Yale Center for Clinical Investigation

ROBERT S. SHERWIN YCCI ALL SCHOLAR DAY

Abstracts

Friday, June 13, 2025
The Anlyan Center, N107
Yale School of Medicine
300 Cedar St.
New Haven, CT 06519

Selected Oral Presentation Abstracts

Speaker 1 Abstract

l-carnitine Drives Pyrin Inflammasome Activation Through Mevalonate Inhibition

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Red meat consumption is epidemiologically associated with numerous diseases of chronic inflammation including cardiovascular disease, diabetes, inflammatory bowel disease, and cancer. However, there is no clearly established mechanism by which red meat drives inflammation. As many of the diseases promoted by red meat are mechanistically tied to inflammasome-mediated IL-1β in model organisms and clinical studies, we hypothesized that red meat contains an inflammatory metabolite or precursor that induces inflammasome activation. The nonessential, nonproteinogenic amino acid L-carnitine is highly abundant in red meat compared to healthier poultry, fish, and plant-based foods. We found that in LPS challenged mice and LPS-primed human and murine macrophages, L-carnitine promotes canonical Caspase-1- and ASC-dependent inflammasome activation defined by Caspase-1 and IL-1β cleavage and secretion. Using RNA sequencing, we determined that L-carnitine treatment of LPS-primed macrophages resulted in transcriptional reprogramming characterized by reduced Rho GTPase activity and decreased cholesterol synthesis, which led to the identification of Pyrin as the inflammasome sensor of L-carnitine. Lastly, by generating a novel conditional knockout for the high-affinity L-carnitine transporter SLC22A5, we determined that myeloid-specific SLC22A5 targeting is a potential therapeutic strategy for inhibiting L-carnitine-induced inflammation. Our future work is focused on examining the relevance of this pathway in inflammatory and autoimmune conditions in which diet, L-carnitine, SLC22A5, and Pyrin are implicated in epidemiologic, metabolic, and genome-wide association studies.

Speaker 2 Abstract

Implementing Accelerated Resolution Therapy (ART) to Improve Sleep and Post Traumatic Stress (PTSD) Symptoms Among Black People Living with HIV

Uzoji Nwanaji-Enwerem PhD, FNP-BC, MSN, RN, BSN, Leo Wilson, PhD, MPH, Theddeus Iheanacho, MBBS, DTM&H, Sangchoon Jeon PhD, Soohyun Nam, PhD, APRN, ANP-BC, FAHA, FAAN, LaRon Nelson PhD, RN, FNP, FNAP, FNYAM, FAAN

Background: Black individuals living with HIV experience disproportionately high rates of trauma exposure and sleep deficiencies, yet trauma-focused interventions are rarely integrated into HIV clinical care. This pilot study evaluated the feasibility and preliminary efficacy of Accelerated Resolution Therapy (ART)—a brief, evidence-based psychotherapy that uses eye movements and guided visualization to reduce the emotional intensity of traumatic memories—for improving PTSD symptoms and sleep health in HIV clinical settings.

Methods: The study was conducted across four HIV clinics—two in Atlanta, GA and two in Broward County, FL. Clinicians (n=4), one per clinic, were trained in ART delivery. Each therapist enrolled five patients (N=20) to receive ART. Participants completed assessments at baseline, post-intervention, and 1-month follow-up. Outcomes included PTSD symptom severity (PCL-5), sleep quality (PSQI Global Score), and sleep-related PTSD symptoms (PSQI Addendum). A repeated measures ANOVA assessed changes over time.

Results: Significant improvements were observed across all outcomes. PSQI Global Scores declined from a baseline median of 15.5 to 10.0 post-intervention and 9.0 at follow-up ($F(1.664, 31.61) = 44.32$, $p < .0001$). PSQI Addendum Scores decreased from 13.5 to 4.0 post-intervention and maintained at follow-up ($F(1.620, 26.73) = 41.06$, $p < .0001$). PCL-5 scores dropped from 36.0 at baseline to 18.0 post-intervention and further to 13.0 at follow-up ($F(1.265, 24.04) = 30.75$, $p < .0001$).

Conclusions: This pilot demonstrates promising efficacy of ART in reducing PTSD symptoms and improving sleep among Black people living with HIV. It also highlights a feasible and scalable model for implementing trauma-informed care in HIV clinical settings. Findings will inform the next phase of our research focused on larger-scale implementation and mechanistic evaluation.

Speaker 3 Abstract

Correlation Between Neighborhood- and Patient-Level Socioecological Determinants of Health Assessed Before Elective Major Surgery

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Introduction
Due to their accessibility, neighborhood-level indices have been utilized as proxies for patient-level SEDOH status. However, neighborhood-level indices are prone to ecological fallacy. This study evaluated the correlation between neighborhood- and patient-level SEDOH domains obtained from patients before elective major surgery.

Methods
This study analyzed a prospective SEDOH assessment tool involving adult patients undergoing elective major surgery within a statewide health system from July 2023 to January 2025. Patient addresses from the EHR were geocoded to U.S. 2020 census data for Area Deprivation Index (ADI) and Social Vulnerability Index (SVI). A patient-reported assessment tool, SEDOH-88, was administered to patients before surgery. Higher scores on the three measures indicate a greater risk. A high SEDOH-88 score was defined as above the 75th percentile.

