY IN A TOXICANT-DRIVEN MODEL OF BRONCHOPULMONARY DYSPLASIA

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Our lab previously reported that offspring sired by adult male mice exposed to TCDD in utero are at risk of premature birth and diseases of prematurity such as New Bronchopulmonary Dysplasia (BPD). New BPD is a developmental lung disease that is characterized by reduced alveolarization and increased inflammation. Beta-catenin and E-cadherin expression and activity are tightly regulated during lung development, but recent reports suggest that dysregulation of these proteins may be involved in the development of New BPD. Therefore, these proteins may be good targets for disease treatment or prevention. Significantly, New BPD begins in utero; thus, it is important to identify therapeutic agents that are safe to use in pregnant women and/or neonates. Dietary interventions have the potential to be a safe and effective therapeutic option to influence the development and progression of neonatal diseases. Herein, we aimed to determine if altering the preconception diet of adult male mice exposed to TCDD in utero, could influence the development of New BPD in their offspring. Fish oil was tested as a therapeutic supplement since we previously reported that this intervention eliminated two risk factors associated with New BPD (preterm birth and low birth weight). Fish oil was also reported to influence the expression of Beta-catenin and E-cadherin in experimental and animal models. We found that a fish oil intervention reduced the risk of BPD, demonstrated by improved alveolarization, and altered Beta-catenin/E-cadherin expression and localization. However, additional signaling pathways should be explored to determine how a dietary fish oil intervention improved lung development in offspring sired by adult male mice exposed to TCDD in utero.

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EVALUATION OF NEURONAL INJURY USING CSF VILIP-1 AND IMAGING BIOMARKERS IN DOMINANTLY INHERITED ALZHEIMER DISEASE

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Alzheimer disease (AD) is a neurodegenerative disease with a long preclinical phase which has been characterized with several imaging and fluid (blood, CSF) biomarkers. With disease progression, changes such as Aβ burden occurs early even before any cognitive symptoms. In dominantly inherited AD (DIAD), a rare familial form of AD due to pathogenic mutations, Aβ burden detected with Pittsburgh compound B (PiB) positron emission tomography (PET) starts 20 years before symptom onset. Then, neuronal dysfunction and injury characterized by decrease of cerebral glucose metabolism detected with fluorodeoxyglucose (FDG) PET starts 10 years before symptoms. Increased levels in CSF visinin-like protein 1 (VILIP-1) has been observed in carriers of a DIAD mutation. This project aims to further describe this new marker of neurodegeneration, including its relationship with well-characterized neuroimaging biomarkers such as FDG hypometabolism, which is believed to reflect neuronal dysfunction and injury. CSF VILIP-1 changes early in disease progression before symptom onset and is associated with imaging biomarkers of neuronal injury in autosomal dominant Alzheimer disease. We evaluated data from participants enrolled in the Dominantly Inherited Alzheimer Network (DIAN) study. DIAN participants are carriers or non-carriers of genetic mutations leading to DIAD. Participants had PiB and FDG PET scans and CSF VILIP-1 measurement. For PET measures, regional standardized uptake value ratio (SUVR) were calculated using MRI-based PET processing. We used estimated year to symptom onset (EYO), Aβ status (positive vs. negative), and clinical status (asymptomatic vs. symptomatic) to define disease stage. Correlations between PET SUVR data and CSF-VILIP-1 levels were performed for cross-sectional and longitudinal analyses. It was found that CSF VILIP-1 levels increase at preclinical stages in mutation carriers who present amyloid burden, high CSF VILIP-1 levels are associated with decreased brain metabolism in the precuneus at preclinical stages, and future evaluations will include assessment of all cortical regions and longitudinal analyses.

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THE DEVELOPMENT OF PAID TO PUBLISH RESEARCH MODEL IN SURGERY

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Predatory journals also called fraudulent, deceptive, or pseudo-journals are publications that claim to be legitimate scholarly journals but misrepresent their publishing practices. The rise of predatory journals and the dubious methods they use to attract researchers to publish in them and serve on their editorial boards is disrupting the scholarly publishing landscape. It is increasingly difficult to distinguish between legitimate and predatory articles and journals. They threaten the credibility of academic publishing and can mislead the public about current scientific thought. Students and practitioners researching unfamiliar topics must also be vigilant. This article reviews the fraudulent behaviors exhibited by predatory journals, their rise in the past decade, their potential impacts, and how they can be identified and combated. Methods used involved data was collected from PubMed and PubMed Central using defining searches between the years 2013 to 2021 to investigate the rise in predatory journals over the decade. A Pearson correlation was made between the two searches of PubMed and PubMed Central to support our hypothesis and results.

