Abstracts of the 2022 American Physician Scientist Association (APSA) Northeast Regional Conference (NERC)

Oral Presentations

01. TRANSCRIPTOMIC PROFILING IDENTIFIES DRIVERS OF INVASIVE LOBULAR CARCINOMA METASTASIS IN MOUSE XENOGRAFT MODEL

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Invasive Lobular Carcinoma (ILC) is the second most frequently diagnosed subtype of breast cancer, after Invasive Ductal Carcinoma (IDC). Although patients with ILC harbor favorable prognostic and predictive factors like hormone receptor expression and low proliferation, they frequently present with long-term recurrences and metastases to unique anatomical sites. The objective of this study is to utilize a novel human ILC cell line xenograft mouse model to elucidate the biologic underpinnings mediating the distinct organotropism of ILC metastasis. Human ILC cell line MDA-MB-MM134 was injected into the mammary fat pad of estrogen supplemented mice to generate ER+ tumors and spontaneous metastases that closely mirrored the clinical dissemination patterns of ILC. We conducted transcriptomic analysis of the cell line, the primary tumor xenograft and metastatic tumors to the brain and ovary. All samples were mapped to the ENSEMBL human reference genome GRCh38 and ENSEMBL mouse reference genome GRCm39. XenofilteR was used to computationally separate human from mouse sequence reads in the xenograft tumor sequence data. We subsequently utilized featureCounts to generate a count matrix, DESeq2 for differential gene expression analysis, and the Gene Ontology gene set for Gene Set Enrichment Analysis. We demonstrated upregulation of pathways related to granulocyte chemotaxis, pro-inflammatory cytokines, and production of extracellular matrix components in the primary tumor versus host cells. Furthermore, action potential regulatory and synapse assembly pathways were upregulated in brain metastatic tissue compared to the primary tumor, whereas extracellular matrix signaling pathways were downregulated. Pathways related to angiogenesis, cell migration, and organization of cellular components were all upregulated in ovarian metastatic tissue relative to the primary tumor. Collectively, this study not only identifies pathways shared with dissemination of IDC but also distinct pathways mediating the dissemination of ILC metastasis.

02. ASSOCIATION BETWEEN EXPOSOME AND SUBSEQUENT MULTIPLE SCLEROSIS OUTCOMES

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BACKGROUND: Environmental factors play an important role in multiple sclerosis (MS) onset and progression, which can be comprehensively assessed through the exposome approach. **METHODS:** We conducted a retrospective, temporal, observational multi-center study incorporating environmental exposures from 2017-2018 and neurological outcomes from 2019-2020. We integrated individual-level demographic and clinical data with area-level climate, air pollution and socioeconomic status (SES) using a published method. Neurological disability was quantified using three interrelated patient-reported outcomes (PROs): Patient Determined Disease Steps (PDDS), Multiple Sclerosis Rating Scale Revised (MSRS-R), and Patient Reported Outcomes Measurement Information System (PROMIS)-Physical Function. We analyzed PROs as continuous outcomes and also dichotomized them based on disease burden (mild, moderate-severe disability). Covariates included demographic, clinical and geo-spatio-temporal features. **RESULTS:** In 2,634 pwMS, aggregate exposures (climate factors, air pollution and SES) were associated with subsequent continuous PDDS (N=2106, R2[95% CI]=0.239 [0.187, 0.255], p<0.001), MSRS-R (N=2279, R2 [95% CI]=0.171 [0.125,0.180], p<0.001) and PROMIS (N=1377, R2 [95% CI]=0.253 [0.193,0.262], p<0.001) scores, after adjusting for covariates. Models containing aggregate exposures performed better than individual exposures in both continuous(aggregate exposures AIC PDDS=9112.52, MSRS-R=14469.61, PROMIS=10640.87; best performing candidate exposure [temperature] AIC PDDS=9556.80, MSRS-R=14740.53, PROMIS=10940.80) and dichotomous regressions (aggregate exposures AUC [95% CI] PDDS=78.8% [76.7%-80.8%], MSRS-R=72.8% [69.5%-6.2%], PROMIS=79.4% [76.6%-82.1%]; best performing candidate exposure [temperature] AUC [95% CI] PDDS=57.5% [54.9%-60.1%], MSRS-R=59.5% [55.6%-3.4%], PROMIS=57.1% [53.3%-60.8%]). **CONCLUSIONS:** Climate factors, air pollution and SES collectively influence subsequent neurological disability over a short time span.

03. **FUNCTIONAL CONNECTIVITY MEASUREMENTS IN APP/PS-1 MICE REVEALED HYPO-CONNECTIVITY WITH TRANSIENT HYPER-CONNECTIVITY**

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Award: Exceptional Graduate Oral Presentation

BACKGROUND: Changes in brain functional connectivity (FC) have gained traction as an early event in Alzheimer's disease (AD), especially reports of increased connectivity in brain networks. In the present study, we characterized changes in network connectivity in AD mice from 3- 12 months of age. **METHOD:** Amyloid precursor protein/presenlin-1 (APP/PS-1) mice (n=8) were injected with AAV-Syn GCaMP6f into cortical regions. Mice were head-fixed and imaged monthly from 3-12 months of age. Simultaneous neuronal and hemodynamic signals were measured using wide-field optical imaging. Plaque characterization was performed via methoxy-04 labelled images. Within (short-range) and between (long-range) cluster resting-state connectivity was calculated via Pearson correlation derived from the average timeseries of functionally clustered brain regions using a K-means algorithm. Differences were determined via Wilcoxon Rank Rum. **RESULTS:** The average short-range neuronal connectivity steadily declined between 3- to 12-mo, with a transient increase in connectivity occurring around 9-mo. Average short-range hemodynamic connectivity decreased between 3- to 12-mo, with no change seen around 9-mo. Average changes in neuronal long-range connectivity patterns occurred until 6-mo and then stabilized. **CONCLUSION:** Changes in network connectivity mirror clinical findings in AD patients. Future work is needed to determine the neurophysiological underpinnings that drive changes in network connectivity.

04. **IS LACTOBACILLUS PHAGE INVOLVED IN THE PATHOGENESIS OF BACTERIAL VAGINOSIS?**

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Bacterial Vaginosis (BV) is the most common cause of vaginal discharge. Although its etiology remains controversial, a Lactobacillus depletion model is one hypothesis. We used shotgun metagenomic sequencing to investigate longitudinal changes in the vaginal microbiota prior to incident BV (iBV), including the presence of Lactobacillus phage, in women with normal baseline microbiota. African American women ages 18-45 were followed for 90 days using daily self-collected vaginal specimens to detect iBV. DNA was isolated from select specimens and sequenced on an Illumina HiSeq. Sequencing reads were processed using Kraken2 to determine taxonomic composition. Following assembly with the Megahit, contigs were analyzed using VIBRANT and PropagAtE to investigate overall phage origin and activity. Six specimens from four women with iBV were sequenced. Normalized estimated reads originating from the Lactobacillus genus declined while BV-associated bacteria subsequently increased prior to iBV. Lactobacillus phages were detected in 2/4 (50%) women, corresponding with a reduction in reads from L. crispatus, L. gasseri, and L. jensenii. These contigs were found to predominately be of lytic phage origin. A possible interplay between Lactobacillus phage and Lactobacillus spp. may occur prior to iBV in some women. The role of Lactobacillus phage in BV pathogenesis should be further investigated.

05. **IDENTIFICATION OF ATF4 AS KEY UPSTREAM REGULATOR OF ACUTE MYELOID LEUKEMIA CELL METABOLISM**

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Compared to other cancers, acute myeloid leukemia (AML) has one of the lowest overall 5-year survival rates, at approximately 25%. While the immediate need for more effective AML therapies is clear, developing such therapies relies on first identifying targetable pathways that support AML pathogenesis. The expression of ATF4 is significantly elevated in numerous genetic subtypes of AML compared to healthy hematopoietic stem and progenitor cells and its inhibition impedes AML in vitro and in vivo, which suggests that ATF4 is broadly deregulated in AML and interventions targeting this pathway may be broadly applicable. A gene expression enrichment analysis of genes that were specifically downregulated by Atf4 inhibition in mouse leukemic cells revealed genes associated with amino acid metabolism, specifically serine metabolism, were affected. Furthermore, chromatin immunoprecipitation assays showed that Atf4 localized to the promoters of many of these genes, suggesting that they are direct transcriptional targets. Lastly, a pathway enrichment analysis of total steady-state polar metabolites indicated that Atf4 inhibition reduces de novo serine synthesis, disrupts de novo synthesis of nucleotides, and affected several additional amino acid pathways. Together, these findings reveal the dependence of AML on ATF4-driven metabolic reprogramming, and the ATF4 pathway could be a viable therapeutic target.

06. **ENDOREPELLIN INDUCED AUTOPHAGY AS A MECHANISM OF AGE-RELATED MUSCULOSKELETAL ATROPHY**

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The extracellular matrix (ECM) is composed of proteoglycans and is the non-cellular, structural material supporting cells. The proteoglycan perlecan is critical in processes such as angiogenesis, membrane stability, and development. When perlecan's C terminal fragment, endorepellin, is cleaved, it acts via VEGFR2 on endothelial cells and has opposite effects from perlecan, inducing autophagy and inhibiting angiogenesis. Sarcopenia, the process of age-related skeletal muscle atrophy has been linked to capillary dysfunction and dysregulated endothelial cell apoptosis. Here, we review endorepellin's implication in age-related musculoskeletal changes as well as its potential as a therapeutic for Sarcopenia. We found that increased levels of endorepellin were associated with animal model Sarcopenia, increased endothelial cell apoptosis, and fibrosis of the ECM. Intriguingly, these endothelial cells accounted for 75% of all apoptotic cells in aged animal muscle. In addition to inhibiting VEGFR2 receptors crucial for angiogenesis, endorepellin was found to trigger autophagy by activating Peg3 in endothelial cells. Thus, endorepellin may negatively impact skeletal muscle capillary health in aging individuals through both autophagic and anti-angiogenic mechanisms, contributing to symptoms such as atrophy, weakness, and stiffness of skeletal muscles. Thus, inhibiting endorepellin signaling through the VEGFR2 receptor and Peg3 may deter age-related musculoskeletal atrophy.

07. **HIERARCHICAL CLUSTERING BY PATIENT-REPORTED PAIN DISTRIBUTION UTILITY IN DIAGNOSIS AND TREATMENT**

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Pain localization and radiation are commonly used in pain diagnosis. The bodily distribution of pain can be measured in the clinic with pain drawings prompting the patient to mark areas of their pain on a "body-map." A previous study found that hierarchical clustering of patients by body-map data alone leads to nine distinct clusters that differ significantly from each other in pain intensity, quality, impact, and treatment outcomes. However, the relationship of body-map cluster to pain diagnosis remains unknown. In this study, chronic pain diagnosis data of 21,423 patients was analyzed to test the hypothesis that cluster membership predicts diagnosis. Data were extracted from a research registry which links patient-reported outcome data with electronic medical record data related to appointments at the University of Pittsburgh Pain Medicine Clinics from 3/17/2016–6/25/2019. Cluster assignment was associated with different diagnoses. Looking specifically at a diagnosis of fibromyalgia, the "Widespread-Heavy" cluster was more likely to receive a diagnosis of fibromyalgia than other clusters, with 47% of fibromyalgia diagnoses belonging to this cluster. Interestingly, only 27% of all patients in the Widespread-Heavy cluster received a diagnosis of fibromyalgia. This study highlights the utility of the pain body-map and suggests that fibromyalgia may be underdiagnosed.

08. **SINGLE-CELL TRANSCRIPTOME ANALYSIS REVEALS DYNAMIC CELL POPULATIONS AND DIFFERENTIAL GENE EXPRESSION PATTERNS IN A MOUSE CEREBRAL ANEURYSM MODEL**

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Cerebral aneurysms (CA) form most commonly in the circle of Willis (CoW). The heterogeneity and relative contributions of the different cells in healthy versus aneurysmal vessels have not been well-characterized. Here, we present the first comprehensive analysis of the lineage heterogeneity, altered transcriptomic profiles and functional states of vascular cells from healthy and aneurysmal mouse CoW using single-cell RNA sequencing (scRNAseq). CA was induced in mice using an elastase model and scRNAseq was later performed on CoW samples. Unbiased clustering analysis of the transcriptional profiles identified 19 clusters representing 10 cell lineages. Seurat clustering analysis identified 5 vascular smooth muscle cell (VSMC) subpopulations and 6 monocyte/macrophage subpopulations. Pathways involving ATP generation were found to be downregulated in 2 major VSMC clusters in CA. CA also induced significant expansion of the total macrophage population which further increased with rupture. Both inflammatory and resolution-phase macrophages were identified, and neutrophils massively spiked with CA rupture. The neutrophil-to-lymphocyte ratio (NLR) in CA mirrored that observed in humans. Our data identify CA disease-relevant transcriptional signatures of vascular cells in the CoW. Furthermore, we characterize the heterogeneity and cellular responses of VSMCs and monocytes/macrophages during CA progression, providing insight into their role in CA pathogenesis.