Results
Of 345 patients contacted, 234 (67.8%) patients agreed to participate, with a median age of 65.0 [IQR, 52.8-72.9], 56.0% (n=131) female, 7.7% (n=18) non-white, and 7.7% (n=18) Hispanic. Overall, the 30-day complication rate was 15.0%. Median ADI score was 31.5 (IQR, 20.3-45.0), median SVI score was 0.29 (IQR, 0.12-0.58), and median SEDOH-88 score was 5 (IQR, 3-8). ADI and SVI had poor discrimination with the SEDOH-88 score, with an AUC of 0.624 and 0.665, respectively. On multivariable logistic regression, high SEDOH-88 was associated with higher deprivation on SVI (OR, 4.86, 95% CI, 1.47-16.33, p=0.010), whereas SEDOH-88 was not associated with neighborhood deprivation on ADI (OR, 1.01, 95% CI, 1.00-1.03, p=0.131). Neither ADI (rho=0.14, p=0.028) nor SVI (rho=0.20, p=0.002) correlated well with SEDOH-88.

Discussion
This study revealed limited agreement between two commonly used neighborhood-level indices and a comprehensive patient-reported socioecological needs assessment obtained before elective major surgery. Neighborhood-level indices identify broad ecological associations that can inform population health policies and resource allocation. Nonetheless, this study cautions against overreliance on neighborhood-level characteristics to stratify individual patients before surgery.

Speaker 4 Abstract

Investigating the impact of common and rare variants on the risk for body-focused repetitive behavior disorders

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Objectives/Goals:
This study aims to characterize the genetic architecture of body-focused repetitive behavior disorders (BFRBs) by examining the distribution of common and rare genetic variants associated with related psychiatric disorders in parent-offspring trios, where the proband has trichotillomania or excoriation disorder.
Required

Methods/Study Population:
This study uses whole-genome array data in 100 parent-offspring trios (309 individuals) where the child has a diagnosis of trichotillomania or excoriation disorder. To assess common variant risk in these trios, polygenic risk scores (PRS) were calculated using summary statistics from the largest available OCD, ADHD, Tourette's disorder, and cross-disorder genome-wide association studies. The polygenic transmission disequilibrium test (pTDT) was used to determine if PRS transmitted to probands from parents is higher than expected by chance. In these same trios, we also examined the frequency of rare de novo and inherited copy number variants (CNVs). Future analyses will investigate how rare CNVs and rare sequence variants from DNA sequencing data impact the transmission of polygenic risk in these same trios.

Results:
Probands with a BFRB show an elevated burden of common variant risk for OCD compared to their parents (pTDT p-value<0.05), suggesting the role of common variants in these families and shared genetic factors with OCD. We also identified rare CNVs in the BFRB parent-child trios, which harbor genes previously associated with neurodevelopmental disorders and are enriched for biological pathways in exploratory analyses. We expect that there will be a negative correlation between the presence of rare variants (including CNVs and gene-damaging sequence mutations) and PRS, as previously described in other neuropsychiatric conditions.

Discussion/Significance of Impact:
Our initial findings provide new insight into how common and rare genetic factors may influence individual risk for BFRBs. Our findings add to our fundamental understanding of the genetic architecture and biological underpinnings of BFRBs.

Poster Abstracts

Poster Abstract 1

Synaptic Density in Frontolimbic Brain Regions and Association with Correlates of Suicide Risk in Middle to Late Adulthood

Ruth H. Asch[1,2], Karina Moisieienko[1], Mia Weed[1], David C. Steffens[3], Richard E. Carson[4,5], and Robert H. Pietrzak[1,2], Irina Esterlis[1,2,4]

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Background.
Adults 65 and older have a higher risk of dying from suicide than any other age group. Therefore, studying suicide risk in this population is crucial. Given prior research implicating stress-related psychiatric disorders and increasing age are independently associated with synaptic deficits, here we aimed to examine the effect of living with stress-related psychiatric disorders on synaptic density and relationships between synaptic density and psychological factors that may be associated with suicide risk specifically in middle to late adulthood.
Methods.
Positron emission tomography (PET) with [^{18}F]SynVesT-1 was used to quantify synaptic vesicle glycoprotein 2A (SV2A) as a proxy measure of synaptic density in frontolimbic brain regions of interest (ROIs) in a total of 55 older adults (57.2±11.5 years), including individuals with any mood disorder diagnosis (clinical group; n=21, 14 female) and unaffected comparison individuals (control; n=34, 14 female). Group differences in synaptic density and relationships with psychosocial corelates of suicide risk were examined.
Results.
Frontolimbic synaptic density was lower in the clinical group relative to controls ($F_{5,45}$=3.48, p=0.010), and was most notably lower in frontal ROIs among individuals with more severe depressive symptoms (n=7; p_{adj}≤0.001) or scan-day suicidal ideation (n=6; p_{adj}≤0.027) relative to controls. In addition to worse depressive symptoms (r=-0.37, p=0.005), lower frontolimbic synaptic density was associated with worse anxiety (r=-4.07, p=0.002) and impulsivity/lack of perseverance (r=-0.419, p=0.001).
Conclusions.
We provide novel evidence of synaptic deficits in older adults with mood disorders and relationships between synaptic density and symptom severity. Future research aimed at identifying psycho-social and biological mechanisms driving synaptic deficits in later life depression and the role these synaptic deficits may play in conferring suicide risk are warranted.

Poster Abstract 2

Sex-differences in Molecular and Synaptic Mechanisms Contributing to Stress-related Pathology: Insight from a Synaptic Density PET and Proteomic Study in Rats

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Background.
Preclinical research indicates chronic stress can induce synaptic loss in corticolimbic brain regions important for emotional regulation and cognition. Synaptic density can be measured in humans with stress-related pathology using radioligands targeting synaptic vesicle protein 2A (SV2A), such as [^{18}F]SynVesT-1, and positron emission tomography (PET), but this method has yet to be investigated in animal models of stress. Therefore, this study aimed to evaluate the potential of using PET to quantify synaptic density following chronic stress in rats and explored relationships with behavior and protein expression.

