15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 1

Presenter: Gustavo Almeida, PT, PhD
Institution: UT Health San Antonio
Category: Faculty

Feasibility of Blood-Flow Restriction Training Prehabilitation in Older Adults Awaiting Total Knee Replacement

Gustavo J. Almeida, Mikaela Gilbert, Zachary Tittle, Diana Gasaway, Leah McBrayer, Jasmine Gongora, Jacob Lewis, Ehab Khalaf, Frank Buttacavoli, Boris Zelle

PURPOSE: Knee osteoarthritis (OA) is characterized by the progressive loss of joint cartilage, particularly in the elderly, leading to limited exercise tolerance. Blood Flow Restriction Training (BFRT) offers a method for building muscle strength with lower loads, thereby reducing joint stress while still achieving exercise-induced benefits. Prehabilitation using BFRT may enhance strength and physical function in individuals awaiting total knee replacement (TKR), potentially accelerating postoperative recovery. However, it is not known if BFRT can be tolerated preoperatively. This study aimed to explore the feasibility of BFRT as a prehabilitation intervention and its impact on physical function and quadriceps strength in older adults awaiting TKR.

MATERIALS AND METHODS: A single-group pre-posttest design was used. Participants underwent 6 weeks of BFRT prehabilitation that included 4 sets (30, 15, 15, 15 repetitions) of bilateral leg extensions, leg curls, and sit-to-stand exercises performed with the blood flow restricted between 50-80% of the full occlusion using pressure cuffs. The primary outcome measured was feasibility. Secondary outcomes included performance-based and self-reported physical function, quadriceps muscle strength, and health-related quality of life. Assessments were conducted at baseline (BA), after 6 weeks of prehabilitation (FU1), and 8 weeks after TKR (FU2). Feasibility was assessed through safety and compliance with intervention. Wilcoxon Signed-Rank Tests were performed to determine changes BA-FU1 and BA-FU2, and Hedges' g effect sizes were calculated.

RESULTS: All participants (10; 5 male, mean age 70.6 ± 7.6) completed the 12 BFRT prehabilitation sessions without adverse events, indicating excellent feasibility and compliance. Across the secondary outcomes, only the 30-second Chair Stand Test showed a trend towards statistical significance. Eight out of 10 participants showed improvements in number of chair stands after at FU1 (Median difference= 1.5 [95%CI: 0.0, 2.5]; p=.065), with 5 of them exceeding the minimal detectable change (i.e., 1.64 chair stands). At FU2, 6 out of 10 participants maintained their gains (Median difference= 1.0 [95%CI: 1.0, 1.0]; p=.253), with 4 participants exceeding the minimal detectable change. Effect sizes were 0.66 (95%CI: 0.22, 1.1), p=.043 preoperatively; and 0.07 (95%CI: -0.52, 0.50), p=.882, postoperatively.

CONCLUSIONS: BFRT is a feasible and safe prehabilitation tool for older adults awaiting TKR. Although there were no significant changes in secondary outcomes, BFRT showed potential for improving sit to stand performance. These preliminary findings suggest that BFRT may be beneficial preoperatively and could help with postoperative recovery. However, the small sample size requires further research to confirm these effects in a larger cohort.

CLINICAL RELEVANCE: Clinicians can consider BFRT as a prehabilitation strategy for patients awaiting TKR, especially for those with reduced exercise tolerance due to OA. BFRT is a promising approach to enhance preoperative strength and function, which are both crucial for mobility and quality of life in older adults undergoing TKR.

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Posterboard #: 2

Presenter: Sevan Alwan, PhD
Institution: UT Health San Antonio
Category: Faculty

Preclinical Impact of New Compound in Schistosoma Therapy

Sevan N. Alwan, Ramiz Shaheed, Alexander B. Taylor, Stanton F. McHardy, Michael D Cameron, Philip T. LoVerde

Human schistosomiasis is a disease caused by parasitic species of the genus Schistosoma. Schistosoma affects over 250 million people worldwide, accompanied by severe clinical symptoms, socioeconomic problems, and more than 200,000 deaths per year. About 90% of the schistosomiasis disease burden occurs in sub-Saharan Africa, where the major forms of schistosomiasis are caused by Schistosoma haematobium (urogenital disease) and Schistosoma mansoni (intestinal-hepatic disease). S. haematobium causes female genital schistosomiasis that leads to formation of lesions within the vaginal tract of women with a risk of progression to infertility and a risk of HIV coinfection if left untreated. S. mansoni is endemic in sub-Saharan Africa. This parasite causes chronic hepatic or intestinal illnesses and malnutrition in both Africa and Brazil and suspected to be directly involved in hepato-carcinogenesis. Due to the large overlap of Schistosoma haematobium - and Schistosoma mansoni -endemic regions in Africa, many people are at risk of co-infection, these mixed foci have a potential adverse effect on their association with bladder and liver pathology. Treatment has relied on the anthelmintic drug Praziquantel (PZQ) for more than 20 years. Mass drug administration in sub-Saharan Africa, where most of the cases occur, has led to the appearance of reduced efficacy of PZQ, which portends the selection of fully drug resistant pathogens. Moreover, PZQ does not prevent reinfection and it is not active against juvenile stages resulting in rapid re-activation after 2 to 3 weeks from PZQ treatment. These limitations strongly warrant the need for new therapeutics with better cure rate. Our focus is on Oxamniquine (OXA), a previous treatment of S. mansoni that fails to treat S. haematobium infections. We have successfully reengineered OXA using structure-function-guided approaches to produce CIDD-0149830 with major advancements over current Schistosoma therapies. CIDD-0149830 reduced the worm burden of S. haematobium and S. mansoni adult worms up to 80% in animal models, an advantage over OXA. Similarly, CIDD-0149830 overcame one of the major limitations of PZQ treatment. CIDD-0149830 kills 100% of juvenile stage of S. haematobium and S. mansoni in vitro. Importantly, CIDD-0149830 kills 100% of PZQ-resistant parasite in in vitro studies. Our goals are to demonstrate the preclinical efficacy of the most effective compound CIDD-0149830 and to prepare for clinical studies. We expect CIDD-0149830 will have broader spectrum activity and a higher clinical impact compared to PZQ, which only targets adult parasites. By targeting juvenile, PZQ-resistant, and adult parasites CIDD-0149830 will eliminate egg production and prevent re-infection and rapidly eliminate tissue damage and disease symptoms.

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Posterboard #: 3

Presenter: Anton Avanceña, PhD
Institution: The University of Texas at Austin
Category: Faculty

Longitudinal trajectories of HIV pre-exposure prophylaxis adherence and their association with alcohol use disorder treatment

Anton L.V. Avanceña, Godwin Okoye, Jamie C. Barner

Background: Pre-exposure prophylaxis (PrEP) effectively prevents HIV, however, alcohol use disorder (AUD) may impact adherence. Routine PrEP care visits could offer opportunities to identify and treat AUD, though the association between PrEP adherence and AUD treatment is unclear. Objective: To examine PrEP adherence trajectories and their association with receipt of AUD treatment among PrEP users diagnosed with AUD.

Methods: We conducted a retrospective cohort study using 2014-2021 MarketScan® claims data. Eligible individuals were aged 16-64 years with a PrEP prescription and an AUD diagnosis within 6 months prior to PrEP initiation. Group-based trajectory modeling (GBTM) identified adherence trajectories over 12 months post-PrEP initiation, selected based on the lowest Akaike information criterion. The proportion of days covered (PDC) was calculated for each trajectory. The primary outcome was receipt of FDA-approved AUD pharmacotherapy. Covariates included age, sex assigned at birth, region, insurance type, employment status, Charlson Comorbidity Index, and mental health comorbidities. Multivariable logistic regression evaluated the association between adherence trajectories and AUD treatment.

Results: We included 3,926 PrEP users and identified 4 distinct PrEP adherence trajectories: (1) non-adherent (32.6%), rapidly declining (21.77%), slowly declining (18.95%), and adherent (26.67%) with mean (SD) PDC of 7.9% (27.24%), 25.24% (34.81%), 59.23% (23.25%), 93.59% (2.95%), respectively. Only about 17.58% of PrEP users received treatment for AUD. Factors associated with AUD treatment were age (OR 1.02, 95% CI 1.02-1.03, $p<0.001$) and diagnoses of depression (OR 1.26, 95% CI 1.04-1.53, $p=0.017$), anxiety (OR 1.42; 95% CI 1.17-1.73, $p<0.001$), bipolar disorder (OR 1.39, 95% CI 1.09-1.77, $p=0.008$), and substance use disorder (OR 1.7, 95% CI 1.42-2.05, $p<0.001$). Adherence trajectories were not significantly associated with AUD treatment. For example, compared to the adherent group, individuals in the non-adherent group had an adjusted OR of 0.981 (95% CI 0.800-1.203, $p=0.8557$).

Conclusions: Despite regular engagement in PrEP care, only a small proportion of PrEP-adherent patients received AUD pharmacotherapy. Our findings highlight the need for integrating AUD screening and treatment within routine PrEP care to address comorbidities and barriers to PrEP adherence.

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Posterboard #: 4

Presenter: Curtis Bone, MD MHS
Institution: UT San Antonio
Category: Faculty

Evaluation of androgen deficiency among people with depression and opioid use disorder-A single center study

Curtis Bone MD MHS, Shorab Syed PhD, Jennifer Potter PhD MPH, Van King MD, Erin Finley Phd MPH, Jimmy Arnold MBA, Meredith Zozus PhD

Background: Depression is the most common mental health comorbidity among people with opioid use disorder (OUD) and may be a direct consequence of opioid-induced androgen deficiency (OIAD), a testosterone deficiency that results from long-term opioid exposure. OIAD has other physiologic consequences including fatigue and sexual dysfunction. Multiple randomized controlled trials demonstrate improved mood, energy, and sexual function when OIAD is treated with testosterone replacement therapy (TRT), but it is not evident whether this clinical research has translated into clinical practice. The purpose of this study is to describe the frequency of OIAD evaluation among people with OUD after a diagnosis of depression in a large health system.

Methods: We conducted a cross-sectional study of a large academic health center using the Epic database. We included men 18 years and older who were diagnosed with OUD between January 1st, 2020 and February 28th, 2025. We reported the number of patients with indications for testosterone levels (diagnosis of depression, fatigue, or sexual dysfunction) as well as the number with documented contraindications to evaluation and treatment of OIAD.

Results: There were 1,213 men with a diagnosis of OUD in our sample. Among them, 416 (34%) had a diagnosis of depression, 73 (6%) had documented fatigue, and 49 (4%) were diagnosed with sexual dysfunction. An initial evaluation of OIAD was conducted in 24 (1.9%) individuals. Among those assessed, 17 (71%) had testosterone level consistent with OIAD. There were 10 (0.8%) patients in the full sample with a diagnosed contraindication to testosterone replacement.

Conclusions: OIAD and depression are prevalent among people with OUD but evaluation for OIAD is not common in this population. Failure to identify and treat OIAD may contribute to depression and treatment-refractory depression. Additional research focused on barriers and facilitators to evaluation and treatment of OIAD among patients with a dual diagnosis of depression and OUD may be warranted.

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Posterboard #: 5

Presenter: Moshtagh Farokhi, DDS, MPH
Institution: UT Health San Antonio
Category: Faculty

Enhancing Oral Health Literacy Among Women Refugees Through a Community-Engaged, Technology-Based Intervention

Moshtagh R. Farokhi DDS, MPH, Andrew Muck MD, MBA, Heidi Worabo DNP, APRN, Dana K English Ed.D., MS, RDH, Alvin Estacio MS, and Benneth T Amaechi BDS, MS, PhD

Introduction. Afghan women with considerable literacy challenges have resettled in San Antonio due to various socio-political factors. This study aimed to understand and mitigate their barriers to accessing oral/healthcare while improving oral health literacy through a technology-based intervention utilizing platforms like WhatsApp.