09. **PRRX1 REGULATES ACINAR CELL PLASTICITY IN PANCREATIC ACINAR-TO-DUCTAL METAPLASIA**

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Award: Exceptional Graduate Oral Presentation

Pancreatic acinar cells can de-differentiate after acute injury to a progenitor-like cell type with ductal characteristics in a process termed acinar-to-ductal metaplasia (ADM). In the absence of oncogenic mutations, ADM lesions can resolve and reform the acinar compartment. However, in the presence of oncogenic Kras mutations, the ADM lesions can continue to de-differentiate to a pre-invasive pancreatic intraepithelial neoplasia (PanIN), which has shown to be a precursor of pancreatic ductal adenocarcinoma (PDAC). Our comprehensive and unbiased approach previously identified the Paired-Related homebox1 (Prrx1) as the most up-regulated transcription factor during pancreatic development, regeneration and evolution of PanIN. We previously showed that Prrx1 expression is upregulated in both ADM and PanIN lesion (Reichert et al.). In the present study, we explore the role of Prrx1 in ADM and PanIN formation using novel mouse models, ex vivo acinar culture systems, and human pancreatitis tissue microarrays (TMA). Our findings suggest that Prrx1 is critical for ADM formation and can facilitate the progression of ADM to PanIN lesions.

10. **GRAFT SUBSIDENCE IN LATERAL LUMBAR INTERBODY FUSION: A PROPENSITY MATCH ANALYSIS OF POLYETHERETHERKETONE VERSUS 3D POROUS TITANIUM**

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OBJECTIVE: Lateral lumbar interbody fusion (LLIF) is an effective method of spinal fusion for select spinal disorders. Polyetheretherketone (PEEK) is widely used, though graft subsidence and low biocompatibility are major concerns. This case-matched study aimed to characterize subsidence rates after LLIF and compare PEEK and porous titanium grafts. **METHODS:** Adult patients who underwent LLIF at UPMC from 2016 to 2020 were included in this study. In total, 86 patients (43 PEEK and 43 porous titanium grafts) were matched 1:1 by age, sex, spinal pathology, level of fusion, and staged posterior fusion. Multivariable regression was performed to evaluate for predictors of subsidence while controlling for follow-up duration. **RESULTS:** In 86 patients, mean age was 62.1 Â± 9.9 years old and 52 (60.5%) patients were female. Fifty-four (72.8%) patients had single-level fusion, 18 (20.9%) patients underwent staged posterior fusion and mean follow-up was 20.3 Â± 17.6 months. In patients with PEEK cages, 58 (73.4%) grafts had grade 0 subsidence, 12 (15.2%) grade I, 7 (8.9%) grade II, and 2 (2.5%) grade III. In patients with porous titanium implants, 59 (89.4%) showed grade 0, 4 (6.1%) grade I, 2 (3.0%) grade II, and 1 (1.5%) grade III subsidence. Compared to PEEK, porous titanium implant was associated with lower odds of developing subsidence (OR = 0.23, 95% CI [0.07-0.78], p = 0.018). Patients who underwent staged posterior instrumentation had decreased risk of developing subsidence (OR = 0.16 (95% CI 0.03-0.93, p = 0.041) compared to lateral fusion alone. **CONCLUSIONS:** This institutional case-matched comparison revealed that patients receiving porous titanium interbody for LLIF experienced lower subsidence rates.

11. **THE ROLE OF METABOLISM IN NEUROFIBROMATOSIS 1**

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Neurofibromatosis 1(NF1) is an autosomal dominant disorder characterized by the propensity to develop benign and malignant nervous system tumors. The disease is also associated with an increased prevalence of sleep disorders and ADHD. A Drosophila model of NF1 recapitulates many aspects of the human disease. Specifically, these animals exhibit reduced and fragmented sleep and marked locomotor hyperactivity. Clinical studies suggest that NF1 is associated with an altered state of metabolism. We conducted unbiased metabolomic analysis and discovered low levels of glycolytic intermediates and high levels of TCA metabolites in Nf1-KO Drosophila. Furthermore, Nf1-KO Drosophila exhibit several markers of starvation, including abnormally enlarged crops, increased ketone bodies, and reduced whole body triglycerides. We also observed that mitochondria in Nf1-KO animals are damaged and exhibit an elevated membrane potential. Nf1-KO animals recover significantly more quickly from cold coma, suggesting excess heat production and inefficient use of metabolic fuel. Finally, a diet consisting of 5 times the typical amount of sucrose rescued hyperactivity and loss of sleep in NF1 mutant animals. These experiments suggest that abnormal metabolism may play a role in sleep behavior in NF1 and may provide paradigms for the use of specific metabolic interventions in its treatment.

12. **TOWARD THERAPEUTIC MODULATION OF P53 ISOFORM Δ133p53α IN THE TUMOR-IMMUNE MICROENVIRONMENT**

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Despite successes of immune checkpoint inhibitors and chimeric antigen receptor T cells in some cancers, challenges remain to extend clinical benefits to a majority of patients due to mechanisms of resistance in the tumor microenvironment (TME). To that end, we have shown that p53-mutant cancer cells secreted miR-1246-high exosomes that reprogrammed macrophages into a tumor-promoting phenotype. We have also found that dominant-negative p53 isoform Δ133p53α rescued senescent T cells and led to attenuated expression of immune checkpoints PD-1 and LAG-3. Given these data, we hypothesized that Δ133p53α (immune cell-autonomously) and tumoral p53 mutations (non-cell-autonomously) regulate macrophage and T cell function and can be leveraged to enhance immunotherapy efficacy. To address this hypothesis, we differentiated monocytic cell lines and primary human healthy donor monocytes into baseline M0, antitumor M1, and pro-tumorigenic M2 macrophages in vitro. RT-qPCR verified macrophage polarization and Western blot analysis suggests decreased Δ133p53α in human M2 macrophages. Future directions will consider immune-augmenting manipulation of Δ133p53α in TME-recapitulating co-cultures of healthy donor immune cells with cancer cell lines of varied p53 mutational statuses. Single-cell transcriptomics and functional and cytotoxicity assays will exemplify ensuing immune responses. Modulation of Δ133p53α to restore cancer-targeting immune function could thus improve immunotherapy response rates.

13. **SEXUAL DIMORPHIC BEHAVIOR IN THE TS65DN MODEL OF DOWN SYNDROME DURING A TIME OF DYRK1A OVEREXPRESSION**

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Award: Exceptional Undergraduate Oral Presentation

Down syndrome (DS) neurodevelopment is influenced by dynamic spatiotemporal expression of proteins in the brain, which is disrupted by the presence of a third copy (aneuploidy/trisomy) of human chromosome 21 (Hsa21). The Ts65Dn mouse model of DS exhibits similar phenotypes to individuals with DS, due to the triplication of approximately one-half of the genes found on Hsa21. Dual-specificity Tyrosine Phosphorylation-regulated Kinase 1a (Dyrk1a), one of these triplicated genes, is an attractive target due to its developmental influence. We hypothesized that DYRK1A expression is dysregulated during early postnatal development, neurobehavioral effects will be seen during development, and that administration of a DYRK1A inhibitor, CX-4945, would normalize aberrant behavior. Our results suggest that increased DYRK1A activity at P15 in male trisomic mice may be associated with observed novel behavior. Administration of CX-4945 had limited beneficial effects on neurobehavioral traits and interfered with growth. This study demonstrates neurobehavioral differences in the third postnatal week in Ts65Dn model of DS, presents a sexual dimorphism of DYRK1A expression at P15 in trisomic mice, and fails to support the hypothesis that CX-4945 treatment can normalize neurobehavioral phenotypes of TS65Dn mice at this age.

14. **IMMUNE MEDIATORS OF INFLAMMATION AND LUNG CANCER RISK IN NESTED CASE-CONTROL STUDY**

Umayal Sivagnanalingam[1], Pamela L. Beatty[1], Camille Jacqueline[1], Matthew Dracz[1], Daniel Y Yuan[1], Jia Xue[1], Jennifer Adams-Haduch[1], Renwei Wang[1], Jian Min Yuan[1], Olivera J. Finn[1].
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Smoking is the leading cause of lung cancer, which is the leading cause of cancer mortality worldwide. Smokers develop multiple lung problems associated with chronic inflammation, which can promote progression to cancer. We hypothesized that smokers who developed lung cancer would have a higher frequency of chronic inflammation induced myeloid-derived suppressor cells (MDSC), regulatory T cells (Treg), as well as higher levels of certain cytokines years prior to lung cancer diagnosis, compared to smokers who remained cancer-free. A case-control study of incident lung cancer was conducted within the participants of the Pittsburgh Lung Screening Study (PLuSS). Live PBMCs were analyzed for MDSC and Treg by flow cytometry. Cytokines were quantified in serum using next generation multiplex immunoassays. There was no statistically significant difference in overall MDSC percentage of PBMC or T reg between cases and controls. CD4 T cells were elevated in cases and were associated with increased risk of lung cancer overall ([OR] = 2.61, 95% [CI] = 0.73-9.32). Cases had significantly higher levels of inflammatory cytokines, IL-17A and IL-12/IL-23p40, at both early (median 84 months) and late time points (7 months prior to cancer diagnosis) (all Ps < 0.05). These cytokines could be used as early biomarkers for risk assessment of lung cancer.

Poster Session

01. CHARACTERIZING THE MACROPHAGE RESPONSE TO HUMAN METAPNEUMOVIRUS (HMPV)

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OBJECTIVE: Human metapneumovirus (HMPV) is a leading cause of acute respiratory illness in children, the immunocompromised, and the elderly. The role of lung macrophages during HMPV infection is incompletely understood. However, CD8+ T cells become functionally impaired during HMPV infection. I hypothesize that macrophages contribute to T cell impairment by expressing inhibitory ligands and producing immunomodulatory cytokines. **METHODS:** Peritoneal macrophages (PMs) and alveolar macrophages (AMs) were harvested from C57BL/6 mice and either cultured for in vitro studies or stained ex vivo for flow cytometry. For select experiments, a fluorescently tagged HMPV virus was used. For co-culture experiments, mice were infected intratracheally with HMPV and lymphocytes were isolated on day 7 post-infection. T lymphocytes and PMs were co-cultured together for 48hrs prior to flow cytometry staining. **RESULTS:** We optimized in vitro and in vivo methods to isolate macrophages with >70% purity. During co-culture, macrophages upregulated the inhibitory receptor, PD-L1, after exposure to HMPV, while T cells decreased expression of CD44 and Ki67. This indicates that macrophages potentially impair T cells during HMPV infection. **CONCLUSION:** This project aims to elucidate the role of macrophages in promoting T cell impairment during HMPV infection

02. INTERROGATING MICROBIOME-DRIVEN TERTIARY LYMPHOID STRUCTURE FORMATION IN COLORECTAL CANCER

Hannah J. Bumgarner[1], Sowmya Narayanan[1], Abigail E. Overacre-Delgoffe[1], Jennifer M. Holder-Murray[1], Ayana T. Ruffin[1], Caleb Lampenfeld[1], Timothy W. Hand[1], Tullia C. Bruno[1].
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Colorectal cancer (CRC) is the second-leading cause of cancer related death with end-stage disease being largely refractory to current treatments. Investigating microenvironment or immune factors that impact immunotherapeutic response is critical in improving treatments for the 70% of patients who develop metastatic disease. Recent literature has demonstrated that specific organisms within the gut microbiome are important for favorable response to PD-1 therapy in melanoma patients. In a mouse model of CRC, we have shown that modification of the colonic microbiome with an immunogenic bacterium activates anti-tumor immunity and drives the formation of tertiary lymphoid structures (TLS). TLS are organized lymphoid aggregates containing T and B cells that can initiate anti-tumor immunity directly at the tumor site. With the opportunity to extend our studies to CRC patients, we are interrogating other immunogenic, mucosal-associated bacteria and assessing how their presence drives TLS formation and maturity. Using 16s microbiome sequencing of the stool and tumor-associated mucous from rectal cancer patients along with flow cytometry to phenotype intratumoral B and T cells and multispectral imaging to assess TLS maturity, we will identify specific organisms associated with mature TLS. Our studies are critical for identifying targets towards microbiome-or TLS-centric therapies to improve survival in CRC.