Methods.
Rats were exposed to Chronic Unpredictable Stress (CUS; n=24/sex) and compared with controls (n=12/sex). Sucrose preference and novel object recognition (NOR) were used to assess stress-related behavioral phenotypes. *In vivo* PET with [^{18}F]SynVesT-1 was used to quantify SV2A as a proxy measure of synapses in a subset of rats (n=8-9/group/sex). After PET imaging, prefrontal cortex (PFC) and hippocampal proteins were quantified *via* LC MS/MS (n=5/group/sex), followed by linear regressions evaluating relationships with PET measures. Additionally, differentially abundant proteins between the CUS and control groups were identified, followed by Ingenuity Pathway Analysis to examine molecular profiles associated with stress exposure.

Results.
Synaptic density was lower in PFC (p=0.012) and hippocampus (p=0.017) in CUS rats relative to control and correlated with blunted sucrose preference (r=0.35, p=0.042) and impaired NOR (r=0.35 p=0.045). Differentially expressed proteins and enriched pathways were minimally overlapping between males and females. Proteins implicated in synaptogenesis and neurodegeneration were positively and negatively correlated, respectively, with the PET measure of synaptic density.

Conclusions.
We demonstrate [^{18}F]SynVesT-1 and PET provide an *in vivo* measure of synaptic density in a rodent model of chronic stress and highlight sex-differences in responses to chronic stress. Critically, synaptic PET imaging has the potential to facilitate translational research investigating synaptic mechanisms in stress-related pathology and treatment response.

Poster Abstract 3

Exploring Pregnant Individuals' Perspectives on the Monitoring and Research of Fetal Health: A Focus Group Study Across Income Levels

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Maternal perception of fetal movement is one of the earliest ways pregnant people assess fetal well-being. While pregnant people are intuitively aware of fetal movement, little is known about how individuals engage with fetal monitoring or experience fetal movement. This gap is particularly pressing for low-income populations, who may have different healthcare access, experiences, and resources compared to their high-income counterparts. To better understand maternal experiences with fetal monitoring and movement, we conducted a qualitative study using income-stratified focus groups. We recruited pregnant people in their third trimester, grouping them by low and high income to examine how socioeconomic differences shape experiences. One high-income focus group has been completed, with additional groups planned. Focus group discussions were audio recorded and will be analyzed using a six-phase thematic analysis framework. Coding followed an inductive approach, capturing participants' own language and conceptualizations. Five initial codes emerged: (1) Reassurance vs. stress: internal fetal movement typically reassured participants, whereas external monitoring tools (e.g., Doppler, kick counts) often evoked stress; (2) Attentional shifts to movement: reduced movement heightened maternal attention toward movement and prompted self-monitoring; (3) Changes across trimesters: early pregnancy was marked by anxiety and greater reliance on external tools, while later stages was marked by reduced fetal health-related anxiety; (4) Reluctance to seek medical care: participants preferred to self-manage concerns rather than contact providers; and (5) Fetal movement as both discomfort and bonding: movement could be physically uncomfortable yet emotionally meaningful, reinforcing maternal–fetal bonding. These insights will inform the development of a standardized questionnaire to assess maternal attitudes toward fetal health monitoring. Findings underscore the need to balance the benefits of fetal monitoring with potential psychological burdens, particularly across income levels. Future work will explore how these attitudes relate to maternal-fetal attachment and anxiety.

Poster Abstract 4

Prevalence and Patient-Level Factors Associated with Common Antibiotic Allergy Labels Among Patients Undergoing Hematopoietic Stem Cell Transplants: A Cross-Sectional Study

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Background: Antibiotic allergy labels (AALs) are common and often limit appropriate treatment. Patients who have undergone hematopoietic stem cell transplants (HSCT) may be at high-risk for harm from AALs, however, few studies have focused on AALs in this population.
Objective: We sought to determine the prevalence and correlates of penicillin, cephalosporin, and sulfonamide allergy labels prior to HSCT. We additionally assessed the incidence of antibiotic allergy testing prior to transplant.
Methods: Using data from an academic transplant center, we conducted a cross-sectional analysis of adult patients who underwent HSCT between 1/1/2013-11/25/2023. Adjusted multivariable models were used to determine independent associations between sociodemographic, clinical, and structural factors and AALs.
Results: Among 1,329 patients who underwent HSCT (mean age 60.0 years (standard deviation [SD] 13.3; 38.2% female; 22.4% Black, 74.2% White; 10% Hispanic/Latino), 18.4% had at least one AAL. 12% patients had a penicillin allergy label (PAL), 6% had a sulfonamide allergy label, and 2% had a cephalosporin allergy label. In adjusted models, female sex was associated with higher odds of having an AAL (aOR 2.42, CI 1.80-3.26) and a PAL (aOR 1.72, CI 1.21-2.42). Compared with White patients, Black patients demonstrated lower odds of having any AAL (aOR 0.49, CI 0.27-0.88). Only 0.23% (3/1,329) patients underwent antibiotic allergy testing prior to transplant.
Conclusions: Among patients undergoing HSCT, AALs were common, associated with female sex and White race, and rarely evaluated. Future studies should examine reasons for differences in AALs by sex and race, and focus on promoting guideline-concordant evaluation of AALs.