Methods. Upon understanding participants' urgent care-seeking patterns and challenges with dental access, an interprofessional (IP) team of providers engaged community advocates to seek and provide culturally relevant insights into prevailing attitudes toward preventive oral/health care. Due to limited literacy, the participants preferred using technology platforms like WhatsApp to access oral/health information.

Trained interpreters as community advocates calibrated to effectively bridge the cultural and linguistic divides while conducting comprehensive pre-surveys about the participants' health practices as availability, accessibility, and affordability to access oral/healthcare. After collaborating with community advocates and participants, we developed a tailored message about oral health and nutrition delivered through the interactive Canva platform. To effectively measure our impact and address ongoing challenges, we created instructional videos that included written messages in English, Pashto, and Farsi. These videos also featured interpreter voiceovers in Pashto and Farsi to ensure accessibility for participants with literacy challenges. We then provided hands-on oral hygiene instructions and used the Teach-Back method to assess participants' brushing and flossing techniques. A structured rubric-based assessment form was created to evaluate and chart participants' progress in their oral hygiene skills. After the training, post-surveys were administered, and the content was easily shared through a link sent directly to participants via WhatsApp.

Results. 43 Afghan women (ages 19-57) participated in this study, with 58% reporting Pashto as their primary language. 46% of participants had limited to no formal education, and 77% identified as homemakers. Participants reported that barriers to accessing dental care included financial constraints (91%), lack of proficiency in English (70%), limited literacy skills (63%), and transportation challenges (56.3%). The engagement with a technology-driven recorded intervention yielded promising outcomes, demonstrating statistically significant increases in oral hygiene and dietary knowledge scores from pre- to post-survey assessments ($p<0.05$). The brushing and flossing techniques evaluation revealed increased proficiency scores from pre- to post-intervention ($p<0.001$), indicating improved oral health literacy and hygiene instructions.

20 participants consented to six-month follow-up care, of which 80% (n=16) reported reduced sugary drink consumption and 95% (n=19) indicated improved oral hygiene practices, including brushing at least once daily and using fluoridated toothpaste.

Conclusions. The intervention highlights pathways to enhance oral health for populations with limited literacy skills. Healthcare providers must implement tailored strategies for oral health promotion to meet their patients' specific needs.

Healthcare providers should consider the complexities of patient access to healthcare systems and leverage technology to empower their patients. Technology-based interventions provide equitable cultural and linguistic approaches to address health literacy constraints.

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Posterboard #: 6

Presenter: Hillary Huber, PhD
Institution: Texas Biomedical Research Institute
Category: Faculty

Estimating health-span and lifespan in 5 nonhuman primate species common to translational aging research

Hillary F. Huber, Hannah Ainsworth, Yaomin Wang, Matthew Jorgensen, Adam Salmon, Paul-Michael Sosa, Eric Vallender, Julie A. Mattison, Kris Coleman, Charlotte Hotchkiss, Michele A. Basso, Ricki Colman, Caroline Zeiss, Corinna Ross, Carol Shively, Laura Cox

There are surprisingly little and contradictory data available about lifespan of captive nonhuman primates (NHP). For example, captive baboon lifespan has been reported as 11, 21, and 37.5 yrs. The purpose of the NHP Lifespan Project is to develop a central primary data source on lifespan of NHP in biomedical research to clarify correspondence between NHP and human ages for translational aging research. We received data from 15 institutions on >110,000 primates for 58 species and subset to animals that survived to adulthood and died of natural causes or were humanely euthanized for health reasons (excluding research-related deaths in the current analysis). Here, we focus on 5 species: Macaca mulatta (rhesus; n=8,207), Papio sp. (baboon; n=1,003), Callithrix jacchus (marmoset; n=831), M. nemestrina (pigtails; n=769), and Chlorocebus aethiops sabaeus (vervet/African green monkey; n=204). We evaluated Kaplan-Meier survival curves by sex and species. Rhesus median lifespan (MLS) was 9.7 yrs and 95th percentile of survival (95th) was 22.4 yrs; maximum age was 44. Baboon MLS was 11.6 yrs and 95th was 21; maximum age was 28. Marmoset MLS was 5.5 yrs and 95th was 12.7; maximum age was 17.3. Pigtail MLS was 9.6 yrs and 95th was 18; maximum age was 24. Vervet MLS was 13.8 yrs and 95th was 26.9; maximum age was 30.6. An important consideration is that research NHP, unlike humans and zoo NHP, are typically euthanized for humane welfare reasons before their natural end of life (although institutional practices vary), often after diagnosis of their first major disease (e.g., endometriosis, cancer, spinal disease), and thus correlated with health-span. Our study clarifies the chronological relationships between NHP ages. Funding from IRP NIA NIH, NIA R01AG087957, NIH 1U19AG057758, P51OD011133, P40-OD010965, P51OD011106, U42OD011123, P51OD010425. Poster presented at the 2024 meeting of the American Aging Association.

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Posterboard #: 7

Presenter: Soumya Maity, PhD
Institution: UT Health San Antonio
Category: Faculty

Endogenous Adenine as a Metabolic Inducer of Senescence in the Aging Kidneys

Soumya Maity, Hak Joo Lee, Ian Tamayo, Afaf Saliba, Guanshi Zhang, Kumar Sharma

Introduction: Cellular senescence is a key contributor to age-related kidney dysfunction. Hallmarks of senescent cells include activation of p53, β-galactosidase positivity, and accumulation of p21 and p16. These long-lived, non-dividing, and metabolically active cells secrete high levels of cytokines, chemokines, growth factors, and immune modulators, collectively referred to as the senescence-associated secretory phenotype (SASP). The SASP contributes to chronic inflammation and disrupts the normal function of surrounding healthy cells. Given the distinct metabolic features of senescent cells, we performed metabolomic profiling in aged kidneys to identify novel mechanisms underlying senescence-associated chronic kidney disease (CKD).

Methods: To overcome the challenge of identifying senescent cells in aging tissue, we used p16-tdTomato reporter mice to visualize senescent cells in situ by detecting red fluorescence from p16 proteins. We applied matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI) to evaluate the metabolomic profile of senescent cells in the kidneys of p16 reporter mice, marmosets, and human kidney biopsies. Additionally, SASP was assessed in kidneys of wild-type (WT) mice treated with adenine.

Results: Using untargeted spatial metabolomics analysis via MALDI-MSI, we identified adenine as one of the top four altered metabolites in the senescence regions of kidneys from 15-month-old p16-tdTomato reporter mice. Notably, multi-modal spatial imaging revealed adenine accumulation in β-galactosidase-positive regions with high p16 expression. Further spatial metabolomics analysis demonstrated increased adenine accumulation in kidney biopsies from individuals over 60 years old compared to those under 40, in the kidney cortex of 15-month-old versus 3-month-old p16-reporter mice, and in 3-year-old versus 16-year-old marmosets. Given adenine's established role in kidney injury and its accumulation in fibrotic regions of diabetic kidneys, we administered adenine to young mice to evaluate its impact on kidney senescence. Adenine treatment led to an increase in p21, p16, and a range of SASP markers in the kidney, effects that were attenuated by the mTORC1 inhibitor rapamycin.

Conclusion: Our results suggest that endogenous adenine acts as a metabolic inducer of senescence in the aging kidney. Furthermore, mTORC1 is regulated by adenine and contributes to adenine induced SASP.

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Posterboard #: 8

Presenter: Sara Masoud, PhD, MPH
Institution: UT Health San Antonio
Category: Faculty

Strengthening partnerships for dementia research: A mixed-methods study of engagement strategies

Masoud, SS., Lesser, J., Escareno, J., Flores, B., Choi, B., Lopez Lorenzo, KD., White, C.L.

Latino communities experience a disproportionately high risk of Alzheimer's disease (AD) yet remain significantly underrepresented in dementia research. Meaningful involvement of communities in research can enhance the inclusivity, responsiveness, and accountability of research but more evidence is needed to ensure that strategies to engage communities are effective. This study utilized a community-engaged approach by establishing a Steering Council (SC) composed of Latino caregivers, individuals living with dementia, community health workers (CHWs), healthcare and social service providers, and dementia researchers. The SC played a key role in designing and implementing culturally tailored engagement activities, known as community pláticas, to identify research priorities and patient-centered outcomes relevant to Latino families affected by dementia. Through an explanatory sequential mixed-methods design, engagement with the SC was assessed longitudinally using surveys and interviews. The Research Engagement Survey Tool (REST) was administered three times to assess quantitative changes in levels of engagement over a two-year period. Qualitative insights were gathered through individual interviews to further explain the quantitative findings. REST results showed significant improvements in collaboration and partnership over time, while qualitative data highlighted an evolving cycle of trust-building, co-learning, and shared decision-making within the SC. An integrated analysis revealed that the SC's structured relationships and iterative engagement strategies fostered strong and sustained partnerships, particularly during the planning and execution of the pláticas. Findings from this study illustrate how culturally responsive, community-led frameworks can enhance stakeholder participation, fostering more inclusive dementia research. This model offers a reproducible approach to addressing health disparities through community-academic partnerships. The study findings underscore the importance of relational, patient- and family-centered strategies in ensuring equitable representation in health research.

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Posterboard #: 9

Presenter: Rahma Mungia, BDS
Institution: UT Health San Antonio
Category: Faculty

Early Life Violent Victimization and Dental Care Use from Adolescence through Adulthood

Rahma Mungia, BDS, MSc, DDPHRCS, Alexander Testa, PhD, Luis Mijares, MS, Dylan B. Jackson, PhD, Daniel Semenza, PhD, Richard Stansfield, PhD, Ian Silver, PhD,

Objectives: This study investigates the long-term impact of early-life violent victimization on dental care utilization patterns from adolescence through middle adulthood (ages 11-43). Given the well-documented association between early-life trauma and health behaviors, we examine whether violent victimization in adolescence contributes to irregular or inconsistent patterns of dental care use across the life course. \

Methods: Data were drawn from Waves I through V of the National Longitudinal Study of Adolescent to Adult Health (Add Health), a nationally representative, longitudinal cohort study. Group-based trajectory modeling (GBTM) was used to identify distinct patterns of dental care utilization over five waves, spanning more than three decades. Multinomial logistic regression models assessed the association between self-reported violent victimization experiences at Wave I and trajectory group membership, adjusting for key demographic, socioeconomic, and health-related covariates to isolate the independent effect of victimization on dental care patterns.

Results: Four distinct dental care utilization trajectories emerged: High Dental Care Use (37.9%), characterized by consistent engagement with dental care services; Intermittent Decreasing Dental Care Use (26.0%), reflecting early engagement followed by a decline in later years; Intermittent Increasing Dental Care Use (23.3%), marked by delayed but eventual uptake of dental care; and Low Dental Care Use (12.8%), representing minimal or infrequent utilization. Adolescents who experienced multiple instances of violent victimization had significantly elevated relative risks of belonging to the Intermittent Decreasing (RRR=2.29, 95% CI=1.31-4.00) and Intermittent Increasing (RRR=1.82, 95% CI=1.10-3.01) trajectories compared to those with consistently high dental care use. These findings suggest that early exposure to violent victimization disrupts patterns of preventive and routine dental care, contributing to disparities that persist into adulthood.

Conclusions: Early-life violent victimization serves as a critical risk factor for irregular and inconsistent dental care utilization over the life course. The cumulative effects of trauma may shape long-term health behaviors, reinforcing disparities in access to and engagement with oral healthcare services. Trauma-informed care approaches and targeted interventions aimed at mitigating these effects could help improve dental care access and promote long-term oral health equity.