03. A RANDOMIZED CONTROLLED TRIAL ASSESSING THE EFFECT OF INTRAOPERATIVE DEXAMETHASONE IN THE MANAGEMENT OF POSTOPERATIVE PAIN CONTROL AND STIFFNESS AFTER DISTAL RADIUS FIXATION

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Distal radius fractures are the most common orthopedic injury, making up 17.5% of fractures among adults. Stiffness and opioid use for pain management are common post-operative problems. Thus, there is a need to find an alternative medication that will both reduce post-operative stiffness and provide pain control in order to curb the opioid crisis. Many studies support dexamethasone administration during surgery as a safe way to reduce post-operative stiffness, swelling, pain, and opioid use. However, there is currently no hand surgery literature on the effects of dexamethasone plus a nerve block on post- operative pain and stiffness. This study is a prospective, randomized, controlled double-blinded trial comparing the use of intraoperative dexamethasone along with a supraclavicular nerve block (treatment) versus a supraclavicular nerve block alone (control) for the management of post-operative swelling, pain control and stiffness after open reduction and internal fixation of distal radius fractures. We hypothesize that patients who receive dexamethasone along with a nerve block will have less post-operative pain and stiffness and require less opioids than those who receive a nerve block alone.

04. CHARACTERIZATION OF LIVER AND LUNG INJURY AND INFLAMMATION IN A HIGH FAT DIET MOUSE MODEL OF NON-ALCOHOLIC STEATOHEPATITIS

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Non-alcoholic fatty liver disease (NAFLD) is a chronic liver condition that affects millions of individuals in the United States, of which ~20% of cases progress to non-alcoholic steatohepatitis (NASH). NASH is characterized by macrovascular steatosis and persistent inflammation, which can lead to fibrosis. Emerging evidence suggests potential effects of NAFLD and NASH on the development of pulmonary pathologies, but the interplay between the liver and the lung remains largely unexplored. In the current study, we assessed the impact of NASH on lung inflammation and fibrosis using a genetically modified mouse model lacking hepatic farnesoid X-receptor (FXR), a nuclear receptor involved in bile acid and lipid homeostasis, and lipocalin-2 (Lcn2), an acute phase protein upregulated in response to stress. Both FXR and Lcn2 are also involved in regulating innate immune responses. Wild type (WT) and Lcn2 hep-/-/Fxrhep-/- (DKO) mice were fed control (10% kCal) or high-fat (HFD) (60% kCal) diets. Liver, lung, serum, and bronchoalveolar lavage (BAL) fluid were collected after 6 months of feeding. Histopathologic evaluation of livers and elevated liver enzymes (ALT, AST, ALP) from HFD-fed mice confirmed the development of NASH. In the lung, we observed histopathologic alterations including inflammatory cell infiltration, lipid-laden macrophages, septal damage, and epithelial thickening; these alterations were most notable in HFD-fed DKO mice. Flow cytometric analysis also revealed increases in BAL inflammatory macrophage populations in HFD-fed WT mice. These results characterize an association of pulmonary complications during simple steatosis to NASH transition, suggesting lung-liver crosstalk.

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05. **EFFECTS OF SLEEP, AGE, AND EDUCATION ON LEARNING AND ANALYSIS OF TECHNICAL AND SCIENTIFIC INFORMATION**

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INTRODUCTION: Education, age, and sleep have been well documented to affect certain aspects of executive function. However, the effect of these factors on the learning, recall, and processing of technical and scientific information remains largely unexplored. These effects, if any, have ramifications for the preferred level of education, understanding what quantity of sleep optimizes performance, and understanding how an individual's abilities change with age. **METHODS:** Participants (n=100) were recruited through an online platform and were tasked with learning from a nuclear engineering diagram, a biological pathway diagram, and a war tactical diagram, and responding to both functional and structural questions about the diagrams. **RESULTS:** There were strong positive correlations between performance and both degree of education (R=0.536) and hours of sleep (R=0.527). However, subject performance strongly peaked at 8 hour of sleep. There was no significant correlation between performance and age (R=0.118). **CONCLUSION:** The results of this study suggest that both sleep and level of education are significant control factors in the learning and analysis of technical information.

06. **CHARACTERIZING PHYSIOLOGICAL MARKERS OF PREMONITORY URGES IN TOURETTE SYNDROME: A MACHINE LEARNING APPROACH**

Nathan Boyle[1,2], Kesley A. Ramsey PhD[2], Joseph F. McGuire PhD[2], Joey Ka-Yee Essoe PhD[2].

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Tourette Syndrome (TS) is characterized by the childhood onset of tics and associated with significant impairment. Patients with TS experience premonitory urges' subjective aversive sensations that precede tics. As urges play a central role in the neurobehavioral model of TS that underlies evidence-based treatment (i.e., behavior therapy), understanding objective metrics of urges can provide new insights into treatment. This study applies machine learning to identify physiological markers of premonitory urges in youth with TS. A custom mobile app collected physiological responses (i.e., skin-conductance, heartrate) from four male participants (11-12y) receiving behavior therapy. Premonitory urges and tics were timestamped by participants and therapist using Bluetooth buttons. After preprocessing, analysis extracted 8-second data-segments from timeseries (Urges: -5s before, +3s after reported urges; Baseline: randomly sampled 8s without button pushes), then balanced to train a shallow neural network classifier (MATLAB nprtool) within-subject. Although data collection is ongoing, procedures demonstrate the feasibility of measuring physiological markers of urges and tics. Preliminary analyses revealed variable accuracy in physiological urge detection (38-77%), with greater accuracy among treatment responders. While limited by sample size, findings suggest that physiological markers can identify urges among treatment responders. Biofeedback training may prove useful to increase urge awareness for treatment non-responders.

07. **ELECTRICAL BRAIN STIMULATION WITH MINIMALLY INVASIVE ELECTRODES TO IMPROVE SPEECH PERCEPTION**

Serder Akkol[1], Jose L. Herrero[1], Elizabeth Espinal[1], Noah Markowitz[1], Ashesh D. Mehta[1], Stephan Bickel[1].

[1] Elmezzi Graduate School at Northwell Health

Electrical brain stimulation (EBS) will potentially become an important tool to ameliorate impairments in speech perception. While intraparenchymal EBS is invasive and presumably focal, transcranial electrical stimulation is noninvasive and delivers current to wider areas, however it is not portable and much of the current is shunted through skin. Minimally invasive stimulation may address these issues. Here, we tested the feasibility of EBS with two types of electrodes in 5 epilepsy patients undergoing intracranial monitoring: subdermal electrodes and cranial bolts that served as reference electrodes for clinical recordings and holding fixture for depth electrodes, respectively. We used matrix sentence speech-in-noise task. Patients listened monoaurally to 20 sentences per condition (no-stimulation, 50ms or 200ms stimulation onset lag relative to sentence onset) presented randomly. Stimulation electrodes were located above superior temporal gyrus contralateral to the listening ear. Electrical stimulation parameters were 100Hz biphasic, charge balanced square wave pulses where amplitudes were modulated by the speech envelope with about 3mA. We found increased correct word perception accuracy in stimulation conditions, although not reaching statistical significance, but we observed in 4 of 5 patients accuracy increased with longer lag. This study provides feasibility of minimally invasive electrodes for EBS to improve speech perception.

08. **TRENDS IN OPIOID PRESCRIPTIONS FOLLOWING ACL RECONSTRUCTIVE SURGERY FROM 2014 TO 2020**

Sabrina Carrozzi[1], Kathleen Poploski, PT DPT MAS[1], Chukwudi Onyeukwu, BS[1], Volker Musahl, MD[1], Jonathan Hughes, MD[1], James Irrgang, PT PhD FAPTA[1].

[1] University of Pittsburgh

The opioid crisis became a nationwide public health concern in 2017. In the same year, Pennsylvania's Department of Health published guidelines for safe and effective opioid prescribing practices for orthopaedic and sports medicine providers. Anterior cruciate ligament (ACL) tears are common and are increasingly treated with ACL reconstruction (ACLR). The goal of this project was to describe opioid prescribing patterns following ACLR within the UPMC Health System between 2014 and 2020. To evaluate changes in ACLR opioid prescriptions pre/post-guidelines, morphine milligram equivalents (MME), min/max MME per day (MMED), and min/max days' supply were calculated. Statistical analysis indicates that whether the surgery was performed before or after introduction of the guidelines was significantly associated with MME, min/max MMED, and min/max days' supply ($p < 0.001$ for all) controlling for demographic and surgical factors. Perioperative opioid prescriptions were on average 202 MMEs lower than pre-guideline MMEs ($p < 0.001$). Likewise, post-guideline min and max MMEDs were on average 26.9 MMEDs and 44.0 MMEDs lower than pre-guidelines ($p < 0.001$ for both). Min and max days' supply were also significantly lower than the post-guidelines with an average decrease of 2.56 days and 4.66 days, respectively, compared to pre-guidelines ($p < 0.001$ for both).

09. **ACUTE HEART FAILURE IN A YOUNG PATIENT WITH ACUTE CORONARY SYNDROME: A CASE PRESENTATION**

Jeffrey Chan[1].
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Acute heart failure can be induced by acute coronary syndrome even in younger individuals. This case presentation describes a case of acute heart failure in a 20-year-old obese male with acute myocardial infarction. The patient had long-lasting substernal chest pain, tachycardia, tachypnea, and hypotension. Lung auscultation revealed moist rales. His peripheral oxygen saturation dropped to 63%. Electrocardiogram showed ST-segment elevation in I, avL, and V2â€"V4. Chest X-ray showed bat-wing opacity, a classical sign of pulmonary edema. Echocardiography revealed pleural effusion and a low ejection fraction of 43%, showing evidence of heart failure. Coronary angiography showed complete occlusion of the left main coronary artery. His cardiac troponin I level was elevated to 0.457ng/mL. Clopidogrel, aspirin, and low-molecular-weight heparin were given as antiplatelets and anticoagulants. Beta-blockers were given to counter his tachycardia. Thrombo-aspiration and intra-aortic balloon pump were performed to remove thrombus and improve myocardial oxygen perfusion and cardiac output, respectively. The patient reached remission after the operations and intensive care. This patient suffered from a combination of cardiovascular conditions and hemodynamic alterations, leading to acute heart failure at a young age. His condition was likely preventable by healthy life-style changes; thus these were encouraged to avoid future relapse.

10. **CHARACTERIZING *CANDIDA AURIS***

Diya Cherian[1], Gabriel K. Innes, PhD[1],Reed Magleby, M.D. [1], Adrienne Sherman, M.P.H. [1], Jessica Arias, M.H.L. [1], Jason Mehr, M.P.H.[1], Rebecca Greeley, M.P.H. [1].
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Candida auris (*C. auris*), an emerging resistant yeast, can cause serious infections in healthcare settings and has led to silent but lethal outbreaks worldwide. The New Jersey Department of Health (NJDOH) conducts *C. auris* surveillance in healthcare facilities to assess patient colonization and transmission events. This research aims to summarize demographics, types of facilities reporting cases, underlying conditions, and other risk factors of *C. auris* infection among patients from 2017 to 2020. Information was obtained from 361 case report forms submitted from 44 facilities. 31% of case-patients were male and 23% were female. Most cases had underlying conditions, the most common being cardiovascular and respiratory disease, ventilator dependence, multidrug-resistant organism (MDRO) infections, and diabetes. Among patients with indwelling devices, the most frequent were catheters, abdominal feeding tubes, and tracheostomies. A majority of patients underwent medical procedures, including wound debridements and line/tube placements. Most patients were on systemic antibiotics, and many received antifungals. Of the forms received, 13.4% of cases were fatal. Data analysis suggests a correlation between co-morbidities, indwelling devices, and cases of *C. auris*. Prioritizing active surveillance, education, infection control measures, and continued research are key in preventing the spread of this emerging fungal pathogen.

11. **ERK5 INHIBITION IN PEDIATRIC GLIOBLASTOMA LEADS TO DECREASED ACTIVATION OF PFKFB3 AND GLYCOLYSIS**

Akanksha Chilukuri[1], Casillo, SM[1], Barber, C[1], Gatesman, T[1], Koncar, RF[1], Golbourn, B[1], Agnihotri, S[1].
[1] University of Pittsburgh

Pediatric glioblastoma (GBM) is an incurable brain tumor that is often marked by a shift from aerobic respiration to glycolysis. Overexpression of PFKFB3, an enzyme that produces fructose-2, 6-bisphosphate in the glycolytic pathway, has been implicated in tumorigenesis. We hypothesize that inhibiting upstream pathways of PFKFB3 such as transcription factors that are activated by ERK5/MAPK7, can be a way to inhibit GBM cell growth. We did an in-silica analysis to identify transcription factors phosphorylated by ERK5 using Phosphosite, proteins that interact with MAPK7 using Biogrid and transcription factors that bind to the PFKFB3 promoter using Jaspar. The overlap of these yielded 4 transcription factors of interest, FOS, ETS1, MEF2A, and MEF2C. Using both siRNA and a drug, ERK5-IN-1, we created a knockdown of ERK5 in SF8628 cells, a GBM cell line. We measured levels of activated (phosphorylated) transcription factor versus total in ERK5 knockdown and control cells. Our results showed that the siRNA ERK5 KD cells had decreased levels of p-MEF2A and p-MEF2C compared to total. In addition, the PFKFB3 KD had more p-MEF2A than the PFKFB3 control. Finally, the SF8628 cells with ERK5-IN-1, showed a dose dependent reduction in p-mef2a compared to the control, b-actin.