Poster Abstract 5

Nanoscale imaging of pT217-tau in aged rhesus macaque entorhinal and dorsolateral prefrontal cortex: Evidence of interneuronal trafficking and early-stage neurodegeneration

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Background: pT217-tau is a novel fluid biomarker that predicts onset of Alzheimer's disease (AD) symptoms, but little is known about how pT217-tau arises in brain, as soluble pT217-tau is dephosphorylated postmortem in humans. Aging macaques naturally develop tau pathology with the same qualitative pattern and sequence as humans, including cortical pathology.
Methods: The etiology of pT217-tau in aging brains can be probed in rhesus macaques, where perfusion fixation allows capture of phosphorylated proteins in their native state. We utilized multi-label immunofluorescence and immunoperoxidase and immunogold immunoelectron microscopy to examine the subcellular localization of early-stage pT217-tau in entorhinal cortex (ERC) and dorsolateral prefrontal cortex (dlPFC) of aged rhesus macaques with naturally occurring tau pathology and assayed pT217-tau levels in blood plasma using an ultra-sensitive Nanoneedle approach.
Results: pT217-tau labeling is primarily observed in postsynaptic compartments, accumulating in: 1) dendritic spines on the calcium-storing smooth endoplasmic reticulum spine apparatus near asymmetric glutamatergic-like synapses, and 2) in dendritic shafts, where it aggregated on microtubules, often "trapping" endosomes associated with Aβ42. The dendrites expressing pT217-tau were associated with autophagic vacuoles and dysmorphic mitochondria, indicative of early neurite degeneration. We observed trans-synaptic pT217-tau trafficking between neurons within omega-shaped bodies and endosomes, specifically near excitatory, but not inhibitory synapses. We also examined pT217-tau in blood plasma in macaques across age-span and observed a statistically significant age-related increase in pT217-tau.
Conclusions: We provide direct evidence of pT217-tau trafficking between neurons near synapses to "seed" tau pathology in higher brain circuits, interfacing with the extracellular space to become accessible to CSF and blood. The expression of pT217-tau in dendrites with early signs of degeneration may help to explain why this tau species can herald future disease.

Advances in Alzheimer's disease (AD) have revealed a novel fluid biomarker, pT217-tau in CSF and plasma, that predicts AD prior to cognitive deficits. Understanding the role of pT217-tau is important in assessing efficacy of novel treatments aimed at early-stage disease. However, it is unknown why pT217-tau is effective in predicting brain pathology, as little is known about early, soluble pT217-tau brain expression. These questions are difficult to address in humans, as soluble p-tau is rapidly dephosphorylated postmortem, and PET scans detect late-stage, fibrillated tau. However, the etiology of pT217-tau can be probed in non-human primate models of sporadic AD. Our data help to explain why pT217-tau predicts degeneration in AD and how it gains access to CSF and plasma to serve as a fluid biomarker.

Poster Abstract 6

Predicting Longitudinal Obesity-Related Outcomes Using Psychological Factors and DNA Methylation in a Cohort of Highly Stressed Parents

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Introduction: Prolonged obesity increases the risk of comorbidities such as type 2 diabetes, and while new treatment options such as GLP1s are effective, access is limited. Thus, identifying individuals in greatest need of such intensive treatment may improve treatment outcomes and reduce treatment risks.
Methods: This study leverages an ongoing randomized controlled trial targeting parenting behavior as a longitudinal cohort to explore psychological and epigenetic predictors of obesity-related outcomes in highly stressed parents with obesity (N = 195). We assess how baseline trauma, emotion regulation, and DNA methylation markers predict changes in BMI, HgbA1C, and biological aging in the parents over a two-year follow up period. We used baseline values of the McCartney-BMI DNA methylation score to predict changes in BMI and HgbA1C. Analyses used linear mixed-effects models accounting for group and age with individual/cohort random intercepts.
Results: We find that a history of trauma predicts changes in BMI ($p < 0.0001$) and HgbA1C ($p = 0.009$), with higher trauma scores predicting worsening metabolic markers but paradoxically lower BMI. Baseline emotion regulation predicted BMI changes ($p < 0.0001$), with poorer emotion regulation linked to weight gain. Baseline trauma also predicted epigenetic age (as measured via GrimAge), with higher trauma predicting age acceleration ($p = 0.003$). Furthermore, we find that baseline methylation scores can predict changes in BMI over the two-year follow-up period ($p < 0.0001$), even after accounting for baseline BMI ($p = 0.013$). Baseline methylation scores also predicted HgbA1C after 2 years.
Discussion: These findings suggest that baseline psychological and epigenetic measures may contribute to prediction of obesity-related outcomes over time, even accounting for baseline BMI and HgbA1C. With sufficient development and validation, these variables could help identify patients at greatest risk of worsening obesity and in need of more intensive treatment.

Poster Abstract 7

Rescuing neoantigen-specific CD8+ T-cell immunity from tumor-microenvironment-mediated immunosuppression in pancreatic cancer

Jeremy B. Jacox, MD, PhD; Chaitanya Vattem, MSc; Gena Foster, MD; Dhruvi Shah, MSc; Jin Woo Yoo, MD; Jess Santana, MS; Akin Sogunro, MPhil; Nikhil Joshi, PhD; Mandar Muzumdar, MD, PhD

Background: Pancreatic ductal adenocarcinoma (PDAC) is highly lethal due to early metastasis and poor immunotherapy responses, driven by a desmoplastic tumor microenvironment (TME) and low immunogenicity. However, long-term human PDAC survivors exhibit higher neoantigen expression, predicted immunogenic neoepitopes, and active T-cell infiltration, suggesting T-cell mediated immunity influences PDAC progression. By contrast, most classical pre-clinical (KPC-based) murine models have low neoantigen burden, limiting their utility for studying anti-tumor T-cell immunity.