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NUCLEOSOME STRUCTURE CHARACTERISTIC OF OPEN CHROMATIN ENHANCES HIV-1 DNA INTEGRATION

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HIV-1 DNA integration into actively transcribing genes is carried out by the preintegration complex (PIC) to establish life-long infection. Here, we report a key biochemical determinant for the preference of the PIC-associated viral DNA integration. We observed that the PIC-mediated DNA integration into chromatin is markedly higher compared to de-chromatinized genomic DNA. Remarkably, nucleosomes without chemical modifications in the histone tails were not preferred for integration compared to the analogous naked DNA. However, DNA integration was markedly enhanced with nucleosomes containing the trimethylated histone 3-lysine 36, an epigenetic modification linked to integration preference *in vivo*. We also observed that nucleosomes with flanking linker DNA promoted DNA integration in the presence of LEDGF/P75-a key host factor of HIV-1 integration. Finally, histone H1, known to condense the chromatin, drastically reduced PIC-associated DNA integration. Collectively, these results provide biochemical evidence that specific chromatin structure may direct HIV-1 DNA into gene dense regions.

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SINONASAL MALIGNANT MELANOMA IN A MINORITY PATIENT – A CASE REPORT

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A 57-year-old Black American male presented with left orbital proptosis and recurrent epistaxis. Endoscopic biopsy revealed the diagnosis of sinonasal malignant melanoma. CT scan revealed a destructive mass involving the left nasal cavity, left maxillary sinus, ethmoid sinus, frontal sinus and orbit. Ear, Nose, and Throat surgeons removed the mass then the patient underwent adjuvant radiotherapy. Due to common presenting symptoms and aggressive nature, this tumor has a poor prognosis by the time it is diagnosed. As the incidence of this melanoma subtype is recorded most frequently in White Americans, this report is the first to present a case highlighting distinct differences among the Black American population. This case report highlights the symptoms, course, and outcome of a rare melanoma diagnosis in a minority patient that is underrepresented in the literature.

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L-TYPE CALCIUM CHANNEL BLOCKADE WITH ISRADIPINE ATTENUATES PRO-DEPRESSIVE AND ANXIOGENIC-LIKE BEHAVIOR INDUCED BY CHRONIC UNPREDICTABLE STRESS

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Major depressive disorder (MDD) is a mentally and physically debilitating disorder with a lifetime prevalence in the United States of 20% (Kessler *et al.,* 2005). Exposure to significant and unpredictable daily stressors, including physical, emotional, and financial, can trigger and exacerbate symptoms of depression, including low mood, anxiety, and an overall reduction in motivated behavior. Vulnerable populations such as those with previous or current mental health challenges, military veterans, first responders, and individuals from marginalized groups are more susceptible to the detrimental effects of daily stressors. In rodent models of mood-related behaviors, including the sucrose preference test (SPT), the elevated plus-maze (EPM), and the forced swim test (FST), chronic unpredictable stress (CUS) has been shown to induce pro-depressive and anxiogenic-like behavioral responses. L-type calcium channels (LTCCs) are expressed in critical brain regions, such as the medial prefrontal cortex, the ventral tegmental area, and the striatum that mediate depressive and anxiogenic-like behavioral responses measured by the SPT, EPM, and FST. The objective of this experiment was to use rodent models of mood-related behaviors to test if LTCC blockade can attenuate the pro-depressive and anxiogenic effects of CUS as measured by the SPT, EPM, and the FST. The results of the experiment show that systemic administration of LTCC blocker, Isradipine, attenuates the decrease in sucrose preference and time spent in the open arms in CUS exposed rats compared to controls. This demonstrates the ability of LTCCs in regulating depressive and anxiogenic behavioral response to CUS.

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INHIBITION OF KDM5 ISOFORMS DECREASES PROLIFERATION AND ALTERS GROWTH SIGNALING PATHWAYS IN CASTRATION-RESISTANT PROSTATE CANCERS