12. **ATN-161 AND INFLAMMATORY PROGRESSION OF CEREBRAL ANEURYSM**

Mitchell W. Couldwell, MS[1], Viktoriya Grayson, BS[1], Timothy E. Gressett, MS[1], Wesley H Chastain, MS[1], Aaron S. Dumont, MD, MBA[1], Gregory J. Bix, MD, PhD[1].
[1] Tulane University

Cerebral aneurysms (CAs) are prevalent in 2-3% in the general population and upwards of 19% in high-risk populations. CAs may progress by rupturing and producing a subarachnoid hemorrhage (SAH). Increasingly, CAs are being detected before rupture through noninvasive imaging techniques. However, the only currently available treatments for these aneurysms is clipping and coiling/endovascular treatment, which are invasive and carry significant risk. Thus, given the potentially lethal complications of CA, there is a need to establish pharmacological therapy for CAs which does not presently exist. ATN-161 is an anti-integrin peptide that has been shown to decrease inflammation and stabilize the BBB in ischemic stroke but has yet to be thoroughly evaluated for efficacy in aneurysm rupture. In addition to affecting cytokines, chemokines, inflammation, and angiogenesis, integrins have also been implicated in the migration of neutrophils and in reducing edema in vascular injury., Thus, ATN-161 may represent a promising pharmacological therapy for CAs. Here we review the therapeutic potential of ATN-161 in preventing CA rupture via the working model of inflammatory control and preservation of the BBB. We discuss the phenotypic response of vascular smooth muscle cells (VSMCs) to local environmental cues involving inflammation, oxidative stress, proliferation, migration, and matrix remodeling.

13. **CHILDREN WITH CEREBRAL VISUAL IMPAIRMENT CAN BENEFIT FROM BOTH IN PERSON AND REMOTE LEARNING**

Ariana Crary[1], Saeideh Ghahghaei[1], Arvind Chandna[1].
[1] Colorado State University

Due to lack of accommodations, inconvenient and embarrassing assistive technology, and lack of support and communication for both parents and teachers, a mainstream classroom is a difficult learning environment for children with cerebral vision impairment (CVI) (Opie 2018) (Blackstone 2021). Students with high-functioning autism reported that remote learning due to COVID-19 actually benefited them (Reicher 2020) and so we hypothesized that aspects of remote learning could also be beneficial to students with CVI. We conducted semi-structured interviews of 6 parents of children with CVI (ages 8-18) who can read print and asked them to share reading difficulties in their children including their view on remote learning. After transcribing and coding the interviews, we found more positive aspects of remote learning were talked about compared to negative aspects. The most talked about theme was material interaction, which included anytime the parents talked about how the child could better engage with and understand the material. We concluded that while remote learning is not the answer, it showed us that by delivering more material in an online/technology based format, it will be naturally more accommodating for children with CVI.

14. **TRENDS IN PEDIATRIC COCAINE EXPOSURE REPORTED TO U.S. POISON CENTERS**

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Cocaine is a central nervous system stimulant responsible for inhibiting the reuptake of biogenic amines. Rise in synaptic concentrations of these neurotransmitters causes euphoria, however, also causes well documented negative effects. Because of the frequency of use/abuse, cocaine has been a commonly studied topic in adults, although, available literature in the pediatric population is scarce. Hypothesis: The number of pediatric patients (ages 0-18) exposed to cocaine is increasing over time, and affected pediatric patients may be at risk for cardiovascular and neurologic toxicity distinct from the adult population. Data for this study was provided by the National Poison Data System database. Data from 2012-2020 was used to analyze trends in incidence rates of exposure. In addition to incidence rates, trends in patient demographics, therapies used, subsequent outcomes, co-ingested substances and geographical distribution was analyzed. Subgroups consisting of two major exposure groups (0-3 y/o & 13-18 y/o) were specifically analyzed. The data indicated a clear bimodal pattern of incidence with two exposure groups of 0-3 y/o and 13-18 y/o. Incidence is increasing, although at a much more alarming rate in younger children. Patients 0-3 y/o presented with increased risk of numerous depressive effects, including respiratory depression, CNS depression, lethargy and drowsiness.

15. **A RETROSPECTIVE REVIEW OF ENDOCRINE MANAGEMENT IN ORGAN DONORS OF THE TRAUMA SURGERY PATIENT POPULATION**

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BACKGROUND: Organ donation in the trauma surgery patient population requires intensive management to sustain organ viability for transplant recipients. Normal regulation of organs by the endocrine system is at risk for disruption in the case of brain death. Endocrine protocols for maintaining homeostasis in transplantable organs of potential donors have been shown to impact organ quality, but controversies remain concerning the best interventions. We investigated the implementation of endocrine protocols at our institution and hypothesized that these interventions would be associated with an increased number of organs donated. **METHODS**: We retrospectively reviewed records of 284 patients from whom organ donation was requested between July 2012 to April 2021. We then identified organ donors and determined if hyperglycemia, hypothyroidism, hypocortisolism, or diabetes insipidus were treated. Finally, we compared the number and type of organs donated when protocols were or were not used. **RESULTS**: Organ donation was completed in 115 of the patients reviewed. Among organ donors, more organs were donated when endocrine protocols were administered relative to when they were not. Administration of multiple endocrine protocols was not associated with a decrease in the number of organs donated. Further study will evaluate how endocrine management relates to post-transplant organ function.

16. **CONCEPTUALIZING OBESITY WITHIN A BIOPSYCHOSOCIAL FRAMEWORK TO ADDRESS ANTI-FAT BIAS**

Sarah Girgis[1], Paavani Lella[1], Ye Kyung Song MD, PhD[1].
[1] Duke University

A significant number of physicians and other healthcare professionals hold fat bias, with many conflating fatness with being weak-willed or lazy. Treating obesity has been described as frustrating and technically challenging. We reviewed the literature and found that several themes need to be addressed in an educational program on anti-fat bias. Clinicians must be aware that anti-fatness in the United States has roots in anti-Blackness. Racial scientific literature since at least the 18th century claimed that fatness was savage and black. Because women are typically reduced to their bodies, fat stigma has commonly targeted racial/ethnic Other women. Additionally, despite research that indicates body weight is affected by interactions of biological and environmental factors, people believe being fat is volitional. This leads to overweight and obese patients receiving substandard care that does not take their set of environmental circumstances and lifestyle preferences into consideration. Diet content is only one of the many factors that affects people's weight.

17. **TELEMEDICINE USE BY CITIZENSHIP STATUS IN CALIFORNIA, 2015-2018**

Panagiotis Gourlias[1], Cem Atillasoy[2], Alexander Adia MPH[3], Kristin Ray MD MS[1].

[1] University of Pittsburgh School of Medicine. [2] Yale School of Medicine. [3] Filipinx/a/o Community Health Association

Telemedicine use in the US is increasing, a phenomenon amplified by state and federal telemedicine policy changes during the COVID-19 pandemic. Immigrants may face unique barriers to telemedicine use, such as lower English proficiency, higher rates of being uninsured, cultural differences, and privacy concerns. To examine the existing relationship between citizenship status and telemedicine use, we conducted a secondary analysis using data from the 2015-2018 California Health Interview Survey. Bivariate analyses using Pearson's chi-squared test were used to compare rates of telemedicine use by noncitizens and naturalized citizens to US-born citizens overall and for specific health services. Our analysis included 84,419 respondents reflecting an estimated population of 29,406,792, 15.2% of whom were noncitizens, 17.6% naturalized citizens, and 67.2% US-born. Of the estimated population, we found that both noncitizens and naturalized citizens were less likely to have used telemedicine overall than US-born citizens (5.30% and 9.14% vs 13.01%, P<0.0001), as well as for upper respiratory issues (0.8% and 1.7% vs 2.7%, P<0.0001), musculoskeletal issues (0.2% and 0.7% vs 1.2%, P<0.0001), and sick visits (1.4% and 1.5% vs 2.5%, P=0.0099). Noncitizens and naturalized citizens used telemedicine at significantly lower rates than US-born citizens prior to the COVID-19 pandemic.

18. **INTRACELLULAR EPHB KINASE INACTIVATION ATTENUATES MECHANICAL ALLODYNIA FOLLOWING SPINAL CORD INJURY**

David Jaffe[1], Nicolette M. Heinsinger[1], R. Vivian Allahyari[1], Jaime L. Watson[1], Aditi Falnikar[1], Rachel Cain[1], Lan Cheng[1], Wei Zhou[1], Eric V. Brown[1], Brittany A. Charsar[1], Matthew B. Dalva[1], Angelo C. Lepore[1].

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Spinal cord injury (SCI) patients often suffer from debilitating neuropathic pain (NP). One mechanism underlying SCI-induced NP is the hyperexcitability of CNS pain circuitry neurons via NMDA-type receptors (NMDARs). EphBs are a family of receptor tyrosine kinases which interact with NMDARs, and studies show EphB activation induces NP-like phenotypes in several chronic pain animal models. We hypothesize inactivation of the intracellular kinase domain in EphB1, 2, and 3 will decrease SCI-induced NP-like phenotypes in a rodent SCI model. We find that mice with cervical contusion SCI display increased EphB2 protein and mRNA levels, as well as increased colocalization of EphB2, GluN1 (an NMDAR subunit), and vGlut2 (an excitatory synapse marker) in the ipsilateral dorsal horn, caudal to the injury compared to uninjured mice. We then use transgenic knock-in mice to chemogenetically inhibit EphB1-3 kinase activity. EphB kinase inactivation in cervical contusion SCI mice significantly reverses already-established mechanical hypersensitivity but not thermal hyperalgesia. This suggests a mechanical sensory modality-specific and an injury-selective role for the EphB kinase domain. Overall, after SCI, we observe an upregulation of EphB2 along with increased EphB2-NMDAR colocalization at excitatory synapses in the dorsal horn, and we show that EphB kinase activity is linked to SCI-induced NP.

19. **PERLECAN LG3 RESCUES MOTOR COORDINATION IN A MOUSE MODEL OF CEREBRAL HYPOPERFUSION**

Viktoriya Grayson[1], Joshua Hanna[1], Joachim Biose Ifechukwude[1], Sharon Ogbonna[1], Scott Hawkins[1], Gregory Bix[1].

[1] Tulane University School of Medicine

Vascular dementia is a major cause of daily functional dependence and currently lacks effective therapy. The small peptide fragment Laminin Globular domain 3 (LG3) of the extracellular matrix component perlecan is a potential therapy shown to improve outcomes in experimental ischemic stroke. Using the bilateral carotid artery stenosis (BCAS) model of brain chronic hypoperfusion in mice we examined the hypothesis that LG3 treatment would improve brain pathology and functional outcomes. Ninety-six adult male C57BL/6J mice were randomly subjected to either BCAS using titanium micro-coils (n=48) or sham surgery (n=48). LG3 (6 mg/kg, i.p.) or saline was administered after surgery and every other day for seven or 14 days to determine whether LG3 treatment in the acute phase of BCAS will ameliorate outcome measures. All animals underwent rotarod test. While histological assay performed on brain tissues for myelin-associated glycoprotein, myelin basic protein, and Iba-1 is in its preliminary stage, our behavioral data suggests that LG3 improves motor function by increasing the latency to fall off of the rotarod ($p<0.05$) when compared to saline and Sham treated groups. Our data suggests that LG3 treatment is neuroprotective in the BCAS model and support its further development as a therapy for vascular dementia.

20. **CASE REPORT: USE OF LURASIDONE IN PREGNANT PATIENT WITH BIPOLAR/SCHIZOAFFECTIVE DISORDER AND COMORBID OBESITY**

Angela Ho[1], Algeny Hernandez[1], Katharine Goebel[1], Agdel Hernandez MD[1].

[1] Touro College of Osteopathic Medicine

We report on a pregnant patient G3P2 with differential diagnosis of schizoaffective disorder and bipolar disorder with psychotic features and comorbid obesity with a significant past medical and mental health history including borderline personality disorder, posttraumatic stress disorder, preeclampsia, and morbid obesity. The patient was in her third trimester of pregnancy with an increased risk for recurrence of preeclampsia. She presented with symptoms of bipolar depression, anxiety, homicidal thoughts, and both auditory and visual hallucinations. She was taking haloperidol 15 mg oral daily; however, it did not control her mood symptoms. Lurasidone has minimal metabolic side effects compared to other SGAs and has lower potential for orthostatic hypertension, hyperprolactinemia, and adverse effects of drug-induced parkinsonism. Therefore, after thorough evaluation and considering the risk/benefit ratio in fetal drug exposure and the degree of severity of maternal psychiatric illness, the treatment team decided to discontinue haloperidol and administer lurasidone 20 mg oral daily. Additional large, controlled studies are needed to determine the safety and efficacy of lurasidone as the treatment of choice for childbearing women with bipolar disorder and/or schizoaffective disorder with comorbid obesity.