Methods: We developed NINJA PDAC, a novel transplantable murine PDAC organoid model, to study neoantigen-specific anti-tumor T-cell responses and their interactions with the TME. The NINJA system affords temporal control of LCMV-based neoantigen (GP33 and GP66) expression in *Kras*-mutated, p53-deficient PDAC organoids, mirroring human PDAC neoantigen affinity for MHC-I. NINJA PDAC orthotopic transplants exhibit physiologic stroma, anatomically correct local-to-metastatic tumor progression, inducible neoantigens, measurable T-cell responses, and T-cell dependent rejection. Using adoptive T-cell challenge, macrophage depletion, checkpoint and chemokine inhibition, and leptin-deficient murine models, we explored rescue of the impact of the TME on anti-tumor CD8+ effector T-cell responses at baseline and in obesity.

Results: Early NINJA neoantigen induction before tumor TME formation leads to partial suppression of tumor growth in a CD8+ T-cell dependent manner. By contrast, late induction post-TME formation revealed heterogenous neoantigen-specific T-cell responses, with tumors splitting into T-cell responders versus non-responders, leading to neoantigen clearance or persistence, respectively. TME differences drive these responses, as activated CD8+ T-cells in non-responders arrest at the tumor periphery alongside cancer-associated myofibroblasts (CAFs) and tumor-associated macrophages (TAMs). Complete TAM depletion (using anti-CSF1/clodronate liposomes) and genetic ablation of B-cells were both insufficient to rescue non-response of T-cells, which remain excluded peripherally. By contrast, fibroblast-derived CXCL12-CXCR4 signaling arrests CD8+ T-cells at the tumor margin, impairing neoantigen-specific tumor clearance. CXCR4-inhibition (AMD3100) partially rescues the response phenotype, and may be further enhanced by combined PD1 checkpoint inhibition. Finally, leptin-deficient obese mice transplanted with NINJA PDAC had larger tumors, fewer neoantigen-specific CD8+ effector T-cells, and altered T-cell activation. This argues that obesity-induced changes in the TME impair neoantigen-specific CD8+ effector T-cells, highlighting obesity as a key host factor in modulating the anti-tumor T cell response.

Conclusions: NINJA PDAC affords a high-fidelity toolset to study how the TME affects murine neoantigen-specific anti-tumor T-cell responses, further modulated by host factors like obesity, with the potential to accelerate the development of new combination immunotherapies.

Poster Abstract 8

1/f Slope and Alpha Peak Frequency as Early Markers of Hyperexcitability in Amnestic and Non-Amnestic Mild Cognitive Impairment

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The aperiodic component of the EEG signal (1/f slope) has recently gained attention as a sensitive marker of cortical excitability, which has been associated with dementia and Alzheimer's Disease. As dementia continues to pose a growing public health challenge, identifying early, non-invasive markers of neural dysfunction is critical for timely diagnosis and intervention. This study investigates whether the aperiodic exponent and individual alpha peak frequency can differentiate between healthy aging and Mild Cognitive Impairment (MCI), and whether these EEG markers are associated with age, memory performance, and cortical structure.

31 MCI patients (17 non-amnestic MCI, aged 58-82, and 14 amnestic MCI, aged 55-79) and 16 healthy elderly individuals (aged 51-83) were recruited in the Department of Psychiatry, Semmelweis University in Budapest, Hungary. All participants completed a comprehensive neuropsychological assessment. Resting-state EEG (64-channel Neuroscan) was recorded under both eyes-open and eyes-closed conditions (4 minutes each). In addition, participants completed the Paired Associates Learning task (PAL) during EEG recording. EEG data were preprocessed using EEGLAB, and the aperiodic exponent and individual alpha peak frequency were extracted using the SpecParam toolbox in Python.

Preliminary results confirm lower individual alpha peak frequency in MCI compared to the healthy control group, with more prominent slowing among the amnestic group. The exponent of the 1/f slope shows a significant decrease in both amnestic and non-amnestic MCI, and a gradual flattening of the aperiodic slope was associated with age. Further analysis is conducted to study the association between the aperiodic component of the EEG signal and working memory and the cortical thickness of the hippocampus and the precuneus.

The flattening of the 1/f slope is suggestive of increased neural noise and a shift towards hyperexcitability in the excitation-inhibition balance in MCI. The slowing of the alpha peak frequency and flatter aperiodic slope could potentially serve as a non-invasive, accessible, and sensitive early indicator of increased dementia risk, highlighting the role of hyperexcitability as a core component of early detection.

Poster Abstract 9

Rebound from the COVID-19 Pandemic on Time to First Colorectal Cancer Screen

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Background
The rising incidence of colorectal cancer (CRC) in younger individuals underscores the importance of understanding age-specific screening trends. The COVID-19 pandemic provided a valuable ‘natural experiment’ in screening rates and practices, but prior studies combined first and repeat screening and did not consider effects among newly eligible individuals.
Objective
Determine temporal trends in time to first CRC screen for newly eligible individuals before and after the start of the pandemic.
Methods
In this observational study of 667,439 individuals who became eligible for CRC screening from 2017 to 2024 within the US Department of Veterans Affairs, we performed Cox regression on time to first CRC screening by any modality, adjusting for demographic and clinical characteristics. Period effects of the COVID-19 pandemic were estimated with time dependent covariates.
Results
Compared to the pre-pandemic period, the hazard ratio of first CRC screening was lowest during the initial three months of the pandemic (nadir hazard ratio 0.58 (95% CI 0.55-0.62), remained below baseline until March 2021, and rose to 1.89 (95% CI 1.80-2.00) by the end of the study. Geographic location, race, ethnicity, and comorbidity-were each independently associated with screening. Being connected to care prior to eligibility also predicted screening completion.
Conclusions
Despite lower screening completion during early phases of the COVID-19 pandemic, CRC screening within the VA now exceeds baseline levels. Strong associations of patterns of care prior to screening eligibility and prompt screening suggests a potential target for improving time to first screening.