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The lysine demethylase 5 (KDM5) family of lysine demethylases is comprised of four isoforms (KDM5A, KDM5B, KDM5C, and KDM5D) known for their ability to decrease methylation of histone H3 lysine 4 (H3K4). While KDM5D functions as a tumor suppressor, the other isoforms are amplified in metastatic prostate cancers. The role of KDM5 isoforms in prostate cancer growth and development is not fully understood. The goal of this study was to characterize the effects of KDM5 family inhibition in castration-

resistant prostate cancers. The LNCaP-MDV 3100, C4-2B, and PC-3 human prostate cancer cell lines were used as models of castration-resistant prostate cancer. KDM5 function within human prostate cancer cells was reduced via two strategies. The compound 2-4(4-methylphenyl)-1,2-benzisothiazol-3(2H)-one (PBIT) was used to inhibit the activity of all KDM5 isoforms, while short interfering RNA (siRNA) SMARTpools targeting KDM5A, KDM5B and KDM5C were used to lower KDM5 protein levels. Presto blue assays revealed PBIT inhibits proliferation of LNCaP MDV3100, C4-2B, and PC3 cells. In each cell line, significant decreases in proliferation were noted following treatment with PBIT concentrations greater than or equal to 5 µM. Furthermore, siRNA knockdown of KDM5C as well as combined knockdown of KDM5A, KDM5B and KDM5C reduced proliferation of PC3 cells. Data from Proteome Profiler Human XL Oncology Arrays demonstrated that PBIT alters expression of proteins involved in the epidermal growth factor receptor (EGFR) signaling pathways in C4-2B and PC3 cells. PBIT also altered the expression of androgen receptor (AR) target genes in C4-2B cells. Together these results suggest inhibition of KDM5 function reduces proliferation of castration-resistant prostate cancer cells by altering activation of the AR and EGFR signaling pathways.

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BIOID APPROACH REVEALED TBTRAP-1 AS A PROXIMAL PARTNER OF TBTIM17

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Trypanosoma brucei (*T. brucei*) is an early divergent parasitic protozoan, the infectious agent for a fatal disease known as African trypanosomiasis. *T. brucei* possesses a single mitochondrion that spreads throughout the cell body. Compared to other eukaryotes, *T. brucei* mitochondrial protein import machinery are significantly divergent. *T. brucei* mitochondrial protein translocation is carried out by the ATOM complex, the translocase of the mitochondrial outer membrane (MOM) and the TbTIM complex of the mitochondrial inner membrane (MIM). It has been shown by our laboratory and other investigators that TbTim17 serves as the major component of the TbTIM complex, and associates with several other trypanosome-specific Tim proteins. However, the actual molecular architecture of this complex is not fully understood. To identify the proximal partner proteins of TbTim17 in *T. brucei* we used Biotinylation Identification (BioID) approach. For this purpose, we expressed a modified biotin ligase-TbTim17 (BirA*-TbTim17) fusion protein in *T. brucei*, from a tetracycline inducible expression vector. BirA*-TbTim17 was properly targeted to mitochondria and assembled in the TbTIM complex. Induced and uninduced BirA*-TbTim17 cell line was grown in the presence of excess biotin and biotinylated proteins were purified by streptavidin agarose affinity pulldown and identified by mass spectrometry. Among the consistently enriched proteins in pulldown fractions, TbHsp84/TbTRAP-1, a mitochondrial Hsp90 homologue, was the highest enriched protein in three independent experiments. To validate our result, we expressed *in-situ* tagged TbTim17-6X-Myc and TbHsp84-3X-HA in the same cell. Co-immunoprecipitation analysis and confocal microscopy clearly showed that these two proteins interact with each other in mitochondria in *T. brucei*. TRAP-1 homologue in human is critical for mitochondrial function and a target for cancer chemotherapy. TbTRAP1 is also found essential in *T. brucei*. This is the first report that TbTRAP1 is associated with a mitochondrial protein translocator in *T. brucei*.

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A COMMUNITY ENGAGEMENT MODEL TO DRIVE ADVANCE DIRECTIVE DISCUSSION AND COMPLETION

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Advance Directives (AD) are used in healthcare to promote autonomous decision-making during a patient's end of life care. In order for an AD to be useful, the document must be entirely completed and made accessible to one's healthcare provider(s) physically or electronically. The difficulty in this process lies in ensuring total completion of the document by an adult with capacity. Several models have been pursued to increase and assess AD engagement, education, and completion. This project's aim was to utilize a community engagement approach to implement AD completion via employee onboarding and orientation processes. Working with Honoring Choices Tennessee's (HCT) The AD at Work in Tennessee (AD@WorkTN) initiative and using HCT's co-branded MYDirectives website, educational resources were provided and website engagement was measured. Over a 2 year period (2019-2021), workforce engagement, educational engagement, and completed AD uploads were measured. Educational resources included lunch and learn workshops, health fairs, videos, person-person interactions, a PBS documentary, and brochures which were made accessible to businesses, employees, and human resource leaders. This approach furthers the workforce population's understanding of an AD, access to AD educational resources, and persons to contact. The results of our work demonstrate an openness towards learning about ADs, but the completion of end of life care planning may require more time.