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Posterboard #: 10

Presenter: Shreya Rao, MD, MPH
Institution: UT Health San Antonio
Category: Faculty

Association between Single-Pill Combination Therapy Use with Blood Pressure Control in the Systolic Blood Pressure Intervention Trial (SPRINT): A Post-Hoc Analysis

*Shreya Rao MD MPH*1, Matthew Segar MD*2, Neil Keshvani MD3,4, Suha Soni MD MPH1, Anubha Aggarwal MD MSc5, Mark Huffman MD MPH5, Priscilla Hsue MD6, Wanpen Vongpatanasin MD4, Vasan Ramachandran MD7, Thomas Wang MD4, Ambarish Pandey MD MSCS3*

Background: Blood pressure (BP) control among patients living with hypertension in the US remains suboptimal. Single-pill combination (SPC) therapies are commonly used as a strategy to improve adherence to BP-lowering therapies. Whether use of SPC agents can facilitate early and sustained intensive BP control and lower adverse CV outcomes is not well-established.

Methods: We performed a post-hoc analysis of SPRINT including 8623 participants with available drug therapy data. The association between time-updated SPC use and rate of change in BP in short- (≤6 months) and long-term (>6 months) follow-up of the trial was assessed by linear mixed-effect model with repeated measures (LMMRM) including an SPC*time interaction term with adjustment for potential confounders. Difference in adjusted estimated marginal means for follow-up BP achieved at different timepoints between the SPC vs. non-SPC groups was also compared using LMMRM. Finally, multivariable Cox proportional hazards models were estimated to evaluate the association of SPC use with incidence of composite CV events (non-fatal myocardial infarction, CV death, and heart failure event).

Results: Among 8623 participants analyzed, 9.3% (N=803) were prescribed SPC at baseline with greater rate of use in the intensive BP control vs. usual care group (5.79[5.61 to 5.97] vs. 3.90[3.75 to 4.06] per 100 person-months; p-diff<0.001). Among those with SPC use, the most commonly used formulation was lisinopril/hydrochlorothiazide (15.1%). SPC use was associated with more rapid BP reduction in the first 6 months (mean monthly change in systolic BP SPC vs. non-SPC[95% CI]: -1.94[-1.65 to -1.22] mmHg vs. -1.33[-1.27 to -1.40] mmHg; p-diff<0.001) with comparable difference across treatment arms. On long-term follow-up, participants using SPCs achieved significantly lower systolic BP at each timepoint. The risk of the primary composite CV endpoint was not different among those with vs. without SPC use during the trial after adjusting for potential confounders (HR[95% CI]: 0.81[0.49 to 1.34]).

Conclusions: SPC use in SPRINT resulted in more rapid BP control and lower BP during long-term follow-up with no difference in the risk of primary composite endpoints, though the results were imprecise. Our findings suggest that SPC therapies may facilitate faster and more sustained achievement of intensive BP control.

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Posterboard #: 11

Presenter: Dan Smelter, PharmD, PhD
Institution: UT Health San Antonio
Category: Faculty

A unique combination of antimicrobials to overcome methicillin-resistant Staphylococcus aureus infective endocarditis

Dan F. Smelter

Infective endocarditis (IE) is a life-threatening systemic disease with significant morbidity and 30-day mortality of 25%. The current age of peak incidence of IE is 70 years of age, and the most common causative organism Staphylococcus aureus, has known mechanisms for robust biofilm production, immune evasion, and antibiotic resistance. With only two standard-of-care antibiotics for methicillin-resistant S. aureus (MRSA) endocarditis (vancomycin or daptomycin), re-assessing traditional monotherapy approaches and repurposing antibiotics toward novel combinations may lead to new breakthroughs for improved treatment algorithms. One novel combination that has demonstrated profound success in treating persistent methicillin-susceptible S. aureus (MSSA) bacteremias, including endocarditis, is cefazolin (CFZ) and ertapenem (ETP). Interestingly, while these two antibiotics are historically considered ineffective against MRSA when used in monotherapy, my recent work has identified variable susceptibility of MRSA to the combination in vitro. While the synergy of the combination is modest when evaluated by in vitro susceptibility testing, it has demonstrated anti-biofilm activity and immunomodulatory behavior that likely enhances the in vivo efficacy seen when used clinically. My data suggests that the combination of CFZ+ETP that has demonstrated great success against persistent MSSA bacteremias may also be an effective MRSA therapeutic option. This combination antibiotic strategy warrants further investigation as we seek improved therapeutic approaches and outcomes in the most vulnerable populations.

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Posterboard #: 12

Presenter: Azam Alamdari, MD
Institution: UT Health San Antonio
Category: Postdoctoral/Clinical Fellow

Hyperglucagonemia and glucose tolerance in humans with and without gastric bypass surgery

Azam Alamdari, Samanth Pezzica, Amallia Gastaldelli, Marzieh Salehi

Introduction and Objective: Glucagon influences glucose tolerance by increasing nutrient-induced insulin secretion. After gastric bypass (GB), prandial glucagon levels rise, independent of the nutrient composition, and remain elevated in the latter phase of the meal, when glycemia dips below fasting level. Here, we investigated the effect of hyperglucagonemia (100-150 pg/ml), created by 'exogenous glucagon infusion', on prandial insulin secretion, clearance and glucose fluxes.

Methods: Nine non-diabetic subjects with prior history of GB and seven healthy non-operated controls (CN), matched for age, BMI, FFM, A1C, were studied twice, with and without intravenous glucagon infusion (2ng/kg/min) during a 3-hr liquid mixed meal test (50-gram whey protein + 50-gram glucose).

Results: Fasting levels of glucose and islet hormones were similar between the 2 studies and among groups. As expected, prandial glucose and insulin secretion shifted to the left and upward in GB compared to CN. Prandial glucagon levels in GB were 1.5 times as high as in CN. Glucagon infusion further increased plasma concentrations by 1.5-fold in each group but had no effect on prandial β-cell secretory response or insulin clearance. Endogenous glucose production, insulin action (metabolic clearance of glucose/ insulin) and glucose tolerance were unaffected by glucagon infusion, but systemic appearance of ingested glucose (RaOral) was significantly reduced ($p<0.05$) by glucagon infusion in both GB and CN.

Conclusion: Our findings indicate that increasing systemic glucagon concentrations within physiological levels has no effect on the overall prandial glucose or insulin secretory response in subjects with normal glucose tolerance with or without bariatric surgery. Whether the excess post-meal 'endogenous glucagon' response after GB contribute to glucose metabolism needs further studies.

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Posterboard #: 13

Presenter: Iriscilla Ayala, PhD
Institution: UT Health San Antonio
Category: Postdoctoral/Clinical Fellow

The Transcriptional Function of TCF7L2 is Spatially Restricted in Liver and Regulates Zonated Metabolic Pathways Which Contribute to Liver Disease

Iriscilla Ayala, Skanda K Hebbale, Chris E. Shannon, Ivan Valdez, Marcel Fourcaudot, Terry M. Bakewell, Sami Heikkinen, Luke Norton

Non-alcoholic fatty liver disease (NAFLD) affects approximately 30-40% of Americans-and its occurrence increases to 40-80% among people with Type 2 Diabetes (T2D). Single nucleotide polymorphisms in the transcription factor 7-like 2 (TCF7L2) gene are highly associated with NAFLD and T2D. TCF7L2 is one of the main effectors of the canonical WNT/β-catenin signaling pathway. The metabolic function of TCF7L2 in the liver remains to be fully elucidated, but we hypothesized that TCF7L2 contributes to NAFLD through the regulation of zonal metabolic pathways. Using single nuclei RNA sequencing (snRNA-seq), we examined Tcf7l2 expression in periportal (PP) hepatocytes around the portal triad and pericentral (PC) hepatocytes surrounding the central vein of the liver lobule. To visualize TCF7L2 transcriptional activity we used TCF/Wnt signaling reporter mice, which express an H2B-eGFP fusion protein downstream of the conserved TCF/Lef DNA binding site. We disrupted Tcf7l2 transcriptional activity in mouse liver by breeding mice with a floxed Tcf7l2 exon 11, which encodes part of the DNA binding domain (DBD), to albumin-Cre mice (Hep-TCF7L2ΔDBD). To investigate the role of TCF7L2 in fibrogenesis, we used eight-week-old control and Hep-TCF7L2ΔDBD mice were fed a choline-deficient amino acid-defined high fat (CDAHFD) diet for 8 weeks. In liver samples harvested from these mice, we examined disruption to several key zonated metabolic pathways including lipid and glutamine metabolism. We prepared histological slides to quantify the development of fibrosis. Single nuclei analysis revealed that Tcf7l2 mRNA was expressed primarily in parenchymal cells of the liver but was ubiquitous across the liver lobule. However, in immunofluorescence analysis of TCF/Wnt reporter mice, the transcriptional activity of TCF7L2 was highly restricted to PC hepatocytes. Classic PC hepatocyte markers, including glutamine synthetase (Glul), were absent in Hep-TCF7L2ΔDBD mice. Following the CDAHFD, Hep-TCF7L2ΔDBD mice developed more severe fibrosis in histological analysis, and expressed elevated levels of genes involved in fibrogenesis, collagen synthesis and TGFβ signaling. Hep-TCF7L2ΔDBD mice also displayed hepatic cholesterol accumulation following the CDAHFD, which was likely the result of impaired pericentral bile acid synthesis. Our results suggest that TCF7L2 plays an important role in the regulation of zonated metabolic pathways, which may contribute to the development of fibrosis. Ongoing analyses are exploring the mechanisms regulating the zonal transcriptional activity of TCF7L2.

Posterboard #: 14

Presenter: Cody Black, PharmD, PhD
Institution: UT Health San Antonio
Category: Postdoctoral/Clinical Fellow

Integrative Genomic and Clinical Modeling Reveals Novel Genetic Determinants Independently Associated with Staphylococcus aureus Purulent Skin Infections

C. Black, W. So, R. Benavides, S. Dallas, C. Frei, G. Lee

Staphylococcus aureus causes a spectrum of infections, with skin and soft tissue infections (SSTIs) and nasal colonization representing divergent clinical phenotypes. The genetic and metabolic adaptations distinguishing these phenotypes remain poorly understood. We performed a bacterial genome-wide association study (bGWAS) and machine learning analysis on 157 S. aureus isolates (126 SSTI and 31 colonization). Unitig-based GWAS, non-synonymous nucleotide variant (NSNV) analysis, and functional annotation revealed associations with metabolic pathways, while XGBoost machine learning identified key predictive features. Copy number variation (CNV) analysis was conducted to assess genomic adaptations. Data were integrated with lineage-specific effects and functional enrichment analyses. SSTI isolates exhibited enriched unitigs and NSNVs associated with metabolic pathways, including purine/pyrimidine metabolism, nitrogen assimilation, and menaquinone biosynthesis. Unitig z-scores highlighted genes involved in nucleotide metabolism (e.g., nirB, narH), anaerobic adaptations, and stress responses, with significant enrichment in SSTI strains (OR > 4.0). Prophage genes contributed to DNA repair and cytolysis processes, enhancing survival in infection contexts. XGBoost identified top features mapping to genes such as purL and menaquinone biosynthesis genes, critical for anaerobic metabolism. CNV analysis revealed significant genomic variations in nitrogen metabolism genes, including nifR3, which co-localized with stress-response and prophage-related elements in 74% of SSTI samples. Restriction-modification systems (e.g., hsdM) were overrepresented in SSTI isolates, safeguarding genomic stability. This study identifies metabolic pathways and prophage elements as critical adaptations for S. aureus pathogenicity. SSTI strains prioritize nitrogen assimilation and anaerobic energy production, with lineage-specific genomic clustering enhancing survival. Machine learning validated these findings, underscoring their potential as therapeutic targets. Disrupting nitrogen metabolism or prophage functions may mitigate S. aureus virulence and infection.