21. **REVIEW OF HIV ACQUISITION CASES WHILE ON PREP**

Gina Kim[1], Clement Haeck[1].
[1] Princeton University

HIV pre-exposure prophylaxis (PrEP) drug regimens have proven to be effective measures of HIV prevention. Of the growing range of PrEP drug formulations, the daily oral emtricitabine/tenofovir disoproxil fumarate tablet is of more common use, but all available PrEP formulations offer a high level of clinical efficacy when taken on a regular basis. However, between the first PrEP formulation approval in 2012 to the present day, a small number of patients have acquired HIV while adhering to consistent drug regimens. To better understand this occurrence, a narrative literature review was conducted that investigates the nature of eleven published cases of HIV acquired while on a stable viral prevention regimen, of which the first U.S. case was documented in New York City. Information on adherence, classes of resistant drugs, treatment regimen types and success, and geographical regions were recorded. Four of the known cases occurred under verified adherence, and the additional seven occurred under self-reported (unverified) adherence. Two of these cases acquired a non-drug resistant HIV strain. With a better understanding of these viral acquisition events, emerging novel methods may provide more effective approaches to HIV prevention and treatment regimens.

22. **A 3-D CELL CULTURE MODEL OF THE NASOPHARYNX REVEALS CELL-TYPE-SPECIFIC SUSCEPTIBILITY TO EPSTEIN-BARR VIRUS INFECTION**

Shweta P. Kitchloo[1], Phillip Ziegler[1], Alex S Reznik[1], Yarong Tian[1], Yulong Bai[1], Sanna Abrahamsson[1], Alan Backerholm[1], Eric Wang[1], Stella E Lee[1], Anthony Green[1], Michael M Myerburg[1], Hyun Jung Park[1], Ka-Wei Tang[1], Clare E. Sample[1], Kathy Ho Yen Shair[1].
[1] University of Pittsburgh School of Medicine

Epstein-Barr virus (EBV) is a human tumor virus that is associated with nasopharyngeal carcinomas (NPC). The progenitor cell for EBV-associated NPC is unknown; however, both latent and lytic infection are thought to be important in preneoplasia. The nasopharynx is composed of pseudostratified and stratified epithelia, which can be modeled in 3-D cell culture. Latent and lytic infection programs are tied to cellular differentiation and are best studied in a 3-D cell culture model. We have developed two 3-D cell culture methods using conditionally reprogrammed cells from the nasopharynx, that are susceptible to de novo EBV infection: (1) a pseudostratified air-liquid interface (pseudo-ALI) model and, (2) an organotypic raft model to study stratified epithelium. In both models, cells in 3-D culture are exposed to EBV inoculum. We demonstrate that EBV latent and lytic infection can be identified in these 3-D culture models, donor variation exists, and the infection program is distinguished cell types. Furthermore, we demonstrate that pseudostratified cultures can be generated from persons without sinus co-pathology, as well as from patients with sinus co-pathology. Thus, these 3-D cell culture models can be used to identify susceptible cell types, and to study the molecular determinants of EBV pathogenesis in the nasopharynx.

23. **SAFETY OF COVID-19 VACCINES USED IN GAZA STRIP: AN OBSERVATIONAL STUDY**

Loay Kanou[1], Hosam Shaikhkhalil[1], Ruba Ismail[1], Nada Abdul Wahab[1], Abd Al-Karim Sammour[1].
[1] The Islamic University of Gaza

OBJECTIVE: To assess the safety of COVID19 vaccines used among the Gazan people, Palestine. **METHODOLOGY**: A two-month safety follow-up was conducted for a randomized sample of vaccinated subjects by phone interviews. **RESULTS:** 755 participants completed follow-up with a median age of 37. 477 (63.2%) were males. About half received Sputnik Light vaccine (n= 376, 49.8%), followed by Pfizer BioNTech (n= 344, 45.6%). 54.3% of the overall sample received a single dose, while 45.7% received 2 doses. 79.3% of Sputnik Light vaccine recipients experienced side effects, whereas 79.1% for Pfizer BioNTech after the first dose and 83.8% after the second dose. Pain at injection site (59.5%), fatigue (33.5%), headache (25.2%) were the most frequent adverse side effects after receiving one dose. Similarly, the same side effects were the most reported symptoms after the second one (63.2%, 35.7%, 27.8%, respectively). 2 cases (0.5%) had strokes within 2 months of Sputnik Light administration. Younger adults (age <50) are more likely to develop adverse side effects than those older than 50, p= .000. **CONCLUSION:** Two-thirds of vaccine recipients develop minimal adverse side effects in the first-week post-vaccination. Moreover, more studies with larger samples are needed to assess the safety of the Sputnik Light vaccine.

24. **ASSESSING BIOMARKERS FOR MONITORING CEREBRAL AUTOREGULATION AT THE RESPIRATION FREQUENCY USING NEAR INFRARED SPECTROSCOPY**

Nikita Kedia[1], Mohini Banerjee[1], Deepshikha Acharya[1], Alexander Ruesch[1], Jana M. Kainerstorfer[1].
[1] University of Pittsburgh School of Medicine

Cerebral autoregulation (CA) is the ability for the brain to maintain a near constant cerebral blood flow despite changes in cerebral perfusion pressure. CA can be impaired in various diseases, thus monitoring CA is important for guiding therapeutic interventions and preventing stroke. Currently, there is no gold standard for evaluating CA clinically because it is difficult to assess global cerebral blood flow. Several methods are being explored that use other biomarkers as a surrogate for blood flow, however, most of these require invasive neurosurgery. An alternative noninvasive diffuse optical modality known as near infrared spectroscopy (NIRS) has been introduced. Previous work has shown that NIRS can monitor CA in response to low frequency changes in pressure that are clinically induced. However, it is still unclear whether CA can be monitored at a higher frequency such as the respiration rate. Monitoring CA at a high frequency is important because inducing low frequency changes is not always practical in clinical settings, especially in surgery where patients may be on a ventilator. In this study, we investigate which NIRS biomarkers can be used to monitor CA at the physiologic respiration rate.

25. **HAPLOTYPIC EFFECT OF MHC ON COMMENSAL COLONIZATION OVER HOMEOSTATIC DEVELOPMENT**

Ming Suet Kwan[1], April Huang BS[1], Wuxing Yuan MS[1], Rashed Shah PhD[1], Jonathan Badger PhD[1], John McCulloch PhD[1], Colm O'Huigin PhD[1].

[1] National Cancer Institute

MHC recognizes microbial peptides to promote immune education as colonization begins at birth. Since MHC polygenicity and polymorphism enable interindividual diversity for peptide recognition repertoires, we investigate whether varying MHC haplotypes are correlated to different microbiome compositions over homeostatic development. We crossed C57BL/6J (B6: Histocompatibility 2bb) and C57BLKS/J (BLKS: H2dd) and homogenized environmental differences between facilities. We generated MIX lineage by crossing females from B6 lineage with males from BLKS lineage. We conducted 16S metagenomic sequencing to examine haplotypic effects among the F2 microbiome. Our results showed that B6 and MIX with shared maternal lineage bore greater similarity in their microbiomes. Both were enriched in Proteobacteria and Verrucomicrobia, whereas BLKS microbiome was enriched in Actinobacteria and Patescibacteria ($p < 0.001$). Lineage-stratified analysis revealed haplotype-associated variations at family level. H2bb from MIX had more Tannerellaceae and Christensenellaceae ($p = 0.004$), while Clostridiaceae and Enterococcaceae were primarily found in H2dd from BLKS (p â‰¤ 0.001). Richness increased over development and was highest in BLKS ($p < 0.001$). Our study demonstrated the influence of maternal lineage and MHC haplotypes on microbiome, resulting in differences in phyla- and family-level, richness, and diversity. Haplotypic effects were limited to interacting with particular species.

26. **UPREGULATION OF IBD-ASSOCIATED CYTOKINES IN INFLAMED RECTUM BRIDGES CROHNS DISEASE AND ULCERATIVE COLITIS**

Rachel Levantovsky[1], Christopher Tastad[1], Shikha Nayar[1], Nai-Yun Hsu[1], Ling-Shiang Chuang[1], Judy H. Cho[1].

[1] Icahn School of Medicine at Mount Sinai

Award: Exceptional Graduate Poster

Regional involvement in Crohns disease (CD) is an important factor in disease course, with more similarity across IBDs in the colon than within CD comparing ileal and colonic disease. To profile differentially expressed genes between regions, bulk RNA sequencing data were analyzed, comparing biopsies from CD (ileum: n=161 infl., n=201 non; rectum: n=116 infl.; n=251 non) and UC (rectum: n=144 infl.; n=168 non). Mean expression, log2 fold change (L2FC) and adjusted p-values were the basis of comparison. Differential expression in pro-inflammatory cytokines, receptors, and signaling mediators were identified with greater contrast between the ileum and rectum in CD than in rectal biopsies from patients with CD or UC. In CD, the mean expression of IL12A, IL12B, IL23A, IL17A, and others is similar between ileal and rectal biopsies; however, the upregulation of these cytokines in rectum is several fold higher than in the ileum (e.g. IL23A means ratio: 1.108; L2FC ratio: 5.188). Comparing rectal biopsies from UC vs. CD, the L2FC across all cytokines and receptors were comparable by linear regression ($Î^2 = 0.98$, $R2 = 0.85$). The same pattern is observed in the expression of TNF and IFNG. This regional dichotomy in cytokine upregulation must be considered in treatment.

27. **ALDH INHIBITION AS MODULATOR OF OVARIAN TUMOR ASSOCIATED MACROPHAGES**

Julia Knight[1], Bingsi Gao[1], Mainpal Rana[1], Ronald Buckanovich[1], Anda Vlad[1].

[1] University of Pittsburgh School of Medicine

Award: Exceptional Graduate Poster

Ovarian cancer (OC) is the 5th leading cause of cancer death in women. There is a crucial need for novel therapies, especially for recurrent, chemoresistant OC. In cancer cells, increased aldehyde dehydrogenase (ALDH) expression correlates with chemoresistance and poor prognosis. Notably, NR4A1, a nuclear hormone receptor transcription factor, is a potential target downstream of ALDH. In immune cells, ALDH inhibitors (ALDHi) support polyclonal expansion of CD8 T cells. In contrast, tumor-associated macrophages (TAMs) are sensitive to ALDHi. TAMs are functionally defined as M1 (pro-inflammatory) or M2 (anti-inflammatory). M2 TAMs predominate in OC and contribute to immune suppression. High levels of M2-like TAMS are a poor prognostic indicator in patients. We hypothesize that ALDHi reduce M2 TAMs and lower NR4A1 expression in human OC ascites samples. Five ascites samples were treated for 72h with ALDHi or DMSO control. Exposure to ALDHi revealed a significant decrease in CD14+ and CD163+ cells via flow cytometry and chip cytometry (ZellScannerONE), indicating a loss of M2 macrophages compared to control. Western blot showed decreased NR4A1 expression in ALDHi treated ascites. Our data reveal that, in OC, ALDHi decrease immune-suppressive M2 TAMs, promote CD8 T cell expansion, and decrease NR4A1 expression.

28. **INTERACTION OF TIM-3 AND PHOSPHATIDYLSERINE IN THE TUMOR MICROENVIRONMENT**

Srividya Kottapalli[1], Hridesh Banerjee PhD[1], Lawrence P. Kane PhD[1].

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T cell (or transmembrane) immunoglobulin and mucin domain 3 (Tim-3) is expressed on many immune cells, including T cell subsets like exhausted CD8+ T cells and regulatory T cells (Treg). Among tumor-infiltrating lymphocytes (TIL), 40-60% of Tregs express Tim-3. Tim-3+ Tregs may mediate Treg suppressive function by producing higher levels of suppressive cytokines. In CD8 T cells, Tim-3 and PD-1 co-expression is associated with more aggressive tumor growth. However, the mechanism behind these phenotypes is unknown. One explanation may be found in evaluating the interaction between Tim-3 and phosphatidylserine (PtdSer), one of its four ligands, and which is flipped onto the surface of apoptotic cells. Recent studies showed that wild-type mice injected with the PtdSer-exposing mutant MC38 had significantly less tumor burden compared to Tim-3 germline knockout mice, indicating that PtdSer:Tim-3 interaction may induce immune suppression. We investigated this by introducing PtdSer-exposing mutant MC38 to transgenic mice overexpressing Tim-3 on CD8 T cells or Tregs. PtdSer-exposing MC38 tumor burden was increased in CD8 Tim-3 transgenic mice, and CD8 Tim-3 transgenic T cells exhibited an exhausted phenotype. While tumor progression in wild-type and Treg Tim-3 transgenic mice did not differ significantly, TIL characterization revealed an effector Treg phenotype in transgenic mice.