This project was supported in part by the Geriatric Workforce Enhancement Program, HRSA Grant: 1-UIQ-HP 033085-01-00. This project was found to be IRB exempt because it is a quality improvement initiative.

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DAYCARE PROVIDERS' OBSERVATION OF AUTISM IN CHILDREN REGARDING NEED FOR REFERRAL

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Autism Spectrum disorder (ASD) is a condition in which early identification can affect the overall outlook of the treatment process. Signs such as difficulty with communication, repetitive behavior and abnormal sensory problems can be the first indicators that a child has ASD (Sicherman et al., 2020). Mandell et al. (2002) found that black children were more likely to receive a diagnosis of ASD and subsequent treatment at a significantly later age than white peers. This delay in identification whether by primary care providers,

family members or caregivers could lead to poorer outcomes for such children that would otherwise be avoidable (Mandell et al., 2002; Donohue et al., 2017). The objective of our research was to determine the most common attributes seen in black children at risk of ASD to develop a survey tool for daycare workers regarding referral of said children. The Achenbach child behavior checklist ages 1½ -5 of 10 children was reviewed to determine common characteristics out of 99 possible items observed by caretakers such as daycare providers or pre-kindergarten teachers. We found that the most common characteristic in children at risk of having ASD was having a speech problem (6 out of 10) followed by qualities such as an inability to maintain focus or stillness, being inpatient, uncooperative, and stubborn (4 out of 10 each). The information found in this review was then used to develop the 9 main questions and 3 groups of behavioral examples that will be used in the survey tool we would create. The formulated questions will assess daycare provider's experiences with children displaying such characteristics, the likelihood that they would refer a child they believe at risk of ASD and their reasons for why and why not. The information gained will help develop a resource network for referrals in the future.

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AUTOMATIC DETECTION AND MEASUREMENT OF SCOLIOSIS IN ADOLESCENT SPINE RADIOGRAPHS USING ARTIFICIAL INTELLIGENCE

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It has been estimated by the Scoliosis Reduction center that 2-3% of the US population is affected by Scoliosis, primarily the pediatric population. Deep learning algorithms can potentially reduce the time necessary for measurements and standardize measurement to aid radiologists. Previous models have been used to classify x-ray images for medical analysis. Therefore, our objective of our research was to propose to build and validate a deep learning algorithm for detection and measurement of scoliosis in pediatric spine x-rays. We have developed an AI model to automatically detect thoracic and lumbar vertebrae and measure the spinal curvature via a cobb angle to determine presence of scoliosis. We found that the AI model was discrepant in 83/343 cases in which AI was correct 66.2%. These results are consistent with the hypothesis that the deep learning model showed some level of agreement for detection and classification of pediatric scoliosis, with lower agreement for radiographic images with hardware. This is very promising as it demonstrates the feasibility of deep learning models in identifying scoliosis in the pediatric population. Our study is limited because we used high school students.

This project was supported, in part, by Stanford Radiology Department via an IRB proposal at a tertiary referral institution.

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UTILIZATION OF DEEP LEARNING NETWORKS TO ENHANCE ULTRA-LOW DOSE TAU PET/MR IMAGES

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Pathological features of AD include accumulation hyperphosphorylated tau into intracellular neurofibrillary tangles and can be identified with positron emission tomography (PET) imaging. Reducing dosing requirements allows for safer scans, potentially increasing screenings and follow-up adherence as well as providing data for pathogenesis and pharmacotherapy research. Convolutional Neural Networks that incorporate MRI and PET information to produce standard-quality PET images from low dose PET acquisitions have been implemented, reducing radiotracer dose by at least 100-fold in Amyloid studies. This study investigated whether similar techniques in deep learning can be used to enhance ultra-low dose tau PET/MR images to produce diagnostic quality images. 44 total participants were recruited for this study. T1-weighted and T2-FLAIR MRI data and tau PET data were simultaneously acquired using 221±61 MBq of the tau radiotracer ^{18}F-PI-2620. The raw list-mode PET data were reconstructed for the full-dose image and were also randomly under sampled by a factor of 20 to produce a simulated ultra-low-dose PET image. An encoder-decoder CNN with the structure ("U-Net") was trained to produce enhanced ultra-low dose images. Quantitative analysis of images showed enhanced images had higher Peak Signal to Noise Ratio, higher Structural Similarity and lower Root Mean Square Error compared to ultra-low dose images, however, these differences were not statistically significant. Three readers also rated all three image types for image quality as well as tau uptake in five regions of interest. Enhanced images are expected to have high accuracy, sensitivity, and specificity for Tau status. It is also anticipated that standard dose images and enhanced images will have higher inter-reader agreement compared to low dose images. Regarding quality metrics, enhanced images are expected to be non-inferior to their standard-dose counterparts. This research increases the potential utility of Tau PET scanning at lower radiotracer doses.