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Posterboard #: 15

Presenter: Kristi Dietert, PhD
Institution: UT Health San Antonio
Category: Postdoctoral/Clinical Fellow

Circadian reprogramming in cellular senescence

Kristi Dietert, PhD; Qing Zhang; Christopher Litwin; Ioannis Tsialtas, PhD; Zhihong Li; Kevin Koronowski, PhD

Aging and age-related diseases have become a public health crisis. Circadian rhythms become dysfunctional with age and disrupted circadian rhythms result in elevated risk for diseases that are associated with aging. We aim to improve our understanding of the reciprocal relationship between aging and circadian rhythms.

A major driver of age-related disease is cellular senescence. Studies suggest that circadian disruptions result in elevated in cellular senescence. Interestingly, there is also evidence that senescent cells display circadian dysfunction. The mechanisms that govern the relationship between circadian rhythms and cellular senescence are incompletely understood and require further investigation.

Our preliminary data suggests expression of prominent players in the cellular senescence program are dependent on Bmal1, a core clock component. Further, we have identified that p21, a cell-cycle protein also responsible for driving cellular senescence is highly upregulated at night, but this rhythm is disrupted with circadian misalignment, suggesting the clock is responsible for regulating its expression. We have also identified that both senescence status and treatment with exogenous SASP factors can robustly alter cellular rhythmicity. Finally, we have identified that increased markers of cellular senescence and disrupted circadian behaviors coincide in aged mice.

Taken together, we hypothesize that the molecular clock regulates cellular senescence and that cellular senescence drives circadian dysfunction with age. We aim to determine how the molecular clock contributes to cellular senescence, define the rhythm of senescent cells, and elucidate how they influence the rhythm and circadian functions of neighboring non-senescent cells.

We use both in vivo and in vitro approaches to strategically manipulate the molecular clock and cellular senescence to disentangle their effects on one-another. A better understanding of the underlying biological processes that drive aging will undoubtedly provide insight toward development of therapeutic interventions capable of ameliorating an array of diseases.

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Posterboard #: 16

Presenter: Marisol Fernandez Ortiz, PhD
Institution: UT Health San Antonio
Category: Postdoctoral/Clinical Fellow

Melatonin as a Preventive and Rescue Strategy to Counteract Doxorubicin-induced Cardiotoxicity and its Link with Sirtuin 3

Marisol Fernandez Ortiz, Logan R. Davis, David Gius, Gregory J. Aune

There are over 500,000 childhood cancer survivors in the USA, many of whom are at increased risk of life-threatening health issues, with cardiovascular disease being the leading cause of early mortality. Most of these survivors received anthracyclines, particularly Doxorubicin (DOX), due to its high efficacy against solid cancer and hematological malignancies. The use of DOX is associated with long-term cardiac risks, including delayed cardiac dysfunction and irreversible heart failure, making the long-term health of survivors a major healthcare concern.

A potential mechanism of DOX induced cardiotoxicity (DOXIC) is the accumulation of DOX in mitochondria of cardiac fibroblasts (CFs), increasing free radicals, which induces mitochondrial oxidative stress and decreases cardiac function over time. We proposed melatonin (aMT), mitochondria-targeted antioxidant, as a strategy to counteract DOXIC. aMT has been shown to enhance chemotherapy efficacy and has been used safely in patients at high doses. Notably, aMT interacts with and regulates mitochondrial Sirtuin 3 (Sirt3), a molecule that plays a crucial role in maintaining mitochondrial redox balance, though the exact link between aMT and Sirt3 remains unclear.

This study aimed to evaluate aMT as a rescue agent against DOX exposure and investigate the role of Sirt3 in aMT efficacy. CFs were isolated from 3-month-old C57BL6/J (WT) and knocked out for Sirt3 (Sirt3-/-) mice. Cells were treated with DOX, followed by continuous aMT treatment during 72 hrs. Confluency, viability, and mitochondria morphology were assessed. Fractional shortening (FS) was determined via echocardiogram to evaluate cardiac function in 12-month-old WT mice. The experimental groups were: 1) Vehicle, 2) DOX, 3) DOX + Early aMT (preventive), 4) DOX + Late aMT (rescue), and 5) aMT. Mitochondrial ultrastructure was analyzed using a 5-grade scoring system.

In vitro, aMT showed a dose-dependent response in WT CFs against DOX toxicity, but this response was absent in Sirt3-/- CFs. aMT improved CFs proliferation, reduced cell death and preserved mitochondrial morphology in WT CFs treated with DOX but had no effect in mutant CFs. In vivo, aMT preserved cardiac function as an early treatment both during and after DOX exposure for the entirety of the 12-month period. As a late treatment, aMT rescued DOX-induced depletion of cardiac function, recovering FS from 28 to 39%. Importantly, this improvement in FS persisted following completion of late aMT treatment. Mitochondrial ultrastructure in DOX mice showed the most damage, with the highest prevalence of mitochondria with a score of 0. aMT prevented this damage as an early treatment and recovered it as a late melatonin, with both groups showing a predominant presence of mitochondria with a score of 4.

These results provide the first evidence demonstrating aMT as a potential preventive and rescue strategy against late DOXIC, with Sirt3 playing a key role in the process.

Posterboard #: 17

Presenter: Alison Luckey, PhD
Institution: Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases / Institute for Integration of Medicine & Science
Category: Postdoctoral/Clinical Fellow

Improving VCID Risk Stratification: A NfL and PSMD Multi-Biomarker Approach

Alison M. Luckey PhD, Rebecca Bernal, MS, Alexa Beiser PhD, Jayandra Jung Himali PhD, Hugo J. Aparicio MD, MPH, Pauline Maillard PhD, Sudha Seshadri MD PHD, Claudia L. Satizabal PhD

Background: Neurofilament Light (NfL) is a broad biomarker of neuroaxonal injury elevated in neurological diseases, including cerebral small vessel disease (cSVD). However, NfL's non-specificity limits its effectiveness in assessing susceptibility/risk for Vascular Contributions to Cognitive Impairment and Dementia (VCID). To improve VCID risk stratification, we propose combining NfL with Peak-Width of Skeletonized Mean Diffusivity (PSMD), a specific neuroimaging biomarker of white matter microstructural damage. Prior research shows NfL and PSMD, individually, are strongly associated with worse cognition. This study aims to (1) provide proof-of-concept validation for a NfL-PSMD multi-biomarker approach, and (2) evaluate a two-step strategy using NfL as an initial screening tool, followed by PSMD measurement to further delineate the presence of cSVD-VCID features.

Methods: Participants (N=1063) from the Framingham Heart Study Offspring (Exam 9; 2011-2014) and Omni-1 (Exam 4; 2011-2014) cohorts, with NfL, neuroimaging, and cognitive data were included. NfL was measured in plasma, and PSMD was derived from magnetic resonance diffusion-weighted imaging. A composite score of general cognitive function was calculated from neuropsychological tests assessing at least three different cognitive domains. Executive function was also assessed through neuropsychological tests, as it is one of the first domains typically affected in cSVD. NfL and PSMD were categorized by the top quartile and combined to indicate heightened VCID risk. Linear regression models examined the association between high NfL-PSMD and cognition, adjusting for age, age2, sex, education, renal function (eGFR), total intracranial volume, time difference between blood draw/MRI and cognitive assessment, and cohort. We then stratified by high and low NfL to assess whether PSMD was differentially associated with cognition.

Results: Key FHS sample characteristics include a mean age of 71 years, 56% female, and a high level of education, with 48% of participants having graduated from college and 28% having attended some college. Regarding vascular risk factors, approximately 58% had hypertension and 14% had diabetes. High NfL-PSMD was significantly associated with worse executive (Beta[95% confidence interval], -0.059[-0.093, -0.025], p=0.001) and general cognitive function (-0.197[-0.314, -0.080], p<0.001). After stratification by NfL, higher PSMD was significantly associated with poorer executive (-0.108 [-0.180, -0.036], p=0.003) and general cognitive function (-0.451[-0.684, -0.217], p<0.001) among those within the high NfL strata.

Conclusion: The NfL-PSMD multi-biomarker approach identifies persons with heightened VCID risk and worse cognition. Further, NfL modifies the association between PSMD and cognition only among those with high NfL. This two-step multi-biomarker approach has the potential to narrow the pool of individuals at risk of developing dementia while reducing the costs of neuroimaging. This approach would be ideal for clinical trial protocols to select participants who are most likely to benefit from interventions. Ongoing analyses are exploring the added specificity of the NfL-PSMD multi-biomarker, with additional validation studies in larger, diverse samples underway.

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Posterboard #: 18

Presenter: Braden Miller, MD
Institution: UT Health San Antonio
Category: Postdoctoral/Clinical Fellow

Ex-Vivo Machine Perfusion of Hemoglobin Based Oxygen Carrier (HBOC) for Extended Procurement-to-Transplantation Timelines after Trauma

Braden Miller, Manuela Gaviria, Dena Norouzi, Shauna Hill, Charles Anton Fries

Background: The efficacy of ex-vivo subnormothermic machine perfusion (SNMP) using hemoglobin based oxygen carriers (HBOC) has demonstrated efficacy in fasciocutaneous graft preservation at extended time points. This study evaluates tissue viability and transplantation outcomes in a myofasciocutaneous graft model comparing ex-vivo SNMP with HBOC, SNMP with University of Wisconsin Belzer Solution (UWS), and cold static preservation (CSP).

Methods: Ten semitendinosus muscle flaps (SMFs) were harvested from five Yorkshire pigs and preserved ex-vivo for 24 hours. Four underwent SNMP using HBOC (HBOC group), 3 underwent CSP using UWS (CSP group), and 3 underwent SNMP using UWS (UWSP group). Three SMF from the HBOC group were transplanted. The CSP group was intermittently perfused for sample collection. Metrics analyzed included venous and arterial blood gas, lactate, creatinine levels, oxygen consumption, and weight change. Lactate values were adjusted for the presence of lactate in HBOC. Perfusate markers were compared at the 24-hour time point using T-test analysis.

Results: One SMF flap failed to perfuse and was excluded. Oxygen consumption was significantly higher in the HBOC group (270.7 mmHg) compared to the CSP (98.7 mmHg, p=0.012) but not significantly different from the UWSP group (134.3 mmHg, p=0.12). Lactate production was lower in the HBOC group compared to CSP (-0.2 vs. 18.5 mmol/L, p=0.0002) and UWSP (-0.2 vs. 1.9 mmol/L, p=0.002). HBOC venous pH was comparable to CSP (7.81 vs. 7.20, p=0.07) but significantly less acidic than UWSP (7.81 vs. 6.82, p=0.003). Creatinine levels were similar across all groups. Preliminary results from the transplantation phase showed two viable grafts at two weeks, while one failed due to vascular thrombosis.

Conclusion: Ex-vivo SNMP using HBOC in a porcine SMF graft model demonstrated superior tissue preservation over CSP by maintaining oxygen consumption, reducing lactate accumulation, and stabilizing pH. The UWSP group confirmed that perfusion alone was not responsible for these differences, highlighting the metabolic advantages of HBOC-based perfusion. These results suggest that HBOC perfusion is a promising technique to improve tissue harvest to transplantation timelines for mycofasiocutaneous grafts for up to 24 hours following trauma.