29. **IMMEDIATE FEEDBACK IMPROVES TASK PERFORMANCE**

Ivonne Morban[1], Zachary Lively[1], Preeti Verghese[1].
[1] Lehigh University

Award: Exceptional Undergraduate Poster

Humans make 2 to 3 saccadic eye movements per second, often to conspicuous items [1]. Studies have shown that these eye movements do not select locations that provide the most information, and are inefficient [2,3,4]. This study investigates the role of feedback in a task where the targets identity is ambiguous, and feedback reveals the true identity of a selected location. We compared two kinds of feedback: immediate feedback following an eye movement and delayed feedback provided at the end of the trial. We hypothesized that immediate feedback would increase eye movement efficiency by helping participants associate motor action immediately with information relevant to the task. Data for 12 participants shows that immediate and delayed feedback had similar effects on eye movement efficiency, although sensitivity (the ability to discriminate target from distractor) was higher for immediate-feedback. We conducted a variant of the original experiment where 3 observers interrogated locations by clicking on them. The click experiment yielded similar results: immediate and delayed feedback had comparable effects on efficiency, although immediate feedback improved sensitivity. The overall efficiency of clicks was higher than that of eye movements, reflecting the longer time required for manual responses compared to eye movements.

30. **TRANSCRIPTOMIC ANALYSIS OF SURAL AND TIBIAL NERVE SAMPLES IN DIABETIC PERIPHERAL NEUROPATHY**

Sanjay Neerukonda[1], Amelia J. Balmain[1], Diana Tavares-Ferreira[1], Theodore J. Price[1].
[1] University of Texas at Dallas

Diabetes mellitus affects approximately 34 million Americans and can cause multiple significant health complications, including peripheral diabetic neuropathy. To investigate the currently unknown molecular mechanisms underlying this complication, which is present in up to half of diabetic patients, paired tibial (n = 13) & sural (n = 5) nerves were collected from advanced diabetic patients who underwent lower limb amputation. Bulk RNA-sequencing of samples was performed with subsequent hierarchical cluster analysis and functional enrichment analysis on differentially expressed genes. Functional enrichment analyses revealed up-regulation of gene ontologies associated with the complement activation cascade and classical pathway as well as associated pathways involving immunoglobulins and other immune cells. Hierarchical cluster analysis revealed multiple distinct patterns of expression. Upon screening differentially expressed genes associated with the complement activation pathway against human dorsal root ganglia nociceptor profiles from utilizing Visium 10X Genomics data, we did not observe significant expression of these genes within specific nociceptor subsets but instead saw increased expression in non-neuronal subtypes. Moving forward, we believe further investigation into the role of the complement system in diabetic neuropathy is warranted. This includes collection and use of qualitative data which would enable us to stratify our analysis and determine how these variables influence neuropathy.

31. **ACUTE TRANSVERSE MYELITIS FOLLOWING SARS-COV-2 VACCINE: A CASE REPORT**

Richard Liberio[1], Mark A. Colantonio[1], Erum Khan[1], Ashish Shrestha[1], Shitiz Sriwastava[1].
[1] West Virginia University School of Medicine

OBJECTIVE: To report a unique case and literature review of post COVID-19 vaccination associated transverse myelitis with abnormal MRI findings. **BACKGROUND:** Coronavirus diseases have been reported to be associated with several neurological manifestations such as stroke, Guillain-Barre syndrome, and meningoencephalitis amongst others. There are only a few reported cases of transverse myelitis associated with the novel coronavirus (n-CoV-2). Here, we identify a post-COVID-19 vaccination patient diagnosed with acute transverse myelitis. **METHODS:** A retrospective chart review of a patient diagnosed with post SARS-CoV-2 vaccination acute transverse myelitis, and a review of literature of all the reported cases of other post-vaccination transverse myelitis, from December 1st, 2010 through July 15th, 2021, was performed. **CONCLUSION:** To our knowledge, this is one of early reported case of transverse myelitis with post SARS-CoV-2 vaccination, who responded well to plasmapheresis. Further studies would be recommended to identify the underlying correlation between COVID-19 vaccination and transverse myelitis.

32. **HOW DOES NUTRITION AFFECT ENDOMETRIOSIS RISK?**

Tamara Marsh[1], Iwona Jasiuk[1].
[1] University of North Florida

Objective: The purpose of this literature review is to analyze key works that investigated how nutrition affects endometriosis development. **Methods:** PubMed was used to find primary literature. The following search terms were used, endometriosis and nutrition and endometriosis risk and nutrition. The following filters were used: free full text and 10 years. The selected research articles included clinical trial results and were published in primary literature. Five primary studies were selected. **Results:** There were mixed results for vegetable and red meat intake and endometriosis risk. Thiamine (B1), folate (B9), vitamin C, and vitamin E supplements were not associated with endometriosis risk, however, these nutrients from foods sources were inversely associated with endometriosis. Poultry (chicken, turkey), fish (canned tuna, dark meat fish, other fish), shellfish (shrimp, lobster, scallops), and eggs were not linked with endometriosis risk. Dairy based yogurt and ice cream as well as fruits especially citrus fruits were linked with reduced endometriosis risk. **Conclusion:** Dietary choices may influence endometriosis risk; however, more research needs to be conducted using a diet record to avoid the limitations of using the food frequency questionnaire (e.g., relies on recall, not quantifiable precise, and does not provide meal pattern information).

33. **NANOSCALE DYNAMIC MECHANICAL ANALYSIS (NANODMA) AND REFERENCE POINT INDENTATION (RPI): A SYSTEMATIC REVIEW OF DIAGNOSTIC TECHNOLOGY USED TO ASSESS THE MECHANICAL PROPERTIES OF BONE**

Pierina Parraga[1].
[1] University of North Carolina at Charlotte

Reference Point Indentation (RPI) and Nanoscale Dynamic Mechanical Analysis (NanoDMA) are novel techniques used to assess the mechanical properties of bones. The first development of RPI technology was through the BioDent then the Osteoprobe. This review demonstrates that the clinical use of the Osteoprobe device in-vivo remains somewhat ambiguous due to a lack of clarity regarding the parameters measured through this methods' assessment of bone. Moreover, past literature demonstrates that the BioDent device can accurately assess fractures in patients. Additionally, this review details the use of NanoDMA through fundamental studies that emphasize its application to assess bone health. Finally, it analyzes the use of NanoDMA in different environmental conditions such as wet and dry testing and its effect on viscoelastic properties. Moreover, this review includes notable trends in moduli observed when examining cross-sections of bone samples in hydrated and desiccated states. This review aims to assess RPI and NanoDMA technology to determine each application's key characteristics, the parameters they measure, and future directions for clinicians. The analysis of bone assessment technology is vital for the development of treatments for bone-related diseases. For this reason, examining different innovations that analyze the mechanical properties of bone is vital for the future of in-vivo studies on the characterization of the bone.

34. **IL-19 ASSOCIATED LYMPHANGIOGENESIS PROMOTES ATHEROSCLEROTIC PLAQUE REDUCTION**

Amanda Peluzzo[1], Tani Leigh[1], Rachel Okune[1], Sheri Kelemen[1], Michael Autieri[1].
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Atherosclerosis is characterized by the formation of fatty plaques which can occlude vessels, causing stroke or myocardial infarction which are the main causes of death due to cardiovascular disease. The role of lymphangiogenesis in atherogenesis is currently controversial. Some consider it protective by promoting reverse cholesterol transport (RCT) or detrimental by promoting plaque instability through white blood cell trafficking. Interleukin-19 (IL-19), an anti-inflammatory cytokine, attenuates plaque progression and is pro-angiogenic. This drives our hypothesis that a mechanism whereby IL-19 is atheroprotective is by driving lymphangiogenesis, allowing the attenuation of plaque progression. Angiogenic assays showed that IL-19 induces lymphatic endothelial cell (LEC) proliferation, migration, and tube formation. RNAseq showed that IL-19 induces an angiogenic transcriptional program in LECs, and notably induces expression of Prox1, a master transcription factor of lymphangiogenesis, 6.2-fold. qPCR confirmed IL-19's induction of proliferation and angiogenic markers. We also analyzed aortic root sections of an atherosclerotic mouse model treated with injections of either IL-19 or saline. Preliminary results suggest an increase in lymphangiogenesis with IL-19 injections. Overall, these data suggest that IL-19 increases lymphatic vessel formation, potentially leading to increased RCT and decreased plaque burden. Future studies will confirm RCT and inflammatory cell egression by intravital microscopy.

35. **GASTRO-INTESTINAL SEPSIS WORSENED COGNITIVE AND BRAIN BARRIER FUNCTION IN A MOUSE MODEL OF ALZHEIMER'S DISEASE**

Divine Nwafor[1], Allison Brichacek[1], Sneha Gupta[1], Nina Bidwai[1], Candice Brown[1].
[1] West Virginia University

Emerging studies suggest a link between Alzheimer's disease (AD) and infection, the role of infection in AD/ADRD pathogenesis remains unclear. In this study, we demonstrate a role for sepsis in AD pathogenesis and elucidated the impact of sepsis on neurological and behavioral outcomes. Male and female APPSwDI/Nos2-/-(CVN-AD) mice were subjected to experimental sepsis. Cognitive deficits were assessed via the 2-day radial arm water maze (RAWM). Brain tissue was evaluated for vascular dysfunction (IgG and fibrinogen) and beta-amyloid burden. In a second cohort of mice, we examined neuroinflammation at 21 days post-sepsis. Our results showed significant deficits in spatial memory and learning in female ADCLP compared to ADsham in the RAWM. Brain IgG levels and fibrinogen infiltration were significantly increased in the female ADCLP compared to ADsham. We found that extravasation of IgG and fibrinogen in female ADCLP mice coupled increased beta-amyloid deposition. No differences were observed between male ADCLP and ADsham in all parameters. Quantification of neuroinflammatory indices in female ADsham and ADCLP mice at 21 days post-sepsis revealed a significant increase in microgliosis and astrogliosis. Taken together, our results suggest a novel interaction between infection and sex in exacerbating the mortality, neuropathology, and cognitive deficits associated with AD/ADRD.

36. **AGE-DEPENDENT DIFFERENCES IN THE IMMUNE RESPONSE TO HUMAN METAPNEUMOVIRUS**

Olivia Parks[1,2], Jie Lan[2], Yu Zhang[2], John V Williams[1,2,3].
[1] University of Pittsburgh School of Medicine, Pittsburgh. [2] Departments of Pediatrics University of Pittsburgh. [3] Microbiology & Molecular Genetics, University of Pittsburgh

OBJECTIVE: Human metapneumovirus (HMPV) is a leading cause of lower respiratory infections in young children, immunocompromised persons, and the elderly, resulting in high morbidity and mortality. Few studies have investigated why HMPV is more severe in the elderly. We hypothesize that severe HMPV infection in the elderly is caused by impairment of the CD8+ T cell response. **METHODS:** We developed an elderly mouse model of HMPV using 72-week-old mice. Aged mice and 6-week-old mice were infected intratracheally with HMPV and euthanized at different time points to measure viral titer and cellular immune response. **RESULTS**: Aged HMPV infected mice exhibit increased weight loss, higher clinical score, increased lung inflammation, delayed viral clearance, and increased CD8+ HMPV-tetramer+ cells co-expressing inhibitory markers PD-1, TIM-3, and LAG-3. Aged CD8+ HMPV-tetramer+ cells display functional impairment compared to young CD8+ T cells when stimulated with HMPV peptide, leading to decreased production of cytotoxic molecules such as granzyme B. **CONCLUSIONS:** Aged mice have a dysregulated CD8+ T cell response to HMPV, increasing disease and delaying viral clearance. Taken together, this project aims to understand the mechanistic differences in the aged host response to HMPV, which will help elucidate why HMPV infection in the elderly is more severe.