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GUIDELINE CONCORDANT USE OF CHILDREN WITH PNEUMONIA

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Pneumonia accounts for twenty percent of the world's morbidity and mortality for children under five years old. The most common reason for hospitalizations for children in the United States is pneumonia. Children with pneumonia are more likely to be prescribed broad-spectrum or macrolide therapy in the emergency department. However, prior evidence associates narrow spectrum and macrolide therapy with risk of worsened severity and antibiotic resistance. A better understanding of risk factors will inform decision-making for Physicians in the emergency department. The Clinical Practice Guidelines for the management of community acquired pneumonia in infants and children over 3 months of age was released in 2011 to address risk factors with care. However, there has been little research that has observed emergency department performance in concordance to the guidelines provided. Bivariate logistic analysis determined

the proportion of antibiotic guideline concordance in children with community-acquired pneumonia in 2 United States hospitals over a 24-month period. Results showed that 56% of all children who presented to the emergency department with pneumonia are guideline-concordant to antibiotic recommendations for the treatment of children with community-acquired pneumonia. Of the population, children were white males at a median age of 7 years old. The next goal is to calculate the association of the risk factors with antibiotic guideline concordance. The risk factors provided can be used as predictors for performance on antibiotic guidelines adherence. The risk factors will be used as a screening tool in order to observe antibiotic treatment in children with community-acquired pneumonia. Using risk factors as a screening tool will serve to decrease overall hospitalizations, probability of complications, length of stay, and overall cost of hospitalizations from community-acquired pneumonia in children.

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ROLE OF SLC38A2 ON SEX – DEPENDENT MEMORY IMPAIRMENT IN MICE LACKING MITOCHONDRIAL CALCIUM PROTEIN FUS1

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Alzheimers Disease is a disorder that affects one's memory and cognitive function. A major player in that memory function are glutaminergic neurons that are present in the brain. SLC38A2 is a glutamine transporter that is expressed on glutaminergic neurons to bring glutamine into the cell and partake in The Citric Acid Cycle. Fus1/Tusc2 is expressed on the mitochondria inner membrane and facilitates in calcium transportation, impairment can lead to enzyme inhibition within the Cycle causing reactive oxygen stress in these neurons and in tandem affecting memory. Our study seeks to understand more about the relationship of SLC38A2 and Fus1 and if dysregulated can lead to memory impairment. Protein expression was determined using mice brain samples using a spectrophotometer readings and Western Blot techniques, along with intermediate metabolites of The Citric Acid Cycle. We found that there is a significant increase of SLC38A2 expression in male mice with Fus1 then without Fus1, also that short term memory is affected in knockout Fus1 male mice over wild type male mice. The results are consistent the hypothesis that there is a relationship between Fus1 and SLC38A2 and memory impairment. Future studies seek to unpack the sex – involvement in this cycle and its development into Alzheimers Disease.

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ARYL HYDROCARBON RECEPTOR OVEREXPRESSION: A STAGE SPECIFIC MARKER OF INVASIVE BREAST CARCINOMA

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Increasing experimental data has provided substantial evidence for the role of aryl hydrocarbon receptor (AhR) in mammary tumorigenesis. AhR is a transcription factor known to bind environmental contaminants such as polycyclic aromatic hydrocarbons (PAH), polychlorinated biphenyls (PCB), and dioxins (TCDDs) and mediate their carcinogenic effects. AhR is involved in a wide arrange of physiological and cellular processes that, if disrupted, can contribute to prooncogenic states. Recent studies also suggest that AhR plays a role in the tumors ability to evade the immune system. High AhR expression levels are found in advanced malignancy human breast carcinoma cell lines, while lower levels are expressed in cells derived from early tumorigenic stages or normal human mammary epithelial cells. Therefore, this study investigated AhR as a potential stage specific marker of breast carcinoma. The study used 192 specimens of human invasive breast cancer with three different clinically defined stages: node negative, node-positive and metastatic carcinoma. AhR immunohistochemical staining was performed and then scored by three evaluators including two pathologists who were blinded to the study. Western immunoblotting was used to investigate the correlation of AhR expression in human breast carcinoma cell lines with the degree of tumor malignancy at the protein level. Statistical analysis revealed that AhR expression is significantly higher in node-positive and metastatic carcinoma and advanced clinical stages. Our findings support that AhR protein is an effective regulator and prognostic clinical marker for therapeutic intervention of metastatic breast cancer. More importantly, AhR overexpression may identify a subset of patients who could benefit from targeted therapy at this receptor. Our study warrants further investigation by the research community and may ultimately yield a novel treatment for breast cancer. One limitation to this study is the need for a larger number of women under 50 years old for the invasive breast carcinoma clinical sample.