Poster Abstract 10

Comparisons of unexpected discrepancies in PTSD and Complex PTSD rates in active-combat soldiers serving in the Israel-Hamas war

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Objective(s): This presentation explores unexpected discrepancies between PTSD and C-PTSD rates in Israeli lone and non-lone soldiers during the Israel-Hamas war.
Background: Previous research on active-duty US military personnel has found PTSD rates to be 1.3%, increasing to 2% - 29% in veterans and among Israeli soldiers, 0.5% to 12%.
Current Study: Lone soldiers, often from the US and abroad, serve in the Israel Defense Forces (IDF) without family support and have unique backgrounds and experiences that may render them more vulnerable to negative outcomes. This study compares PTSD and C-PTSD rates in lone versus non-lone soldiers during the Israel-Hamas War.
Methods: Soldiers (N =576) initiated in-person and online surveys that measured childhood trauma, war-related experiences, loneliness, social experiences, and PTSD/C-PTSD symptoms.
Results: Lone soldiers had significantly higher histories of child abuse and neglect, $p \leq .001$. A chi-square test showed a significant relationship between lone soldier status and a C-PTSD diagnosis, $\chi^2(2, N = 160) = 94.28$, $p \leq .001$, $V = .77$, with 75% of lone soldiers meeting diagnostic criteria for C-PTSD, compared to 0% of the non-lone soldiers. For PTSD, the test was also significant, $\chi^2(2, N = 194) = 96.87$, $p \leq .001$, $V = .71$, with 78% of lone soldiers meeting criteria compared to 8% of non-lone soldiers.
Conclusions: Lone soldiers struggle emotionally and interpersonally, more than non-lone soldiers, with higher PTSD/C-PTSD rates than the US and Israeli averages.
Future Research: Further studies should explore the context of endorsed differences between lone and non-lone soldiers. Data should inform policymakers about the need for additional support programs and lone soldier resources. Measures should be examined more closely to assess if soldiers are not endorsing trauma items based on measure limitations, cultural interpretations, or mental health stigma.

Poster Abstract 11

Trends and Disparities in Cardiovascular Screenings Among Cancer Survivors with and without Atherosclerotic Cardiovascular Disease

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Background: Cancer survivors have an increased risk of atherosclerotic cardiovascular disease (ASCVD) due to shared risk factors and treatment-related cardiotoxicity. Despite recommendations that cancer survivors should receive annual screening for cardiovascular risk factors, disparities and trends in cardiovascular screenings among by ASCVD status remain understudied.
Methods: We analyzed cross-sectional data (2012-2018) from the National Health Interview Survey including adults aged ≥18 years with a self-reported history of cancer and stratified by ASCVD status (defined as prior myocardial infarction, stroke, angina, or coronary heart disease). The primary outcome was receipt of screenings for three primary cardiovascular risk factors (high cholesterol, hypertension, and diabetes) within the past 12 months. We compared screening rates by ASCVD status and examined factors associated with not receiving all screenings using multivariable logistic regression.
Results: The sample included 16,420 cancer survivors, of which 21.4% had ASCVD, representing approximately 3.1 million individuals annually. Screening rates increased from 67.5% to 69.0% in cancer survivors without ASCVD, and 65.9% to 71.9% in those with ASCVD. There were no significant differences based on ASCVD status during the study period. Certain subgroups of cancer survivors with ASCVD were at higher risk of not receiving all cardiovascular screenings including those with a lower level of education (aOR, 1.20 [95% CI, 1.02-1.41]), without insurance (aOR, 1.96 [95% CI, 1.19-3.22]), and without a usual source of care (aOR, 2.13 [95% CI, 1.35-3.36]). While these differences were similar or more pronounced among those without ASCVD, additional disparities emerged in younger adults, females, and those with lower family income (all $p<0.001$).
Conclusion: While cardiovascular screenings rates among cancer survivors marginally increased from 2012 to 2018, there were no significant differences by ASCVD status. With nearly 1 in 3 cancer survivors lacking comprehensive cardiovascular assessment and socioeconomic disparities persisting, novel approaches are needed to equitably increase screening uptake.

Poster Abstract 12

N-glycoproteomic profiling of the hookworm *Ancylostoma ceylanicum* reveals stage-specific and phosphorylcholine-substituted motifs

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Glycosylation is one of the most common eukaryotic protein modifications. In helminths, N-glycans, carbohydrate chains attached at asparagine residues of proteins, have been identified as drivers of complement activation and a Th2 immune response. Glycosylation patterns have also been linked to the recognition of helminth proteins by host macrophages, B cells, and dendritic cells throughout infection. Little is known about glycosylation patterns in the hookworm *Ancylostoma ceylanicum*, an intestinal nematode parasite of humans and animals. We first treated excretory/secretory products of *A. ceylanicum* with PNGase F, an amidase that removes most N-glycans. After treatment under non-denaturing conditions, several protein bands were no longer recognized by infected host serum IgG or intestinal IgA by immunoblot. These results suggested that host antibodies recognized specific hookworm glycoproteins. Next, we developed a glycoproteomic workflow to identify hookworm glycoproteins and define their glycan structures. Glycopeptides are limited in complex protein samples and require enrichment prior to analysis. We compared three enrichment methods and found that strong anion exchange-electrostatic repulsion liquid chromatography performed best, leading to the identification of 326 unique larval glycopeptides, or 95% of those identified across the three methods. Screening 3 replicates of larval and adult proteins with this workflow revealed 77 larval and 157 adult N-glycoproteins, all with a high confidence of identification in the Byonic search algorithm (score >150, LogProb >1.5). The majority these proteins were stage specific. Of particular interest, phosphorylcholine, a known immunomodulatory glycan substitution, was detected in both larvae and adults. These results identify, for the first time, intact glycopeptides in *A. ceylanicum*, and validate a method to further characterize the glycoproteomes of other hookworm species. In addition, the data confirm the presence of glycoproteins throughout hookworm development and suggest a role for changing glycosylation patterns in parasite development and pathogenesis.