37. **WHAT IS THE PREDICTIVE VALUE OF INTRAOPERATIVE SOMATOSENSORY EVOKED POTENTIAL (SSEP) FOR POSTOPERATIVE NEUROLOGICAL DEFICIT IN CERVICAL SPINE SURGERY?**

Brian Rosario[1], Rajiv P Reddy[1], Jeremy D. Shaw[1], Robert Chang[1], D. Thirumala MD[1].
[1] University of Pittsburgh

INTRODUCTION: Cervical decompression surgery risks spinal cord and nerve root injury. Neuromonitoring with SSEPs is often used, but therapeutic value remains unknown. We hypothesized that significant intraoperative SSEP changes are predictive for postoperative neurological deficit, with irreversible changes indicating higher injury risk. **METHODS:** We conducted a systematic review and meta-analysis of literature for studies with patients undergoing cervical spine surgeries with intraoperative SSEPs. Inclusion criteria: 1) prospective/retrospective cohort studies, 2) elective cervical spine surgery (no aneurysm or trauma) with intraoperative SSEP monitoring, 3) reporting postoperative neurological outcomes, 4) sample size of 20 patients, 5) patients â‰¥ 18 years old, 6) English publication, 7) abstract included. **RESULTS:** Total cohort was 7,747 patients; rate of postoperative neurological deficits was 2.50% (194/7747). 7.36% (570/7747) incurred significant intraoperative SSEP changes. Incidence of postoperative neurological deficit in patients with intraoperative SSEP changes was 16.49% (94/570) while only 1.39% (100/7177) in patients without. Reversible and irreversible SSEP changes had sensitivities of 17.7% and 37.1% and specificities of 97.5% and 99.5%, respectively. **CONCLUSION:** SSEP monitoring is highly specific but weakly sensitive for postoperative neurological deficit following cervical spine surgery. Patients with new postoperative neurological deficits were nearly 27 times more likely to have significant intraoperative SSEP change. Loss of SSEP signals and irreversible SSEP changes indicate higher risk of injury than reversible.

38. **A CRISPR/CAS9-MEDIATED METHOD TO EDIT THE MAJOR ONCOPROTEIN OF EPSTEIN-BARR VIRUS**

Alex Reznik[1], Robert Zhang[1], Kathy HY Shair[1].
[1] University of Pittsburgh

Award: Exceptional Undergraduate Poster

DNA tumor viruses disrupt cellular equilibria and facilitate host cell transformation. Epstein-Barr virus (EBV) is a human tumor virus associated with nasopharyngeal carcinoma (NPC). While EBV infection is ubiquitous, it isn't clear why some individuals are at risk of developing NPC. One possibility may be the genetic variation in EBV's principle oncoprotein, latent membrane protein 1 (LMP1), which is phylogenetically classified into seven strains. Curiously, NPC tumor-derived LMP1 is conserved in comparison to sequences detected in saliva and blood. CRISPR/Cas9 can manipulate the host genome, but has not been exploited as a genetic-editing tool to manipulate herpesvirus genomes. Despite the multi-copy episomal nature of EBV genomes, genetic editing of EBV is in theory possible by repeat transfections of CRISPR/Cas9. We screened a panel of sgRNA candidates targeting the 5 and 3 of *LMP1* and selected efficient sgRNA pairs for generating an LMP1 knock-out (KO). Our goal is to introduce LMP1 mutants into the *LMP1* KO by transient expression of Cas9D10A nickases that encourage homology-directed repair and knock-in (KI) of a donor LMP1 template. This method for generating recombinant EBV with LMP1 mutants is anticipated to facilitate LMP1 functional mapping studies in human cells and elucidate the functional significance of LMP1 polymorphisms.

39. **REGRESSION PATTERNS OF CENTRAL SEROUS CHORIORETINOPATHY (CSCR) USING EN-FACE OPTICAL COHERENCE TOMOGRAPHY (OCT)**

Brian Rosario[1], Supriya Arora[1], Oliver Beale[1], Amrish Selvam[1], Abdul Rasheed Mohammed[1], Jay Chhablani[1].
[1] University of Pittsburgh School of Medicine

OBJECTIVE: We studied subretinal fluid(SRF) regression patterns in central serous chorioretinopathy (CSCR) on sequential en-face optical coherence tomography (OCT) and its relationship to leak locations. **METHODS:** We retrospectively sampled acute CSCR patients. Inclusion criteria: i)data availability, sequential OCT and OCT angiography(B scan and en-face OCT) biweekly until SRF resolution or 6 months,ii)single active leak. Exclusion criteria: i)presence of macular neovascularization or atypical SCR,ii)Diffuse pigment epitheliopathy,iii)multiple leaks. Serial en-face OCT scans were evaluated and SRF area was measured using Image J software. Correlation coefficient was calculated for SRF area regression rate and central retinal thickness(CRT) over first month of follow-up and time of SRF resolution. **RESULTS:** From 25 eyes;20 eyes demonstrated centripetal regression. 5 eyes demonstrated centrifugal regression. In eyes with leakage point <1000Âµ from fovea, 86% resolved in a centripetal fashion. In eyes with leak site >1000Âµ away from fovea, 70% eyes resolved centripetally. There was good correlation(r=-0.47,p=0.018) of NSD area rate regression during first month and resolution timing. In contrast, correlation was absent (r=-0.16,p=0.44) for CRT regression. **CONCLUSION:** En-face analysis of sequential OCTs of regressing CSCR demonstrated tendency for subfoveal SRF to resolve towards the end or a centripetal pattern of regression. 1 month SRF resolution prediction is better with SRF en-face area than CRT.

40. **SURGICAL INTERVENTION AND STENT PLACEMENT FOR PATIENT WITH MAY-THURNER SYNDROME AND DOUBLE INFERIOR VENA CAVA ANATOMY: CASE REPORT**

Brian Rosario[1].
[1] University of Pittsburgh

BACKGROUND: May-Thurner Syndrome (MTS) is caused by left iliofemoral vein compression by the right common iliac artery against vertebral bodies which can cause deep vein thrombosis (DVT) or venous flow obstruction resulting in lower extremity edema and tenderness. Double inferior vena cava (IVC) is a rare congenital anomaly arising from persistence of embryonic venous systems during fetal development. Although normally clinically insignificant, it may have significant implications in treatment of thromboembolic diseases. We report treatment of May-Thurner Syndrome in a patient with double IVC causing bilateral lower extremity edema. Surgical intervention is discussed. **PRESENTATION:** 65-year-old Caucasian male with left lower extremity ulcer and bilateral lower extremity lymphedema with intact valves in greater and lesser saphenous veins. No evidence of DVT. **SURGICAL INTERVENTION:** Venogram showed a double IVC; intravascular ultrasound showed stenosis of right and left iliac veins and left vena cava. Stenosis was treated bilaterally individually using standard angioplasty and stenting techniques. A 16mm x 100mm Venovo stent was placed in the left inferior vena cava. A second 16mm x 100mm Venovo stent was deployed into the left common iliac vein. **RESULTS/CONCLUSION:** Intervention resolved stenosis in affected vasculature. Within one week, venous flow returned to normal. The ulcer healed and lymphedema resolved bilaterally.

41. **HIGH-DEFINITION FIBER TRACTOGRAPHY (HDFT) MAY IDENTIFY TRACT-SPECIFIC OVERLAP WITH TUMORS IN PATIENTS WITH GLIOMAS AND PREOPERATIVE LANGUAGE DEFICITS**

Nikhil Sharma[1], Arka N. Mallela MD, MS[1], J Raouf Belkhir BA[1], Fang-Cheng Yeh MD, PhD[1], Bradford Z. Mahon PhD[1], Nduka Amankulor MD[1].

[1] University of Pittsburgh School of Medicine

INTRODUCTION: While maximum safe resection of glioma is well-established to increase overall survival, the effects and etiology of more subtle language deficits has not been well-established. Utilizing high-definition fiber tractography (HDFT), we sought to investigate the relationship between specific preoperative language deficits and injury to specific white matter (WM) tracts. **METHODS:** We performed a retrospective review of 31 patients who underwent glioma resection and had preoperative concern for language involvement. Patients underwent preoperative HDFT, structural MRI and postoperative MRI. We collected clinical data, demographics, and outcomes. For initial analysis, we examined overlap between tumor volumes and superior longitudinal fasciculus (SLF) I and II and the frontal-aslant tract (FAT). **RESULTS:** 24(77.4%) patients had high-grade glioma, 7(22.6%) had low-grade glioma. Left hemispheric (p=0.009), frontal lobe (p=0.018), and high-grade tumors (p=0.008) were associated with more severe preoperative language deficits. Tract-specific overlap analysis revealed moderate association between preoperative language deficit and higher overlap of tumor volume with left FAT (R=0.279) and left SLF II (R=0.156). Conversely, overlap of tumor with right SLF I and II was negatively associated with the presence of language deficit. **CONCLUSION:** HDFT can reliably identify WM tract-level changes that are associated with preoperative language deficits.

42. **AN EDUCATIONAL SURVEY OF THE CENTRAL PA GREEK AND MEDITERRANEAN DIASPORA REVEALS A NEED FOR INCREASED β -THALASSEMIA CARRIER STATUS SCREENING AND PUBLIC HEALTH EDUCATION**

Rhea Sullivan BS[1], Bridget Rafferty MPH, MD[1], Daniel McKeone MD, FAAP[1], Zissis Chroneos PHD[1].

[1] Penn State College of Medicine MSTP

β-thalassemia, a heritable hemoglobinopathy, has high prevalence in people of Mediterranean descent. With the increasing number of immigrants from the Mediterranean region relocating to Central Pennsylvania, the population density of β-thalassemia carriers is also increasing. Without a Pennsylvania state β-thalassemia newborn screening program and robust studies quantifying carrier burden, generations of this at-risk diaspora continue to have a gap in preventative healthcare. In order to address a potentially growing knowledge gap, an educational survey was administered to 141 members of this population to assess perception of disease symptoms, prevalence, inheritance, pathogenesis, treatment, diagnosis, and known carrier status. Overall, the population of participants aged 45 years and older felt more familiar with the disease compared to those that are younger. Unfamiliarity with the disease in younger cohort was prominent, with 25% of participants having never heard of the disease. With 44% of participants between 13-24 yrs having had no educational source contribute to their knowledge of β thalassemia in their lifetime, there is a need to increase educational efforts and sustainable screening access to this at-risk population.

43. **PREDATORY JOURNALS: DO NOT JUDGE JOURNALS BY THEIR EDITORIAL BOARD MEMBERS**

Leon Ruiter-Lopez[1], Sandra Lopez[1], Diego A. Forero[1].

[1] University of Pittsburgh

Award: Exceptional Undergraduate Poster

BACKGROUND: Predatory journals, pseudo-journals, are low-quality scientific journals with an exploitative business model. They fail to provide scientific rigor or transparency, failing to provide adequate quality control, editorial services, peer reviews, or proper indexing. **OBJECTIVE:** Given that often the quality of journals is based on their editors, the objective of this study was to quantitatively describe the profiles of members on editorial boards (MEBs) of predatory journals. **METHODS:** Information was retrieved from 1015 editors found on journals on Beall's list: country, university, position, and degree. The Scopus website was used to identify the number of citations, documents, and h-index. **RESULTS:** Presumed open-access predatory journals include several profiles as MEBs, including fake and unqualified editors, and very high-qualified scientists who are professors, medical doctors and/or had a PhD. Located in 74 different countries, most had an affiliation in the United States of America (USA) (44.4%). The median of publications per editor was 43, citations 664, and h-index 14. **CONCLUSIONS:** The results dispute the common belief that it is possible to identify predatory journals through their editorial boards. Scientists should not rely on editors to determine a predatory journal. If an author has doubt, the editors should be contacted.

44. **TESTING VARIANTS OF UNCERTAIN SIGNIFICANCE IN A HEK293T MODEL FOR VERY LONG-CHAIN ACYL-COA DEHYDROGENASE DEFICIENCY**

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Newborn screening identifies inborn errors of metabolism, often confirmed by DNA sequencing. Variants of uncertain significance (VUS) result in ambiguity in diagnosis and need for treatment. Mutations in ACADVL result in very long-chain acyl-CoA dehydrogenase deficiency (VLCADD), impairing energy production from long chain fatty acids. Over 300 VUSs have been reported in ACADVL. We developed an ACADVL null HEK293T cell line to determine pathogenicity of ACADVL VUSs. CRISPR/Cas9 genome editing was used to ablate ACADVL with dual guide RNAs targeting the catalytic site. We measured VLCAD protein by Western blot and enzyme activity by electron transfer flavoprotein fluorescence reduction enzymatic assay. Control or variant ACADVL plasmids were transfected into ACADVL null HEK293T. Droplet digital PCR confirmed homozygous deletion of the catalytic site. ACADVL null clones contained no residual VLCAD protein and had 84% reduction in measured enzyme activity (residual activity due to enzymes with overlapping specificity). Transfection of control ACADVL restored normal VLCAD protein. Four mutant alleles produced reduced VLCAD protein and/or activity. We generated an ACADVL null HEK293T that has no residual VLCAD protein and reduced measured enzyme activity. Transfection of plasmids with control or variant ACADVL allows us to perform functional studies to examine variant pathogenicity.

45. **ANTIBIOTIC USE IN ACUTE DIVERTICULITIS: ADMISSION RATES AND ANTIBIOGRAM COMPLIANCE IN A RURAL CENTER**

Niteesh Sundaram[1], Kevin Reilly[2], Luke Dombert[2], Robert Behm[3].