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WHAT CAN WE LEARN FROM PATIENTS? PATIENT PREFERENCES AND RECOMMENDATIONS FOR CLINICIANS TO DISRUPT RACISM AND PROMOTE HEALTH EQUITY

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Far too often in modern medicine, Black patients are the recipients of differential treatment which leads to adverse effects on their healthcare (Saha et al. 2008). This mistreatment is due to the unconscious bias that

clinicians exhibit when interacting with Black patients (James et al. 2017). Results in one study show that while clinicians often use similar communication behaviors when interacting with terminally ill Black and White patients, they exhibit significantly less positive, trust-reaffirming nonverbal cues with Black patients (Elliot et al. 2016). This is one reason why Black communities have developed mistrust towards institutionalized healthcare (Gamble et al. 1997). The Covid-19 pandemic has further reinforced the consequences of inequality in healthcare between Black patients and their white counterparts (Metzl et al. 2020). At Stanford University, the Presence for Racial Justice (PRJ) has evolved from a framework (Presence 5) centered on teaching clinicians how to better communicate with patients in a manner that builds trust and results in improved patient satisfaction.

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LEAD (Pb) REPRESSES ASTROCYTIC GLUTAMATE TRANSPORTER EAAT2 TRANSCRIPTION

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Chronic exposure to lead (Pb) causes neurotoxicity, including cognitive and behavioral deficits and brain damage. The mechanisms underlying Pb neurotoxicity are not well understood, but include the cellular accumulation of Pb in astrocytes and consequent apoptosis, neurotransmitter receptor dysregulation, and excitotoxicity. In particular, studies have demonstrated that Pb decreases expression and function of the astrocytic glutamate transporter GLT-1, rodent form of human excitatory amino acid transporter 2 (EAAT2) in rat models. But the molecular mechanisms by which Pb decreases GLT-1 (EAAT2) have not been investigated. Moreover, since Pb is an environmental neurotoxin, Pb neurotoxicity may also be potentiated by exposure to other environmental neurotoxins including manganese (Mn), a heavy metal which is known to impair EAAT2 transcription. In the present study, we investigated if Pb causes cytotoxicity and impairs EAAT2 transcriptional expression, which is exacerbated by Mn in H4 human astrocytes. Our results demonstrate that Pb caused cytotoxicity as it decreased cell viability. Pb also reduced EAAT2 promoter activities and mRNA/protein levels and these Pb effects were exacerbated by Mn in H4 astrocytes, which can lead to excitotoxic neuronal injury. Taken together, the results from the current studies indicate that exposure to two common environmental neurotoxins, Pb and Mn, which is likely occurring in the human environment, could have a deleterious impact on human brain health.

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ASSOCIATION OF OBESITY AND BREAST CANCER SUBTYPES AMONG BLACK WOMEN

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Problem Statement: Is there a positive correlation between lack of exercise and energy-related risk factors and different subtypes of breast cancer in Black women? Background: Our hypothesis is that Black women with the triple negative breast cancer (TNBC) subtype are less likely than women with other subtypes to

have activity-related risk factors. TNBC means tumor cells do not have receptors for estrogen, progesterone, or human epidermal growth factor receptor 2. Approach: About 2000 Black women 25-75 years who were diagnosed between 2009-2019 with primary invasive breast cancer in Tennessee, South Carolina, and Georgia. Eligible patients provided information on physical activity, diet and other related risk factors on a telephone interview and gave consent for review of their tumor tissue. Activity-related risk factors were described as: no physical activity, heavy meat intake, upper obese class II/III, accompanied by high weight gain since age 18. Breast cancer subtype information was obtained from pathology reports and tumor tissue samples were requested after consent was provided. Discussion: We are still waiting on tissue to be examined, questionnaires to be completed, and saliva samples to be submitted. While the pathology reports have been completed recently, without the rest of the data being analyzed and logged new results are not final yet. However, the previous data from a smaller sample size showed women with TNBC have a higher meat intake compared to women with estrogen+ disease and many gained significant weight since 18. Estrogen- women usually had a higher meat intake, were obese, and had more weight gain than the estrogen+ group. Conclusions: So far subtyping has been performed and recorded on collected tissue to confirmed by the pathology reports. The large number of Black women participating will allow us to better understand the correlations between activity/energy-related risk factors and breast cancer subtypes in this population.