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Posterboard #: 19

Presenter: Carlos Rivera, PhD
Institution: UT Health San Antonio
Category: Postdoctoral/Clinical Fellow

A humanized mouse that mounts mature class-switched, hypermutated and neutralizing antibody responses

Carlos E. Rivera, Daniel P. Chupp, Yulai Zhou, Yijiang Xu, Zhenming Xu, Patrick S. Ramsey, Belinda R. Lopez, Amy Bible, Bhuwaneswor P. Kandel, Mia C. Pickens and Paolo Casali

Humanized mice are limited in terms of modeling human immunity, particularly with regards to antibody responses. We have constructed an advanced (THX) humanized mouse by grafting non-γ-irradiated, genetically myeloablated (KitW-41J mutant) immunodeficient NBSGW and NSGW41 mouse neonates with human umbilical cord CD34+ cells by intracardiac injection, followed by hormonal conditioning with 17β-estradiol (E2), the most potent and physiologically abundant estrogen, to promote immune cell differentiation. THX mice reconstitute an immune system with human CD45+ cells accounting for virtually all lymphoid and myeloid cells, including human marginal zone B cells, germinal center (GC) and memory B cells, follicular helper T cells, NK cells, dendritic cells, monocytes/macrophages and neutrophils. These human lymphoid and myeloid cells populate all lymphoid organs, including lymph nodes and Peyer's patches, and THX mice developed a thymus housing human thymic epithelial cells and B cells. THX mice express diversified B cell receptor (BCR) and T cell receptor (TCR) repertoires reflecting those of humans and develop a gut microbiome consisting of Muribaculaceae and other bacterial families characteristic of human gut microbiome. They mount mature high-affinity antibody responses to T-dependent and T-independent conjugated haptens, as well as specific and neutralizing antibody responses to Salmonella Typhimurium and SARS-CoV-2 Spike S1 RBD upon vaccination with Salmonella Typhimurium flagellin and Pfizer COVID-19 mRNA, respectively. Such mature human antibody responses entailed somatic hypermutation (SHM), class-switched DNA recombination (CSR), GC B cell and plasma cell differentiation, and the generation of memory B cells, as accompanied by blood incretion of human APRIL, BAFF, TGF-β, IL-4, IFN-γ and other human cytokines, all at physiological levels. THX mice also develop human-like lupus autoimmunity and immunopathology after one pristane injection. Thus, by leveraging crucial estrogen activity to support human immune cell differentiation and maturation of antibody responses, THX mice overcome the limitations of current humanized mouse models and provide a platform for in vivo studies of human immune responses, development of human vaccines and therapeutics and modeling human diseases.

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Posterboard #: 20

Presenter: Afaf Saliba, PhD
Institution: UT Health San Antonio
Category: Postdoctoral/Clinical Fellow

Inhibition of methylthioadenosine phosphorylase protects against acute kidney injury

Afaf Saliba, Yidong Chen, Jonathan W. Nelson, Abhinav Vetcha, Wei Wei Wang, Li Kang, Nagarjunachary Ragi, Soumya Maity, Hamid Rabb, W. Brian Reeves, Kumar Sharma

Acute kidney injury (AKI), the sudden decline of kidney function, is a major clinical challenge associated with high morbidity, increased mortality, and a strong predisposition to chronic kidney disease (CKD). Despite advances in understanding AKI pathophysiology, effective therapeutic strategies remain limited. Metabolic dysregulation plays a central role in AKI pathogenesis, yet targeted interventions remain elusive.

Methylthioadenosine phosphorylase (MTAP) is a key enzyme involved in purine and polyamine metabolism. While MTAP inhibition (MTAPi) has shown renal protective effects in diabetic kidney disease, its role in AKI remains unexplored.

In this study, we examined the effects of pharmacological MTAP inhibition using MT-DADMe-ImmA, a small-molecule MTAP inhibitor, in ischemia-reperfusion (IR) and cisplatin-induced AKI mouse models. Male 10-12-week-old C57BL/6J mice were used, and the inhibitor was administered intraperitoneally. Kidney injury was assessed through renal biomarkers, histology, and RNA sequencing. Additionally, single-cell RNA sequencing (scRNA-seq) data from 32 human kidney biopsies (20 healthy, 12 AKI) retrieved from the Kidney Precision Medicine Project (KPMP) were analyzed.

MTAPi significantly reduced kidney injury, as evidenced by decreased blood urea nitrogen (BUN) levels, reduced expression of injury markers Havcr1 (hepatitis A virus cellular receptor 1, also known as Kim-1, kidney injury molecule-1 and Lcn2 (Lipocalin 2, also known as NGAL, neutrophil gelatinase-associated lipocalin), and attenuation of tubular necrosis. To gain mechanistic insight into MTAPi protection during AKI, bulk RNA-seq analysis of kidney cortex lysates revealed that MTAP inhibition modulates key metabolic and inflammatory pathways, suppressing maladaptive renal tubular repair programs while enhancing protective metabolic processes such as fatty acid oxidation and oxidative phosphorylation.

To determine the relevance of MTAP in the clinical manifestations of human kidney disease, we analyzed single-cell RNA sequencing (scRNA-seq) KPMP data from human AKI kidney biopsies. Our analysis demonstrated increased MTAP expression in proximal tubule (PT) cells, particularly within HAVCR1-expressing cells associated with injury. Furthermore, MTAP was enriched in adaptive PT cells, which are involved in tissue repair but may contribute to maladaptive responses in AKI.

Our findings establish MTAP as a novel modulator of AKI pathophysiology, with its inhibition conferring renal protection through metabolic and inflammatory modulation. The strong correlation between MTAP expression and injury markers in human AKI underscores its clinical relevance. These results position MTAP inhibition as a promising therapeutic strategy to enhance kidney recovery and mitigate AKI severity. Future preclinical studies and in-depth mechanistic studies are warranted to refine MTAP-targeted therapies and evaluate their efficacy potentially addressing the urgent need for novel AKI treatments.

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Posterboard #: 21

Presenter: Shilpa Thakkar, BDS
Institution: UT Health San Antonio
Category: Postdoctoral/Clinical Fellow

Exploring Stem Cells for Management of Post-Operative Endodontic Pain

Shilpa Thakkar, Josue Murillo, Phoebe Chang, Brett Chapa, Kaila Nip, Nikita B. Ruparel

Persistent post-endodontic pain affects ~2 million patients. The chronic use of current analgesics yields to serious adverse effects including the contribution to the opioid epidemic. Thus, it is imperative to investigate novel classes of compounds devoid of adverse effects for lasting pain relief. Stem cell-induced analgesia has shown promising efficacy in clinical and preclinical studies. Objective: To evaluate the role of human stem cells of the apical papilla (hSCAP) and its potential mechanisms in attenuating apical periodontitis (AP)-induced pain. Methods: Baseline mechanical thresholds of BALB/c mice were obtained using von Frey behavioral assay. AP was induced via pulp exposures of the maxillary left 1st molar. Following this, mice received weekly intravenous hSCAP injections for three weeks. Orofacial behavior was evaluated each week. hSCAP homing was evaluated using immunohistochemistry. Bulk RNA-sequencing was performed of mouse periapical lesions to determine potential targets mediating hSCAP effect. Intraoral recombinant drug injections of macrophage migration inhibitory factor (MIF) for three days were performed to evaluate its effect on mechanical allodynia. Data were analyzed by 2-way ANOVA with Tukey's post-hoc test. Results: Orofacial behavior demonstrated that hSCAP significantly reversed AP-induced mechanical allodynia. Immunohistochemistry showed hSCAP selectively home to periapical granulomas. RNA sequencing of granulomas from mice injected with hSCAP revealed a 133-fold increase in MIF expression. Intraoral recombinant MIF injections significantly reversed AP induced pain. Conclusion: Collectively, we demonstrate the effectiveness of stem cells in attenuating AP-induced pain via hSCAP-derived MIF release. These studies highlight a novel analgesic drug class potentially devoid of serious adverse effects. This study was supported by NIDCR R01 DE031352

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Posterboard #: 22

Presenter: Leen Abazid, MD, PhD candidate
Institution: UT Health San Antonio
Category: Student

Brain Alterations in Prader-Willi Syndrome: A Coordinate-based Meta-analysis of Case-Control Contrasts

Leen Abazid; Crystal G. Franklin; Ralph A. DeFronzo; Amy S. Garrett; Peter T. Fox

This study conducted a coordinate-based meta-analysis (CBMA) of voxel-based neuroimaging studies to identify consistent brain abnormalities in Prader-Willi Syndrome (PWS). Analysis of 25 experiments from eight studies (131 PWS patients, 99 controls) revealed alterations in regions linked to self-regulation and reward processing, including the anterior cingulate cortex, striatum, and frontal and temporal lobes. While PWS and non-syndromic obesity shared similarities in reward-related regions, distinct alterations were observed in the cingulate cortex, mid-frontal gyrus, and precentral gyrus. Notably, the absence of hypothalamic alterations challenges the traditional view of PWS as primarily a hypothalamic disorder. These findings offer insights into the neural mechanisms of PWS, potentially guiding targeted treatments for hyperphagia and associated behaviors.

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Posterboard #: 23

Presenter: Emily Aller, BA
Institution: UT Health San Antonio
Category: Student

Development of a novel MDK targeted therapy for the treatment of Endometrial Cancer

Emily J. Aller, Alondra L. Rodriguez Sanchez, Megharani Mahajan, Xue Yang, Paulina Ramirez, Panneerdoss Subbarayalu, Manjeet K. Rao, Edward R. Kost, Hareesh B. Nair, Ratna K. Vadlamudi, and Suryavathi Viswanadhapalli

BACKGROUND: Endometrial (ECa) is the fourth most prevalent women's cancer and its incidence is rising rapidly in women under 40. Currently, recurrent ECa is treated with hormonal therapy, chemotherapy, and targeted therapies, such as bevacizumab and everolimus. However, the response rates and progression-free survival (PFS) are still poor in advanced ECa with high risk of cancer recurrence and mortality. New targeted therapies are urgently needed. Midkine (MDK), is a heparin-binding growth factor that regulates multiple oncogenic signaling pathways and its expression is commonly deregulated in cancers including ECa. The objective of this study is to develop a potent inhibitor that targets MDK for treating ECa.

METHODS: Using the three-dimensional structure of human MDK, we rationally designed a small organic molecule (HBS-101) that directly binds with MDK and that functions as a MDK inhibitor. In silico docking studies were used to identify the putative interaction site of the HBS-101 on MDK. Direct binding of HBS-101 to MDK was confirmed using microscale thermophoresis technique (MST) assay. In vitro activity was tested using MTT, clonogenicity and apoptosis assays. Mechanistic studies were conducted using Western blot, RT-qPCR and STAT3 reporter gene assays. Status of MDK in ECa was determined using TNMplot database. Pharmacokinetics and Maximum Tolerable Dose studies were conducted using in vivo mice models.

RESULTS: TNM plot results showed that MDK is highly expressed in ECa tumors compared to normal tissues. Western blot analyses confirmed expression of MDK and its receptors in established and primary ECa cells. Molecular docking studies identified an HBS-101 interacting surface on MDK. MST studies confirmed the direct interaction of HBS-101 to MDK. The MTT assay results indicated that HBS-101 significantly reduced the cell viability of ECa cells, with an IC50 of 1-5 μM. HBS-101 treatment also reduced the survival of ECa cells in colony formation assays. Further, HBS-101 treatment promoted apoptosis. Additionally, HBS-101 treatment substantially diminished the activity of STAT3, a downstream effector of MDK. PK studies confirmed that MDK has distinct pharmacologic advantages, including oral bioavailability, and in vivo stability. HBS-101 up to a dose of 10 mg/kg showed no observable organ toxicity and had no effect on the mice's body weight. Ongoing studies are evaluating the efficacy of HBS-101 using xenograft models.

CONCLUSION: Collectively, our findings indicate that HBS-101 is a novel therapeutic agent targeting MDK through a unique mechanism of action, good PK and HBS-101 blocking MDK signaling triggers apoptosis in ECa cells.