[1] University of Pittsburgh. [2] Binghampton University. [3] The Guthrie Clinic

BACKGROUND: Acute diverticulitis (AD) refers to the inflammation of colonic diverticulum. AD is typically self-limited and managed conservatively with or without antibiotics as an outpatient. The standard outpatient antibiotic regimen for AD involves 7-10 days of ciprofloxacin/metronidazole (Cipro/Flagyl), amoxicillin/clavulanate (Augmentin), or a cephalosporin. Providers must consider local antibiotic sensitivities before choosing a regimen. Our study aims to determine the admission rate for patients treated for AD as an outpatient and if they were on optimal antibiotic regimens. **METHODS/RESULTS:** A single-center retrospective review from January 1, 2016 to December 31, 2018 with 3,105 unique outpatient AD visits. Antibiotics were prescribed for 1,141 (36.7%) patients, with 780 (68.4%) receiving Cipro/Flagyl, 184 (16.1%) Augmentin, 36 (3.2%) Avelox, 24 (2.1%) cephalosporins, and 117 (10.3%) alternative regimens. The admission rate was 6.9% for patients treated with Cipro/Flagyl, 15.8% with Augmentin, and 0% with cephalosporins. There was significant inconsistency between the effectiveness of antibiotics versus our antibiogram: Cipro (93.1% vs 74%; $p < 0.01$) and Augmentin (84.2% vs 57%; $p < 0.01$). **CONCLUSION:** There was a lack of concordance between antibiotic selection and our antibiogram. Furthermore, our low admission rates for those receiving Cipro/Flagyl or Augmentin imply our antibiogram is inaccurate or that AD was misdiagnosed.

46. **IMPACT OF EDUCATIONAL ATTAINMENT, INCOME LEVEL, AND FAMILY HISTORY ON COLON CANCER SCREENING RATES IN A RURAL HEALTH SYSTEM**

Briana Sylvester[1], Giovanni Baiamonte[1], Niteesh Sundaram[2], Mohammad Yousef[3], Swadha Guru[3], Robert Behm[3], Matthew Lincoln[3], Burt Cagir[3].

[1] Geisinger Commonwealth School of Medicine. [2] University of Pittsburgh. [3] The Guthrie Clinic.

BACKGROUND: Colon cancer remains a significant cause of morbidity and mortality despite updated screening programs and an array of screening modalities. Our study aims to assess the prevalence of colon cancer screening among distinct patient populations in a rural community hospital setting. **METHODS/RESULTS:** A single-center retrospective review of 52,103 patients, of which 36,853 patients (70.7%) underwent colon cancer screening. Our study showed that rates of colon cancer screening were not significantly affected by bachelor's diploma status (R2: 0.06, F(1,12): 0.78, p: 0.39), high school graduation status (R2: 0.12, F(1,12): 1.74, p: 0.21), or median household income (R2: 0.01, F(1,18): 0.29, p: 0.59). Of the 3,417 total patients who had a family history of colon cancer, 2,957 (86.5%) were screened. Individuals with family history of colon cancer were more likely to be screened than those without (86.5% vs 69.6%; $p < 0.01$). **CONCLUSION:** In our population, traditional metrics associated with superior health outcomes were not shown to affect colon cancer screening rates. Patients with family members personally affected by colon cancer correlated with a higher rate of colon cancer screening. Our findings emphasize the responsibility of providers to provide patient education about colon cancer screening as it is an esoteric topic.

47. **UNDERSTANDING THE ETIOLOGY OF INFLAMMATORY BOWEL DISEASE IN A NOVEL LCK VARIANT**

Ngoc Truong[1], Victor Lui[2], Elena Hsieh[2].

[1] Cornell University, [2] University of Colorado Anschutz Medical Campus

Lymphocyte-specific protein-tyrosine kinase (LCK) is a tyrosine kinase that initiates T cell receptor (TCR) signaling upon T cell activation through a network of cell surface receptors and proteins. A novel LCK mutation (Pro440Ser) was identified in two siblings presented with recurrent viral and fungal infections, failure to thrive, and inflammatory bowel disease (IBD) since infancy. A mouse model harboring the knock-in homologous mutation recapitulated human immunological and clinical phenotype. Our goal is to determine the underlying immunopathology of IBD using Lck mutant mice. We hypothesize that deficiency of regulatory T cells (Tregs) contributes to IBD development. We developed an optimized antibody panel that identifies and measures T cell populations pertinent to disease, such as antigen-experienced (CD44+ CD49d+) and regulatory (CD25+ FoxP3+) T cells. We adoptively transferred wild-type (WT) Tregs into Lck mutant mice and recorded IBD progression to determine whether Treg deficiency is an underlying contributor. 12 weeks after adoptive transfer, Lck mutant mice that received WT Tregs did not develop IBD while those that didn't receive exogenous Tregs did not, though longer incubation periods are needed for definitive conclusions. Future findings will advance our understanding of IBD in the context of disturbed T cell development from defective TCR signaling.

48. **TRIBBLES-1 AND ITS CORRELATION WITH CORONARY ARTERY DISEASE**

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Coronary artery disease (CAD) is a deadly chronic disease that affects the coronary arteries of the heart. CAD is characterized by the accumulation of fatty deposits in the walls of the coronary arteries that can harden into plaques restricting oxygen flow into the heart. These plaques can rupture, triggering heart attacks that can lead to sudden death. Risk factors include a smoking, poor diet, lack of physical activity, diabetes, hypertension, family history/genetic predisposition, high cholesterol, high levels of lipids and lipoproteins such as total cholesterol, and low-density lipoprotein-Cholesterol (LDL-C), and triglycerides. Genome-wide association studies (GWAS) have been broadly used to identify common genetic variants associated with diseases such as (CAD) and identify novel aspects of disease biology. The most common type of variants examined by GWAS are single nucleotide polymorphism (SNPs), which are biological single nucleotide variations between individuals. In some cases, single variants or combinations that define polygenic risk scores, allow researchers to predict an individual's response to certain drugs, susceptibility to environmental factors such as toxins, and risk of developing diseases. This poster looks at the recent studies which have started to unravel the genetic architecture of CAD as well as CAD response and prevention.

49. **MEDIAN ARCUATE LIGAMENT SYNDROME MASQUERADING AS FUNCTIONAL ABDOMINAL PAIN SYNDROME**

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BACKGROUND: Median arcuate ligament syndrome (MALS) refers to anatomical compression of the celiac artery and/or ganglion by fibrous attachments of the median arcuate ligament. It typically presents as a vague constellation of abdominal symptoms that are often initially attributed to various other gastrointestinal pathologies; thus, it can be very difficult to diagnose. Surgical decompression is an effective and safe treatment for this condition. **CASE SUMMARY:** We present a case of median arcuate ligament syndrome in a 68-year-old woman. Her diagnosis and treatment were delayed as her symptoms were felt to be the result of functional abdominal pain syndrome. Once the diagnosis of MALS was confirmed, the condition was ultimately treated by laparoscopic release of the median arcuate ligament. **CONCLUSION:** This case demonstrates that surgical decompression of the celiac axis is an effective treatment for median arcuate ligament syndrome and highlights the importance of continuing to reassess the clinical picture of patients labeled with functional abdominal pain syndrome.

50. **STEADY STATE PATTERN ELECTRORETINOGRAM PREDICTS CHANGES IN OPTICAL COHERENCE TOMOGRAPHY IN GLAUCOMA SUSPECTS**

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BACKGROUND: Steady state pattern electroretinogram (ssPERG) parameters have been shown to be associated with structural changes on optical coherence tomography in glaucoma patients. However, no previous studies have investigated the use of ssPERG parameters in predicting structural changes in glaucoma suspects. **METHODS:** Patient data from glaucoma suspects, identified based on suspicious optic disc features and glaucoma risk factors, were prospectively collected. Statistical analyses were performed using ssPERG parameters Magnitude (Mag), Magnitude D (MagD), and MagD/Mag ratio and OCT measurements. **RESULTS:** A total of 49 eyes of 26 patients were included. ssPERG parameters Mag and MagD were significantly correlated to superior, inferior, and average RNFL thicknesses. All ssPERG parameters were significantly correlated with average and minimum GCL/IPL thickness and the inner macular sector thicknesses. Mag and MagD were found to significantly predict the superior, inferior, and average RNFL thickness. All ssPERG parameters were found to significantly predict GCL/IPL thickness in all sectors as well as all inner macular sector thicknesses. **CONCLUSION:** In glaucoma suspects, ssPERG can predict structural changes in RNFL, GCL/IPL and macular thicknesses on OCT and may serve as a more sensitive screening tool in patients with early glaucoma compared to current methods.

51. **ANNOTATING DATA TO TRAIN MACHINE LEARNING MODELS TO CLASSIFY CITATIONS IN BIOMEDICAL PAPERS**

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References provide the foundation and context for new biomedical science. Previous work defined keystone citations as references that logically support a paper's claims. This study aims to test whether methods keystone citations, defined as citations supporting research methods and materials, can be consistently identified by different people (i.e., consensual). Four students annotated citations from biomedical papers using a prior manual. Afterwards, they compared and discussed the results and updated the manual accordingly. Substantial inter-annotator agreement was found for the upper-level categories is methods keystone and not methods keystone (Cohen's kappa = 0.671), supporting that they are consensual. During the process, we discovered several subcategories. For the is method keystone category: used the method, used the material, used output of a paper in methods, and justify decisions made in the design of the methods. For the not methods keystone category: cited as background information, citing/cited agree, citing/cited disagree, used in knowledge synthesis, and qualifying method. This study furthered our understanding about how references were used to support a paper's claims. Future research is required to determine whether the subcategories are consensual and exhaustive, build a training dataset, and train supervised machine learning models to identify methods keystone citations.

52. **MICROSTRUCTURE OF EQUINE HOOF WALL**

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Equine hoof is highly impact resistant and lightweight, and the ability to absorb high energy is attributed to its hierarchical structure. Tubules are embedded within the lamellar intertubular matrix and have areas made of keratin crystalline intermediate filaments and amorphous keratin cells. The tubular and intertubular regions at the microscale are investigated using micro-computed tomography and image preprocessing with ImageJ. Throughout the hoof walls, tubules have circular cross-sections near the palmar region and become more elliptical near the dorsal region. The elliptical cross-sections closest to the dorsal region are the result of permanently tubule deformation from galloping. Preliminary studies assume that tubules are completely hollow, but with new micro-computed tomography analysis, we observe that the tubules are partially filled. The tubules have multiple bridges, which vary in frequency, thickness, and orientation relative to the length of the whole tubule. We believe that the bridges that fill the tubules are made of soft keratin and that the structural differences between different bridges are correlated to the mechanical properties of the hoof wall.

53. **GETTING A GLIMPSE INTO NEURO-OPHTHALMOLOGY MALPRACTICE: A REVIEW OF THE WESTLAW DATABASE**

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BACKGROUND: Neuro-ophthalmologic conditions are at a higher risk of misdiagnosis compared to other ophthalmic conditions. Increased awareness of the most common diagnostic errors in neuro-ophthalmology that lead to malpractice claims can allow ophthalmologists to further improve their diagnostic workup to reduce delays in diagnosis and management, while also mitigating the risk for litigation. **METHODS:** Malpractice trials in the Westlaw Legal Database involving cases of neuro-ophthalmologic diagnostic errors or failures by ophthalmologists were included. **RESULTS:** A total of 44 cases were included, all citing failure to diagnose as the main reason for litigation. The most common diagnoses missed were cerebrovascular pathologies (29.5%), intracranial tumors (27.3%), and giant cell arteritis (25.0%). The majority of verdicts were in favor of the defendants (47.7%). After adjusting for inflation, the average amount awarded was $1,909,501. **CONCLUSION:** Nearly half of the cases resulted in a defendant verdict. Settlement and plaintiff verdicts were costly, with average awards of approximately two million inflation-adjusted dollars. Failure to diagnose cerebrovascular pathologies was the most common diagnostic error followed by failure to diagnose intracranial tumors and GCA. It is crucial for ophthalmologists to be aware of the most common pitfalls that lead to misdiagnosis or delays in diagnosis of neuro-ophthalmologic conditions.

54. **EFFECT OF CANDIDATE CIS-REGULATORY ELEMENTS ON GENE REGULATIONS**

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Many studies have been trying to find the possible relations between candidate cis-regulatory elements (cCREs) and their target gene. It still remains unclear how the cCREs influence target genes and if cCREs are corresponding with certain target genes. Based on the benchmark study, we utilize single-cell analysis to categorize the cCREs with the possible target genes using multiple standards. Using the method of clustering, the frequency of cCREs appearing in each category has been analyzed. We found that on certain chromosomes, the cCREs have higher counts in one or few categories than others. The study may help with the development of future regulatory elements and gene prediction models and lead to possible explanations of the role cis-regulatory elements played in gene regulations.

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