Poster Abstract 13

Application of large language models to electronic health record text-based data to infer ischemic stroke etiology

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BACKGROUND: Stroke etiology is critical for optimal delivery of secondary prevention strategies. Artificial intelligence may efficiently infer acute ischemic stroke (AIS) etiology when applied to the electronic health record (EHR). We previously trained an ensemble machine-learning algorithm, *StrokeClassifier*, comprised of traditional algorithms, to classify stroke etiologies. We subsequently aimed to evaluate the performance of large language models (LLMs) to discharge summary text to classify AIS etiologies.
METHODS: We assembled a cohort of AIS hospitalizations at Yale-New Haven, Massachusetts General, and Beth Israel Deaconess Hospitals. The outcome was stroke etiology per TOAST classifications: (1) large artery atherosclerosis, (2) cardioembolism, (3) small vessel disease, (4) other determined etiology, (5) undetermined etiology. We tested Me-LLaMA, a medically pre-trained and instruction-tuned LLaMA-2 13B model, and the general foundation LLaMA-3 8B. We compared LLM predictions to the gold standard etiologies ascertained by consensus of $\geq$ 2 vascular neurologists.
RESULTS: The sample consisted of 3,062 patients with AIS (adjudicated TOAST classes: TOAST 1 n = 588 (19.2%); TOAST 2 n = 1007 (32.9%); TOAST 3 n = 362 (11.8%); TOAST 4 n = 317 (10.4%); TOAST 5 n = 788 (25.7%)). The limited context length of Me-LLaMA resulted in 860 outputs (28.1% throughput). Me-LLaMA accuracy rates were: TOAST 1: 77.6%, TOAST 2: 47.1%, TOAST 3: 52.3%, TOAST 4: 5.6%, TOAST 5: 3.7%. LLaMA-3 resulted in 3,048 outputs (99.5% throughput). LLaMA-3 accuracy rates were: TOAST 1: 86.2%, TOAST 2: 89.8%, TOAST 3: 67.8%, TOAST 4: 11.0%, TOAST 5: 4.2%.
CONCLUSION: We provide proof-of-concept for automated inference of stroke etiology from EHR. The performance of the general LLaMA-3 was superior to Me-LLaMA. Further model fine-tuning, architecture customization, and quantization are needed to improve predictive performance, explainability, and output readability. LLM-based stroke etiology assignment may serve as the basis of a clinical decision support tool.

Poster Abstract 14

Perturbational single-cell RNA sequencing of patient tumors in Merkel cell and small cell lung carcinomas

Mentor: Jeffrey Ishiuzuka, MD/MPhil.

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Background:
Although immune checkpoint blockade has revolutionized cancer therapy, many patients do not achieve durable survival. This study tested the hypothesis that the novel double-stranded RNA sensor RIG-I agonist, SLR14, can induce cytotoxic transformation of T cells in immunologically "cold" human tumor specimens.

Methods:
An *ex vivo* platform, PERCEPT, was developed to evaluate patient tumor and immune responses to novel and established therapies using perturbational single-cell RNA sequencing. Tumor and lymph node metastasis samples (n=9) from primary or metastatic melanoma and Merkel cell carcinoma (MCC) were collected and processed into suspension replicates of tumor-infiltrating immune co-cultures. Samples were stimulated for 42–48 hours (Table), followed by Fluorescence-Activated Cell Sorting (FACS) of live cells and barcoding for multiplexed single-cell sequencing via 10x scRNA-seq. CINEMA-OT analysis identified factors associated with therapeutic response and resistance. CRISPR knockout (KO) MCC and small cell lung cancer (SCLC) cell lines were developed, validated, and co-cultured with CD14+ monocytes or monocyte-derived dendritic cells (DCs).

Results:
SLR14 stimulation induced gene expression beyond canonical interferon-stimulated genes in tumor cells, NK cells, and T cells. In tumor-immune co-cultures, SLR14 promoted antiviral states in tumor-infiltrating T cells and primed IFNγ production. CINEMA-OT analyses identified midkine (MDK), a multifunctional cytokine, as associated with nonresponse in MCC. MDK knockout restored sensitivity to IFN and SLR14 in MCC and SCLC cell lines and in co-cultured CD14+ monocytes or monocyte-derived DCs.

Conclusions:
Midkine was identified as a critical suppressor of innate immune sensing of IFN and SLR14 in both tumor and immune compartments, disrupting multiple stages of the tumor immunity cycle. This resistance mechanism, while infrequent in melanoma, was markedly enriched in MCC and SCLC. These findings, based on direct assessment of patient-derived tumor and immune samples, reveal a novel pathway of immune evasion in MCC and SCLC.