Posterboard #: 24

Presenter: Adriana Baker, BS
Institution: UT Health San Antonio
Category: Student

ERX-315: A Potential Treatment Option for Hepatocellular Carcinoma

Adriana Baker1, Xue Yang1, Uday P. Pratap1, William C. Arnold1, Alyssa D. Friudenberg1, Gaurav Sharma1, Chia-Yuan Chen2, Scott Elmore2, Sukeshi Patel Arora3, LuZhe Sun1,3, Suryavathi Viswanadhapalli1,3, Ganesh V. Raj4, Jung-Mo Ahn2, Ratna K. Vadlamudi1,3

Background: Hepatocellular carcinoma (HCC) accounts for more than 90% of instances of liver cancer, which ranks as the fifth most frequent cancer in the United States. Furthermore, Texas leads the nation in the age-adjusted incidence of HCC. Most patients are diagnosed with advanced, unresectable HCC, and their 5-year survival rate is less than 5% when using current systemic treatments. Therefore, there is an immediate unmet need for new treatment approaches for HCC. Recently, the unfolded protein response (UPR) and endoplasmic reticulum (ER) stress have been recognized as targetable vulnerabilities. From a curated screen, we have previously identified that a synthetic oligo-benzamide, ERX-315, that targets protein encoded by lysosomal acid lipase A (LIPA), causes ER stress and cancer cell death without affecting normal cells. This study aims to evaluate the utility of ERX-315 for treating HCC by targeting ER stress

Methods: Tissue micro arrays (TMAs) and Immunohistochemistry (IHC) were used to confirm the expression of LIPA in HCC. LIPA expression in HCC tumors was also confirmed using TNM database. The impact of ERX-315 on 6 well-established HCC cell lines was evaluated using the MTT and colony formation assays. The specificity of ERX-315 targeting activity was confirmed by CRISPR-KO of LIPA in one of the HCC cell lines. For mechanistic investigations, Western blotting, RT-qPCR, and splicing assays were employed. Huh7 organoids generated from xenografts were utilized to evaluate the effects of ERX-315 ex vivo. Huh7 cell-based xenografts and patient-derived xenograft (PDX) models were used to validate the efficacy of ERX-315 in vivo.

Results: TNM plot analysis revealed that HCC tumors exhibited elevated levels of LIPA expression in comparison to normal tissue. Analysis of TMA samples showed that compared to normal tissue, HCC samples exhibit increased levels of LIPA expression. ERX-315 treatment significantly decreased both colony formation and cell viability (IC50 between 30-150nM) and promoted apoptosis in HCC cells. In contrast, ERX-315 did not cause apoptosis in normal liver epithelial cells. Compared to wild type cells, KO of LIPA dramatically attenuated the effect of ERX-315 on colony formation and cell viability in HCC cells. Mechanistic studies using splicing assay, RT-qPCR, and Western blotting demonstrated elevated levels of ER stress indicators upon treatment with ERX-315 in a dose dependent manner. Xenograft-derived Huh7 organoids' cell viability was considerably reduced by ERX-315. ERX-315 therapy dramatically decreased the tumor volume in Huh7 xenograft and PDX models in both male and female mice.

Conclusion: Collectively, our results suggest that ERX-315 promotes ER stress and cell death in HCC in vitro, ex vivo, and in vivo. ERX-315 represents a promising novel therapeutic option for HCC. Since ERX-315 is in clinical trials, these data strongly support evaluation of ERX-315 in patients with liver cancer.

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Posterboard #: 25

Presenter: Ramya Smithaveni Barre, MS
Institution: UT Health San Antonio
Category: Student

A Human H5N1 Influenza Virus Expressing Nluc for Real-time Tracking Viral Infection and Identification of Therapeutic Interventions

Ramya Smithaveni Barre, Ahmed Mostafa, Ruby Escobedo, Esteban Castro, Roy N. Platt, Anastasija Cupic, Mahmoud Bayoumi, Nathaniel Jackson, Chengin Ye, Timothy J C Anderson, Adolfo García-Sastre, Luis Martinez-Sobrido

A multistate outbreak of highly pathogenic avian influenza virus (HPAIV) H5N1 in dairy cows was first reported on March 25, 2024, marking the first discovery of this virus in cattle. Soon after, a dairy worker on an affected farm became the first human case linked directly to the cattle outbreak. Influenza A virus (IAV) studies typically require secondary methods to detect the virus in infected cells or validated animal models. To address this challenge, we modified the non-structural (NS) gene of the human A/Texas/37/2024 H5N1 virus to create a recombinant virus with a nanoluciferase (Nluc) reporter gene, enabling easy tracking of the virus in cultured cells and mice via in vitro, ex vivo, and in vivo imaging systems (IVIS). In vitro, the Nluc-expressing recombinant A/Texas/37/2024 H5N1 showed growth and plaque characteristics similar to its wild-type counterpart. Remarkably, in vivo, the recombinant virus allowed effective tracking of viral infection in whole mice and in the organs of infected animals using IVIS. Additionally, the morbidity, mortality, and replication rates of the Nluc-expressing recombinant virus were similar to those of the wild-type virus. In vitro, the recombinant A/Texas/37/2024 H5N1 expressing Nluc was successfully neutralized by monoclonal antibodies (MAbs) and antivirals, with neutralization and inhibition levels comparable to those in wild-type virus-infected cells. We also utilized the Nluc-expressing virus to evaluate the neutralizing and antiviral effects of monoclonal antibodies and antivirals in vivo. Our findings show that the recombinant A/Texas/37/2024 H5N1 with Nluc is an excellent tool for tracking viral infections and discovering new prophylactic and therapeutic treatments for this newly circulating HPAIV A H5N1.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 26

Presenter: Puneet Basra
Institution: UT Health San Antonio
Category: Student

The impact of Adverse Childhood Experiences (ACEs) on oral health

Puneet Basra, Alex Testa, Erica Wallace, Rahma Mungia

Background: Adverse Childhood experiences (ACEs) are early-life traumatic events that occur before the age of 18, including experiences of abuse, neglect and household dysfunction. These experiences can disrupt neurodevelopment, impair stress regulation, and hinder coping mechanisms, increasing the risk of chronic diseases, mental health disorders, and health-risk behaviors in adulthood. Despite the well-established link between ACEs and overall health, limited research has examined their impact on oral health and the role dental practitioners play in mitigating these effects through trauma-informed care. This study investigated dental practitioners' awareness of ACEs and their role in incorporating trauma-informed care into patient interactions.

Methods: A brief targeted five-question survey ("Quick-Poll") was conducted through the South Texas Oral Health Network (STOHN) Practice-Based Research Network (PBRN). A total of 41 participating dental practitioners responded to assess their familiarity with ACEs, knowledge of trauma-informed care, and interest in further education and research on the topic.

Results: 43 dental practitioners completed all five questions in the quick poll. Most dental practitioners had some level of familiarity with ACEs, yet only a small fraction (N=4, 9.3%) reported being highly knowledgeable. Conversely, 14.0% (N=6) were completely unfamiliar with the concept, underscoring the need for further education. Critically, 76.8% (N=33) of practitioners acknowledged that ACEs negatively impact a patient's likelihood of seeking dental care, highlighting the necessity for a trauma-sensitive approach in dentistry. When assessing trauma-informed care knowledge, the largest proportion of respondents (N=17, 39.5%) remained neutral, indicating uncertainty about their ability to implement trauma-informed strategies. Furthermore, over one-fifth (N=10, 23.2%) of practitioners admitted they lacked the knowledge to apply trauma-informed counseling techniques for patients with ACEs. Encouragingly, 65.2% (N=28) expressed a strong interest in receiving training on ACEs screening and counseling, demonstrating a willingness to bridge this knowledge gap. Additionally, more than half (N=24, 55.9%) of respondents indicated enthusiasm for participating in an ACEs and counseling study, signaling a commitment to advancing trauma-informed practices in dentistry.

Conclusion: The findings highlight a moderate level of ACEs awareness among dental care practitioners but reveal a significant knowledge gap in trauma-informed screening and counseling. While most practitioners recognize the impact of ACEs on oral health and patient behavior, many lack the training necessary to provide appropriate support. Encouragingly, the majority of participants expressed a strong interest in further education and research involvement, presenting a valuable opportunity to integrate trauma-informed care into dental practice. Expanding ACEs education for dental practitioners may enhance patient-centered care, improve health outcomes, and foster a more compassionate dental environment for individuals with a history of trauma.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 27

Presenter: Kaitlyn Bejar, MS
Institution: UT Health San Antonio
Category: Student

The Analysis of N-glycans and Collagen to Predict Prostate Adenocarcinoma Outcome

Kaitlyn Bejar, Jordan Hartig, Richard Drake, Peggi Angel, Teresa Johnson-Pais, Robin Leach

Background: Prostate cancer is the most common non-cutaneous cancer and the second leading cause of cancer related death in American men. However, the majority of men with prostate cancer die with their cancer and not from their cancer. Distinguishing indolent from aggressive disease and early identification of men at risk of developing aggressive, metastatic disease is of great clinical importance. Genomic classifiers that analyze RNA expression of various genes have been found to predict risk of metastasis with areas under the curve (AUCs) averaging 0.70. These classifiers can be improved and additional biomarkers for aggressive prostate cancer are still needed. Tumor extracellular matrixes are comprised of fibrillary and non-fibrillary collagens, fibronectin, and proteoglycans. Collagen is a main component of reactive stroma and changes in collagen types to reflect the course of prostate cancer have yet been defined. It has already been observed that collagen type 1 may promote metastasis in multiple cancers. Observed with the reactive stroma changes in collagen peptides and extracellular matrix are alterations in N-linked glycans attached to glycoproteins in the stroma and tumor regions. Recent technological advances allow for the analysis of N-glycans and collagens on the same tissue specimen, leading to the potential of glycan- and collagen-based biomarkers for prostate cancer.

Methods: Matrix assisted laser desorption/ionization mass spectrometry can be utilized to characterize N-glycan profiles in formalin fixed paraffin embedded tissues. Collagen may also be characterized using ECM-targeted collagenase MALDI imaging. These approaches were used to analyze prostatectomy samples with different clinical outcomes. Tissue microarrays containing tissues from 75 non-progressors (no evidence of disease; NED) and 50 metastatic cases (MET) were examined. From a combined list of 90 N-glycans and 500 collagenase peptides, the average AUC intensity value for each glycan and collagen peptide was extracted and assessed as a predictor of metastatic progression.

Results: Three N-glycans and three collagen peptides were found to discriminate between NED and MET cases with statistical significance. The best performing N-glycan was Hex6HexNAc6Fuc1 with an AUC of 0.77 ($p<0.001$). While the best performing collagen peptide was COL3A1 with an AUC of C 0.95 ($p<0.001$). When treated with ENDO F3 prior to PNGase identification of core fucose species significantly improved and AUCs increased.

Conclusion: Both a collagen peptide (COL1A2) and N-glycan (Hex6HexNAc6Fuc1) were discovered as promising biomarkers to predict metastasis. Future validation studies are needed utilizing an independent cohort to confirm biomarker potential. There is also a need to determine if the addition of these biomarkers can strengthen current genomic classifier's ability to predict metastatic prostate cancer.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 28

Presenter: Marissa Brown, BS
Institution: UT Health San Antonio
Category: Student

Harmonization of Diffusion MRI Parameters in the Liver

Marissa Brown, Luke Norton, John Blangero, Geoffrey D. Clarke

Introduction One of the challenges in analyzing quantitative diffusion MRI data acquired from multiple scanners is the variability in the measured parameters introduced by differences in magnetic field strengths, vendors, hardware, and scan parameters. ComBat is a popular batch-effect correction tool originally designed for use in genomics, however, it has seen success when applied to MRI data. ComBat has been successfully applied to DTI images of the brain to remove inter-site variability while preserving biological variability in fractional anisotropy and mean diffusivity maps. ComBat has also been applied to harmonize radiomic features extracted from T2-weighted abdominal MRI data in subjects with chronic liver disease. To the authors' knowledge, ComBat's effectiveness in harmonizing IVIM parameters in the liver has not been studied.