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IMPROVING SUBSTANCE USE DISORDER EDUCATION IN STAFF AT A MULTI-SITE FEDERALLY QUALIFIED HEALTH CENTER

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Substance use disorder ranges in severity from mild to severe reflecting how use of a substance such as caffeine, alcohol, opioids, or illicit drugs has impacted an individual's life through four main domains: impaired control over use of substance, social problems, risky use, and physical dependence.[1] Substance use disorders impact over 20 million people 12 years and older annually in the US; lifetime prevalence is ~10%.[2] Current guidelines indicate benefit to screening for substance use with brief interventions and referral to treatment (SBIRT), to aide in recognizing disease and facilitating treatment initiation.[3] Screening and intervention for substance use disorder is widely supported, but lack of provider knowledge and training are barriers to care.[4] When primary care providers are educated to treat substance use disorder, outcomes are significantly improved; however, substance use disorder is not well-integrated into medical education.[5] Expanding medical education to include substance use disorder improves skills, knowledge, and attitudes of medical learners in a meaningful way.[6] Biases and stigmas are prevalent but correctable barriers that can improve patient care when addressed.[7] Neighborhood Health is a multi-site, federally qualified health center that provides primary care services to a large population in the middle Tennessee area. Their substance use treatment program internally has policies regarding medical provider and staff education; but training is not universal for all employees. Monthly all-staff meetings will be utilized to implement substance use disorder education to improve patient care and staff medical knowledge. Pre and post surveys will be utilized to assess substance use disorder knowledge and comfort before and after education sessions. We hypothesize knowledge of and comfort with substance use disorder will be improved at Neighborhood Health through education sessions. We intend to advocate for improved medical education on substance use disorder to improve patient care in a prevalent disease.

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THE EFFECT OF NALOXONE STANDING ORDERS ON FATAL SYNTHETIC OPIOID OVERDOSE FATALITY RATES

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Significant increases in fatal synthetic opioid overdoses over the past eight years have left states scrambling for effective means to curtail these deaths. Many states have implemented policies and increased service capacity to address this rise. To better understand the effectiveness of these policy level interventions we aimed to estimate the impact of the presence of naloxone access laws (NAL) such as standing order's and Good Samaritan Laws as well as capacity for medication for opioid use disorder (MOUD) on the synthetic opioid fatalities at the state level. A multivariable longitudinal mixed effect model was used to determine the relationship between the NALs and MOUD capacity and synthetic opioid overdose death rates, while controlling for several other variables. Data for the study was collected from the National Vital Statistics System using multiple cause-of-death mortality files linked to drug overdose deaths. The presence of a naloxone standing order had the single strongest negative relationship to fentanyl overdose rates, with states with the standing order reporting an average 2.93 reduction in deaths per 100,000. Naloxone standing orders are strongly related to fatal synthetic opioid overdose reduction. The combination of naloxone and MOUD treatment capacity also have strong potential to reduce fatality. The use of these two medications should be a central part of any state strategy to reduce overdose.

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THE RELATIONSHIP BETWEEN HEALTHY EATING INDICES AND SCHOOL ABSENCES

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COVID-19 has contributed to increased child poverty and food insecurity in the United States, and while government programs help alleviate food insecurity, they do not always ensure nutritional security. Prior research has demonstrated a correlation between food insecurity and increased school absences. However, the role of child nutritional quality is less well understood. The current study enhanced this understanding by merging two data sources to create a novel dataset and analyzing the association between child nutritional quality and school absences. A subset of the data from a 3-year randomized control trial to prevent obesity in 3-5-year-old children was linked to data from a public school system. Data from 354 children were analyzed using negative binomial regression models to examine the relationship between school absences and nutritional quality as measured by the 2010 Healthy Eating Index (HEI) and each of its 12 subcomponents. The primary model found a significant relationship between healthier total HEI scores and fewer school absences (IRR=0.989; 95% CI=[0.981, 0.996]; p=0.003). Subcomponent analyses found that absences were significantly related to intake of whole fruits (IRR=0.934; 95% CI=[0.878, 0.993]; p=0.03) and marginally significantly related to whole grains (IRR=0.975; 95% CI=[0.949, 1.002]; p=0.07), sodium (IRR=0.968; 95% CI=[0.934, 1.002]; p=0.07), and refined grains (IRR=0.975; 95% CI=[0.949,

1.003]; p=0.08).nThe relationship between HEI and school absences among young children in public school suggests that it could be beneficial to direct funding towards improving nutrition in school settings in addition to meeting USDA requirements.