Poster Abstract 15

Postmortem Computed Tomography of COVID-positive Decedents: Complementary Roles for Antemortem and Postmortem Imaging and Autopsy

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Background: Ongoing international shortages in the forensic pathology workforce have led to increased application of postmortem computed tomography (PMCT) for medicolegal death investigations. The COVID-19 pandemic and associated temporary halt in some hospital autopsy practices highlighted a need for alternative investigations to improve diagnostic accuracy of death determination in hospitals when autopsy is forgone or cannot be performed. This study examines the application of PMCT in the hospital setting for deaths suspected to be related to COVID-19 and evaluates its utility as a comparative timepoint to antemortem imaging.

Materials and Methods: In an academic teaching hospital, full-body PMCT was conducted between June 2020 and May 2022 for decedents who had tested positive for COVID-19 and were consented for unrestricted autopsy. PMCTs were interpreted by fellowship-trained radiologists, and PMCT findings were compared to autopsy findings, antemortem imaging examinations, and clinical data.

Results: 19 decedents with either a positive postmortem COVID-19 nasal swab (n=18) or COVID-19 test during hospitalization (n=1) were scanned. Autopsy-proven causes of death were categorized as ‘cardiovascular disease’ (CVD, 21%), ‘COVID’ (42%), combination ‘COVID/CVD’ (26%), and ‘other’ (11%). An antemortem CT from the visit/admission preceding death was available for 11 decedents. Of these, 5 PMCTs demonstrated worsened findings and 3 PMCTs demonstrated pertinent new findings compared to most recent antemortem CT.

Conclusions: PMCT of COVID-19 decedents in a hospital setting allows for correlation with autopsy, histopathology, and other medical data, and can suggest the acuity of findings when antemortem imaging is available. PMCT demonstrates direct and indirect findings consistent with autopsy-proven cause of death, a feature which may improve the accuracy of cause of death determinations when autopsy is forgone or cannot be performed, such as during epidemics or pandemics, when epidemiological data including geographic distribution of infections, rate of spread, and morbidity and mortality become of vital importance.

Poster Abstract 16

Nucleosides Accelerate Membrane Transit by a Tumor Targeting Anti-DNA Autoantibody

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Objectives/Goals
ENT2 regulates nucleoside flux at the BBB and the nucleoside-rich environment created by necrotic tumors & damaged tissues attract variants of 3E10. We conducted cell penetration assays to see if added nucleosides increase the cell penetration ability of Deoxymabs, engineered versions of 3E10.

Methods/Study Population
We conducted cell penetration assays to see if added nucleosides increase Deoxymabs's cell penetration ability. We also conducted cell penetration assays with nucleobases, nucleotides and pentoses. Our lab's previous research determined that combining Deoxymabs and olaparib was a weaker treatment for glioblastoma than the singular treatments. Olaparib may be binding to Deoxymabs, making it unable to be transported through ENT2. We conducted cell penetration assays using olaparib to determine its effect on the cell penetration ability of Deoxymabs. We plan on conducting SPR binding assays to prove that these molecules bind to Deoxymabs.

Results/Anticipated Results
Nucleosides increase the cell penetration ability of Deoxymabs. Both nucleobases and pentoses decreased the cell penetration ability of Deoxymabs. The nucleoside as a whole increases Deoxymabs's cell penetration ability. Nucleotides had a varying effect on the cell penetration ability of Deoxymabs. Nucleosides may be prioritized by ENT2 over nucleotides. Olaparib decreased the cell penetration ability of Deoxymabs. Olaparib may be unable to cross the BBB via ENT2, but Deoxymabs bind to it, which makes it also unable to bypass the BBB. We predict that our SPR binding assay data will show that Deoxymabs bind to nucleosides, nucleobases, pentoses, nucleotides, and olaparib.

Discussion/Significance of Impact
Deoxymabs have potential use as biologics that engage hard to reach intracellular targets & exert synthetically lethal effects on vulnerable cancer cells. They are currently in clinical trial planning for use against DNA repair-deficient malignancies. Nucleosides could strengthen those treatments.

Lay Summary)
Deoxymabs have potential use as treatments for DNA repair-deficient malignancies and could be improved with nucleosides.

Poster Abstract 17

Antisense Oligonucleotide-Mediated Gene Therapy for KCNT1 Epilepsy

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Gain-of-function (GOF) mutations in the *KCNT1* gene, which encodes the sodium-activated potassium channel Slack (KCNT1, $K_{Na}1.1$), lead to network hyperexcitability, refractory seizures, and severe intellectual disability. Antisense oligonucleotides (ASOs) have emerged as promising therapeutic agents for KCNT1 epilepsy, although their mechanisms and broader effects remain unclear. In a mouse model of KCNT1 epilepsy with the *Kcnt1-R455H* mutation, we demonstrate that knockdown of *Kcnt1* with an ASO targeting the core domain of the channel reduces both Na^+-activated K^+ (K_{Na}) currents and voltage-dependent sodium (Na_V) currents, alleviating mutation-induced hyperexcitation in excitatory neurons and restoring inhibition in interneurons. Moreover, *Kcnt1* knockdown releases its binding proteins FMRP (Fragile X Mental Retardation Protein) and CYFIP1 (Cytoplasmic FMR1 Interacting Protein 1) from the channel to eIF4E (Eukaryotic Initiation Factor 4E), where they normally inhibit translation initiation. As a result, ASO treatment reduces the synthesis of Na_V channels, specifically $Na_V1.1$, $Na_V1.2$ and $Na_V1.6$, and their localization to the axon initial segment (AIS), further contributing to the reduction in Na_V currents. Together, these findings provide new insights into the role of ASOs in modulating neuronal excitability and mRNA translation, supporting their therapeutic potential for refractory epilepsies and developmental disorders.