Methods Data for this study will be obtained from participants in two ongoing NIH studies, "Identification of the Exposome in Fatty Liver Disease in Mexican American Families Using Genetic Correction" and "Quantifying Hepatic Mitochondrial Fluxes in Humans Sub Study Treatment of NAFLD." Abdominal DWI examinations were performed on one of three scanners (i) a 3T Siemens TIMTrio (n = 26), (ii) a 3T Siemens Prisma (n = 35), or (iii) a 1.5T GE Signa Voyager (n = 15). Each DWI sequence was acquired using respiratory triggering with 10 b-values however, the number of diffusion weighting directions, the number of gradient sampling orientations, and the b-values themselves could not be matched between each scanner due to software and scan time limitations. All IVIM parameters will be estimated using a physics-informed convolutional neural network that fits the images to a bi-exponential model to predict estimates for perfusion (D*), perfusion fraction (f), and diffusion (D) (Submitted Abstract ID: 4667). ComBat has been very successful in harmonizing data when the sample sizes are small however, the effectiveness of ComBat to harmonize data using small sample sizes depends on the amount of variability between the groups.

ComBat harmonization will be performed using equal numbers of subjects from each group that are age- and sex-matched. Liver steatosis measured as percent fat fraction by hydrogen MRS will be used as a confounder. To assess the effectiveness of ComBat, a small sample of healthy volunteers (n = 5) will undergo DWI acquisitions on each scanner. Additionally, a NIST diffusion phantom will be used to assess differences in apparent diffusion coefficient (ADC) values. Differences in IVIM parameters before and after harmonization will be analyzed using repeated measures ANOVA for normal data or Friedman test for non-normal data, with Tukey HSD correction for multiple comparisons. The successfully harmonized IVIM data from multiple scanners will be combined for further analysis.

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Posterboard #: 29

Presenter: Elena Camargo, MS
Institution: UTSA & UTHSA
Category: Student

Diagnosis and treatment of chronic disruptive dizziness in Post-911 Veterans following mild traumatic brain injury

Elena Camargo, M.S. & Kelly Cheever, Ph.D.

Introduction/Background: While post-9/11 Veterans often experience dizziness following traumatic brain injuries, whether the dizziness persists over time, if that persistent dizziness leads to a clinical diagnosis, what treatments are sought, and the extent to which that treatment is working is not well understood. Objective: This study aimed to explore what treatments post-9/11 Veterans with and without a formal diagnosis seek to treat their long-term dizziness following a brain injury.

Methods: This cross-sectional study used a sample of 928 post-9/11 Veterans with at least three years of VA care, who reported moderate or more severe dizziness symptoms on initial Neurobehavioral Symptom Inventory -Vestibular sub scores (NSI-V) administered via comprehensive TBI evaluation (CTBIE) and were surveyed between April 2019 through January 2021. Chi square tests were used to assess whether differences between diagnostic groups (those with a specific diagnosis and those without) varied significantly by demographics, reported current dizziness (Dizziness Handicap Inventory; DHI), number of treatment modalities attempted and perceived success of those treatments.

Results: More than 98% (n=914) post-9/11 Veterans reported experiencing dizziness at the time of the survey. In total 78% of the sample population reported trying at least one type of treatment to reduce their dizziness, and those veterans with a specific diagnosis were more likely to have attempted any form of treatment and attempted a broader range of treatment modalities than those with no diagnosis. For all respondents, the most attempted treatments were counseling (55%) and medication (51%). Interestingly, only 32% of respondents reported having attempted balance training and a mere 13% indicated having tried vestibular therapy. Veterans without a formal diagnosis reported the highest percentage of perceived success following surgery and counseling reporting vestibular rehabilitation to be the least effective.

Conclusions: Veterans in this sample who screened positive for moderate to severe disruptive dizziness at the time of initial assessment continue to experience dizziness 3 - 19 years after their initial assessment. Our data indicate that having a specific diagnosis increases the likelihood of seeking treatment for disruptive dizziness but did not increase the likelihood of seeing an improvement in symptoms over time. Further research is necessary to explore the appropriate interventions to increase the utilization of evidence-based treatments such as balance and vestibular therapy in clinical pathways for veterans experiencing disruptive dizziness during the CTBIE.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 30

Presenter: Monica Dorman, MS, CCC-SLP, LSLS Cert. AVEd
Institution: UT Health San Antonio
Category: Student

A Quantitative and Qualitative Analysis of the Articulation in Children with Unilateral Hearing Loss

Monica Dorman, Fang-Ling Lu, Ph.D., CCC-SLP, FASAHP

It is estimated that unilateral hearing loss (UHL) occurs in 0.4 to 34 per 1000 babies and 1 to 50 per 1000 school-aged children, according to Lieu, Tye-Murray, Karzon, & Piccirillo (2010). Research indicates that children with unilateral hearing loss (UHL) experience delays in speech and language development by the time they enter school (Gordon et al., 2023). While hearing health providers and families of children with UHL are cognizant of the research needs, there continues to be a lack of published research studying speech articulation development among children with single-sided deafness (SDD) and unilateral microtia/atresia (UMA).

This study used mixed methods analyzing retrospective data obtained from nationwide listening and spoken language programs to compare children with UHL, either with SSD or UMA, to children with normal hearing on standardized articulation assessment. Articulation test scores of 306 children between 24 and 71 months were analyzed. One-sample t-tests showed that children with UHL performed significantly lower than the normative articulation scores. A two-sided t-test indicated insignificant differences in articulation scores between children with SSD and UMA at 36 months or older.

Below-average articulation scores in children with UHL from 36 to 47 months compared to normal-hearing children support the need for hearing health providers to recommend formal speech evaluation and intervention for children with UHL before 36 months of age to prevent further delays in speech and language development.

Qualitative information was collected through a survey from healthcare providers and parents with children enrolled at Sunshine Cottage, A Listening and Spoken Language School, regarding the service's recommendations that families of children with UHL typically received. Common suggestions from hearing health providers to improve the standard of care for UHL include a comprehensive medical evaluation and early intervention, the similar services provided for children with bilateral hearing loss. Ninety-five percent of parent respondents suggested their child's speech needs be addressed early and consistently, and 70% advocated for at least three to four speech therapy sessions monthly.

The study's quantitative and qualitative analyses led to the same conclusion that formal speech evaluation and intervention should be recommended and implemented for children with UHL before 36 months of age to prevent further delays in speech development and future academic deficits.

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Posterboard #: 31

Presenter: Nomie Fairley
Institution: UT Health San Anotnio
Category: Student

Exploring Dental Practitioners' Confidence in Delivering HPV Vaccine Information

Nomie Fairley (presenter), Erika Thompson, Caitlin Sangdahl, Rahma Mungia

Background: Human Papillomavirus (HPV) is the most common sexually transmitted infection (STI), it is estimated that 80% of sexually active adults will get HPV in their lifetime. Of the over 200 identified HPV types, 15 are classified as high-risk and strongly associated with multiple cancers, oropharyngeal being the one of most common HPV-related cancers. Notably, oropharyngeal cancers linked to HPV surged by 225% between 1988 and 2004, making HPV the leading cause of oropharyngeal cancers in the US. Although initially developed for cervical cancer prevention, the HPV vaccine has emerged as a critical tool in reducing the burden of other HPV-associated cancers. This has led the ADA to recommend dentists to educate their patients about the HPV cancer prevention that the vaccine can provide.

Objective: to gage the confidence of dentist on their understanding and dissemination of HPV-related cancer prevention

Methods: A five-question survey ("Quick Poll") was distributed through the South Texas Oral Health Network (STOHN) Practice-Based Research Network (PBRN) to assess dental practitioners' perspectives on HPV-related cancer prevention during Month 2024 - February 2025. The survey included two hypothetical case-based questions featuring Jordan, an eleven-year-old patient, and his parent, prompting respondents to consider their approach to discussing and recommending the HPV vaccine. A total of 59 dental practitioners participated. Descriptive statistics were estimated.

Results: Among respondents, 59.3% felt "very confident" or "somewhat confident" in explaining the connection between HPV and oropharyngeal cancer to patients and parents; none reported being "not confident at all." However, when it came to actively recommending the HPV vaccine to a hypothetical patient, confidence levels were roughly the same, with 40.6% stating they felt "very confident" or "somewhat confident" and 42.4% felt "not very confident" or "not confident at all". Alarmingly, 37.3% never recommend the HPV vaccine to eligible patients, while only 5.1% do so frequently. To improve HPV-related discussions in dental settings, practitioners identified patient education materials (87.9%), communication training (44.8%), and example intake forms (36.2%) as the most helpful resources. Additionally, 43.1% expressed interest in participating in a study on HPV vaccination, highlighting a willingness to engage in efforts to enhance their role in cancer prevention.

Conclusion: While most respondents feel confident explaining the link between HPV and oropharyngeal cancer, far fewer are comfortable recommending the vaccine. This gap underscores the need for targeted interventions, such as patient education materials and communication training, to enhance dental practitioners' role in HPV-related cancer

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Posterboard #: 32

Presenter: Layla Garcia
Institution: UT Health San Antonio
Category: Student

Glial Fibrillary Acidic Protein (GFAP) is Elevated in Acute Psychiatric Episodes Among Older Adults

Layla Y. Garcia, Thiago Macedo e Cordeiro, Ana Ruiz, Scott Lane, Natalia Pessoa Rocha, Sudha Seshadri, Antonio L. Teixeira, Vanessa M. Young

Background: Psychiatric symptoms in older adults are associated with complex neurobiological processes, with symptom severity varying between acute (inpatient) and stable (outpatient) phases of illness. Some evidence suggests potential associations between psychiatric symptoms and biomarkers of neural injury and inflammation, including neurofilament light chain (NfL), glial fibrillary acidic protein (GFAP), and S100 calcium-binding protein B (S100B). However, differences in these biomarkers based on clinical state remain understudied, particularly in geriatric populations. This preliminary study aimed to explore whether blood-based biomarkers of neural injury and inflammation differ between older adults with acute versus stable psychiatric symptoms.

Methods: We conducted a cross-sectional study of 40 older adults (mean age 66.0 years; 58% male) with psychiatric disorders from two clinical settings: inpatients (n=23) from UT Health Houston Harris County Psychiatric Center with severe symptoms requiring hospital-based care, and outpatients (n=17) from UT Physicians Psychiatry Outpatient Clinic managing chronic conditions. Blood samples were analyzed for NfL, GFAP, and S100B. Biomarker levels were log-transformed, and linear regression models compared levels between groups, adjusting for age and sex. Wilcoxon rank-sum test provided additional group comparisons.

Results: GFAP levels were higher in the inpatient group compared to the outpatient group ($\beta = 0.61$, 95% CI: 0.08-1.1, $p = 0.026$) after adjusting for age and sex, with similar findings using non-parametric analysis ($p = 0.00356$). NfL ($\beta = 0.12$, $p = 0.6$) and S100B ($\beta = -2.6$, $p = 0.5$) were not significantly associated with inpatient status in our sample.

Conclusion: These findings suggest a potential association between elevated GFAP and acute psychiatric states in older adults, which may indicate astrocytic responses during acute symptom phases. This exploratory study provides initial data on possible biological differences between acute and stable psychiatric states in older adults. Further research with larger samples, longitudinal designs, and more comprehensive clinical characterization is needed to validate these findings and investigate their clinical significance.