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ROLE OF RACE AND INSURANCE IN ANTERIOR CRUCIATE LIGAMENT BIODEX AND FUNCTIONAL TESTING

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ACL injury and reconstruction have become increasingly common in the pediatric and adolescent populations. This patient population is known to have a high rate if repeat injury compared to adults with some studies showing as high as 25% repeat injury and thus careful attention should be paid not only to surgical technique, but the rehabilitation after surgery and criteria for return to sport. The objective of our research was to discussion the role of race and insurance in pre and post opt isokinetic as well as time to MRI and surgery. After IRC approval we used our existing Biodex database at Children's Mercy Hospital to collect race and insurance type. We modeled the deficiency at post-surgery visits as a function of gender, race, age at baseline, insurance status, inv side, months since surgery, Biodex speed, and surgical procedure, controlling for deficiency at baseline. Statical results are pending. We hope the results will prove our hypothesis that patients with a Primary ACL tear with public insurance will have an increased deficit between pre-operative, post-operative Biodex scan and have an increased time between surgery and MRI.

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METABOLIC DEPENDENCIES OF ANNEXIN A6 LOW AND LAPATINIB-RESISTANT TNBC CELLS

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The ability of cancer cells to alter their metabolism is one of the major mechanisms underlying therapeutic resistance in multiple tumor types, including triple-negative breast cancer (TNBC). TNBCs are among the most aggressive and deadly breast cancer subtypes, with high rates of tumor recurrence and poor overall survival. Significant effort has thus far been devoted to epidermal growth factor receptor (EGFR) targeted

therapies as 70% of TNBC tumors overexpress EGFR. However, clinical trials utilizing anti-EGFR therapies have been largely unsuccessful in TNBC due to the lack of understanding of TKI-acquired resistance. We have shown that the expression status of annexin-A6 (AnxA6), a calcium-dependent membrane binding tumor suppressor, stabilizes activated EGFR on the cell surface. We have also shown that chronic treatment of AnxA6-low TNBC cells with Lapatinib induces AnxA6 expression and accumulation of cholesterol in late endosomes suggesting a novel mechanism for resistance of TNBC to EGFR-TKIs. However, whether the EGFR-TKI induced upregulation of AnxA6 is associated with metabolic reprogramming in TNBC cells remains unclear. Using the Seahorse XF Analyzer, we assessed the live-cell oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) of 10 TNBC cell lines. We demonstrate that AnxA6-expression in TNBC cells sustains an energetic phenotype while AnxA6-depletion renders a quiescent phenotype. Induction of AnxA6 expression following chronic treatment of AnxA6-low TNBC cells with Lapatinib (LapR) reverted these otherwise quiescent metabolic phenotypes to the energetic phenotype associated with higher OCR/ECAR ratios and cellular ATP production capacity. However, down regulation of AnxA6 in AnxA6 high TNBC cells attenuated the mitochondrial and glycolytic function with reduced OCR/ECAR ratios and decreased cellular ATP production capacity. NMR-based metabolomics revealed that AnxA6 depleted and/or lapatinib-resistant TNBC cells have a greater dependency on gluconeogenic amino acids including alanine, cysteine, glycine, and proline. These data suggest that altered expression of AnxA6 is accompanied by significant bioenergetic adaptations and provide novel insights into the failure of EGFR-targeted therapies as therapeutic options for TNBC.

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FACILITATORS AND BARRIERS TO COVID-19 RESEARCH PARTICIPATION IN THE BLACK COMMUNITY OF THE SOUTHERN UNITED STATES

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Introduction: The SARS-CoV-2 pandemic has illuminated underlying social and economic inequalities in access and use of healthcare in the United States. Low-income persons and racial/ethnic minorities disproportionately bear the brunt of morbidities and mortalities but are not well represented in clinical trials or research participation. Efforts to understand the opinions and potential barriers limiting participation of these groups will improve the relevance and effectiveness of current and future pandemic interventions and treatments. **Methods:** A phenomenological qualitative study design with a total of 61 in-depth interviews were conducted between May – Sept 2020 and led by trained researchers and medical students. Participants fell into one of the following four categories: essential workers, young adults, parents, and immunocompromised individuals. **Results:** All groups expressed a positive opinion regarding the importance of research, however, there was consensus across all groups that historical injustices against Black communities in the United States by scientific researchers play a large role in perceptions of research and willingness to participate in SARS-CoV-2 research. **Conclusions:**

This study indicates several barriers contribute to the low interest in research participation within Black communities. Prominent factors are distrust in academic and medical institutions, limited health literacy, little to no access of information about clinical trial participation, as well as incomplete understanding of the various ways to participate in research. Providing accessible and reliable information through engagement with trusted clinicians and researchers will play a pivotal role in increasing participation in research in Black communities, particularly in the southern United States.

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