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Posterboard #: 33

Presenter: Elisabeth Halm, BS
Institution: UT Health San Antonio
Category: Student

Outcomes and Resource Utilization Before and After Development of Protocol for the Management of Pediatric Mild TBI

Elisabeth Halm BS, Brent Janda MS, Christian Gerhardus BS, Lauran Barry BS, Nicholas Taylor MD, Katie Wiggins-Dohlvik MD

Traumatic brain injury (TBI) is a major cause of trauma in children, leading to about 500,000 ED visits and 60,000 hospitalizations in the United States each year. TBI is defined as a physical trauma to the head, which can result in complications secondary to the impact, including hemorrhage, ischemia, edema, vasospasm, and hypoxemia. TBI is commonly delineated using a patient's Glasgow Coma Scale (GCS) score - 14-15 (mild), 9-13 (moderate), and 3-8 (severe). While most TBIs are mild, severe TBI-related injuries cause death in more than 3000 U.S. children annually. Measures to improve outcomes in patients with TBI are crucial and have the potential to impact many children. A variety of methods have been employed to improve outcomes in TBI with many showing promise. Organized trauma protocols for standardized evaluation, triage, and disposition of patients depending on injury pattern, GCS, and clinical presentation have improved TBI management in adults. Evidence-based algorithms in pediatric TBI management are less well-established. With growing constraints on our health system and resources, our aim was to develop and implement a standardized protocol for the evaluation, triage, and disposition of pediatric patients presenting with mild TBI at our institution. We hypothesized that a standardized care pathway would allow for optimization of resource utilization and have no detrimental effect on patient outcomes. Our institution developed an algorithm to aid in management of mild TBI in the pediatric population in early 2023. It was introduced in January 2023 and was finalized for use in April 2023. We developed a database of pediatric trauma patients with mild TBI that received treatment at University Hospital between 2021 and 2024. We used trauma registry data and retrospective chart review to compare the outcomes of 100 patients before the introduction of the protocol (BP group) to 100 patients after the finalization of the protocol (AP Group). This study showed similar results in both groups regarding resource utilization and clinical outcomes. However, the AP Group had more severe injuries, with a significantly higher head abbreviated injury score and nearly double the number of skull fractures. The mean injury severity score was also higher in the AP Group, although the findings were not statistically significant. Based on these findings, we have shown that a standardized protocol for the evaluation, triage, and disposition of patients with mild TBI does not negatively impact patient outcomes. Limitations to our study include small sample size and a single institution. Further investigation including newer data would be useful in determining if the injury severity has changed, and if outcomes have remained favorable.

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Posterboard #: 34

Presenter: Haeram Han
Institution: University of Incarnate Word School of Osteopathic Medicine
Category: Student

Hypomineralized enamel analyzed by microcomputed tomography

Hae-Ram Han, Yong-Hee Patricia Chun, Roberto J Fajardo

The mineralization of enamel into the hardest mineralized tissue of the body underlies a highly regulated stepwise process. Disruptions in the developmental process may result in under-mineralization of enamel. Molar-incisor hypomineralization (MIH) is a developmental defect of enamel manifesting with lesions of reduced mineral density that are mechanically weak, susceptible to caries, and unesthetic. Instead of accumulating mineral, matrix proteins are retained in MIH teeth from children. While the pathophysiology is still not known, a mouse model overexpressing the enamel protein ameloblastin (Ambn) has been developed to mimic MIH. The goal of the study was to analyze the spectrum of density and the regional distribution of mineralization in enamel by utilizing the ameloblastin overexpressing mice.

Methods: Transgenic Ambn was overexpressed in mice from the amelogenin promoter encoding full-length Ambn. Mandibular incisors of separate mouse lines overexpressing Ambn at four increasing concentrations were scanned (Skyscan, Bruker), reconstructed and analyzed for low-, medium- and high-density areas and volumes using microCT.

Results: Mice overexpressing Ambn displayed demarcated lesions of reduced mineral content were found depending on the Ambn concentration. At high Ambn concentrations, lesions appeared one after the other from transition stage to erupted enamel. At low Ambn concentration, hypomineralized enamel opacities started close to the dentino-enamel junction (DEJ), coinciding with delayed conversion from medium to high density. At high Ambn concentration the low-density areas expanded to the surface of enamel. The conversion from low-density to medium and high density was delayed at early maturation. At mid maturation the mineral density was halted at medium density and failed to further increase mineral to high density levels. The opacities may contain Ambn cleavage products of higher molecular weight than found in wild type. Ameloblasts demonstrated prolonged secretory and transition stages, thin basement membrane and shortened maturation stages. When opacities expanded to the enamel surface adjacent ameloblasts were detached and formed cysts within the enamel organ.

Conclusion: The overexpression of Ambn in murine secretory ameloblasts results in a failure to convert mineral density from medium to high density. The enamel hypomineralization with sharply demarcated enamel is phenotypically like MIH.

Posterboard #: 35

Presenter: Brent Janda, MD, MS
Institution: UT Health San Antonio
Category: Student

Open versus Endovascular Approaches in Subclavian and Axillary Artery Trauma

Brent Janda, Richard Walsh, Lauran Barry, Brian Eastridge, Donald Jenkins, Susannah Nicholson

Subclavian and/or Axillary Artery injury can lead to severe complications: limb ischemia, hemorrhage, and death. An open surgical approach has traditionally been employed for these injuries. Recent improvements in endovascular methods have led to an increase in use in arterial injury repair. The National Inpatient Sample Database suggests an endovascular approach is the preferred treatment in terms of outcomes and mortality. Our hypothesis is that with the continued advent of novel endovascular approaches and improvement in trauma care, we will see an increase in endovascular repair, particularly for blunt mechanisms.

This is a retrospective review study. All data is from the National Trauma Data Bank (NTDB) from the years 2016, 2017, 2021, and 2022. Pediatric and adult patients were included. ICD10 diagnostic codes describing any type of injury to the subclavian or axillary artery were used to filter patients with such injuries. Patients were further filtered by ICD10 procedure codes for any type of open procedure, endovascular procedure, or both simultaneously (Hybrid). Two sample t-test and chi squared tests were used for analysis.

Within the four years of collected data, there were 4068 injuries, 1165 Open repairs, 634 endovascular repairs, and 68 hybrid repairs. Endovascular patients were older (41.5 v. 35.7, p=9.5E-11), less likely to be male (79.3% v. 83.8%, p=0.022), and more likely to be white (54.4% v. 46.4%). Endovascular treatment had lower associated in-hospital mortality (5.7% v. 10.6%, p=4.48E-4) yet similar initial Injury Severity Scores (19.5 v. 19.0 p=0.32). Endovascular patients took longer to go to the OR (16.9 hours v. 8.0 hours, p=8.67E-7) and spent more time on a ventilator (7.6 days v. 6.3 days, p=0.04). Endovascular patients were much more likely to present with a blunt mechanism of injury (50.9% v. 33.8%, p=1.33E-10). Endovascular and Open treatments had similar reoperation rates (4.6% v. 6.2%, p=0.16), hospital length of stays (13.0 days v. 12.6 days, p=0.61) and Intensive Care Unit length of stays (7.8 days v. 7.1 days, p=0.16). The number of all treatment types has been increasing yearly along with the number of injuries in the database. There was an increase in use of endovascular treatment compared to open treatment from 2016 and 2017 to 2021 and 2022 (32.0% v. 37.5%, p=0.018).

Endovascular methods led to lower in-hospital mortality with an increase in usage compared to open approaches. The next step in this project is to determine factors that influenced the choice of an open versus endovascular approach in addition to penetrating or blunt mechanisms of injury. The end goal of this research is to help develop an algorithm to choose candidates for open or endovascular surgery which could improve outcomes and decrease mortality.

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Posterboard #: 36

Presenter: Niya Joy
Institution: UT Health San Antonio
Category: Student

JATRORRHIZINE ENHANCES SOCIAL NOVELTY PREFERENCE AND REDUCES BURYING IN FEMALE MICE

Niya Joy, P. Bridgette Stewart, Karina Cantu, Georgianna Gould

Social behavior impairments are prevalent in many different psychiatric disorders, yet current treatments have limited efficacy to ameliorate them. Organic cation transporters (OCTs) of the solute carrier family SLC22A play a crucial role in neurotransmitter regulation that is underappreciated. Recent research has shown that blocking OCTs increases extracellular monoamine levels, suggesting a novel therapeutic approach that may enhance social behaviors. Jatrorrhizine, an isoquinoline alkaloid, shows promise as it inhibits serotonin and norepinephrine clearance via OCTs at high nanomolar concentrations in vitro, and at 20 mg/kg has antidepressant-like effects comparable to venlafaxine. The goal of this study was to test our hypothesis that the same dose of jatrorrhizine could enhance social preferences and dominance in male and female mice acutely. To accomplish this, we examined its effects in two inbred strains of mice differing in innate social behaviors. We used BTBR T+ Itpr3tf/J (BTBR) mice with social interaction deficits and C57BL/6J mice that are gregarious. The vehicle was 20% ethanol in saline, as this was required to keep jatrorrizine in solution at 2 mg/ml. An hour after acute injection and acclimation the behavior tests commenced. Social interaction and social novelty preference were examined in three chamber tests first, followed by marble burying tests to assess anxiety-like behaviors, followed by tube tests for social dominance. While jatrorrhizine had no apparent effect on social interaction preference, it enhanced social novelty preference and reduced marble burying in female C57BL/6J mice. This was evident in measurements of time in chamber and by observation of social sniffing time. Interestingly, BTBR mice did not exhibit any responses to jatrorrhizine treatment in the behaviors measured. Thus, the beneficial effects of Jatrorrhizine appear to be sex and strain dependent in behavior tests relevant to autism spectrum disorders or schizophrenia symptoms.

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Posterboard #: 37

Presenter: George Naratadam, PhD
Institution: UT Health San Antonio
Category: Student

A Peripheral Pro-Inflammatory Axis Governs Sex-Specific Resolution of Neuropathic Pain

George T. Naratadam, Priscilla A. Barba-Escobedo, Jennifer Mecklenburg, Sergey Shein, Alexei V. Tumanov, Theodore J. Price, and Armen N. Akopian

Introduction. Neuropathic pain remains a significant clinical challenge due to its complex pathophysiology and resistance to conventional treatments. Emerging evidence suggests that immune cells and cytokine signaling play crucial roles in modulating pain trajectories, with differences potentially existing between males and females. However, the specific immune-related cellular and molecular mechanisms that drive the transition from persistent pain to resolution remain poorly understood. In this study, we aimed to elucidate the cellular contributors and signaling pathways that regulate pain resolution, focusing on immune system involvement and sex-specific differences.

Methods. Neuropathic pain models were developed in male and female mice, including chemotherapy-induced neuropathy and peripheral nerve crush injury. In chemotherapy-induced neuropathy, paclitaxel dosing was titrated to yield resolving or persistent pain trajectories. At multiple stages (initiation, pre-resolution, post-resolution, and persistence), RNA sequencing was conducted on peripheral tissues (hind paw and dorsal root ganglion), selecting differentially expressed genes (P-adj < 0.05, FC >2). Immune cell populations were quantified through CD45+ cell isolation and flow cytometry, while Cre/LoxP models, diphtheria toxin receptor-mediated ablation, and antibody inhibition dissected cell-specific contributions.

Results. Mechanically-evoked hypersensitivity was more chronic in females. RNA sequencing showed immune-related gene upregulation during resolution in males, absent in persistent pain or at any stage in females. A peripheral population of myeloid cells was essential for resolution in males. Flow cytometry showed no quantitative differences in immune cell populations between sexes, suggesting qualitative immune responses contribute to male-specific resolution. The pro-inflammatory cytokine CCL2 was associated with resolution in males. Global CCR2 deletion or antibody inhibition impaired resolution in the chemotherapy-induced neuropathy model, while keratinocyte-specific CCL2 deletion impaired resolution in both models in males. Peripheral administration of recombinant CCL2, but not anti-inflammatory IL-4 or IL-10, resolved persistent pain.

Conclusion. Our findings reveal sex-specific immune mechanisms in neuropathic pain resolution, with peripheral myeloid cells and CCL2-CCR2 signaling pivotal for resolution in males. Females exhibited prolonged pain independent of these pathways, suggesting that mechanistic differences underlie sex-specific outcomes and may guide development of targeted treatments for chronic neuropathic pain.

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Posterboard #: 38

Presenter: Khaled Nassar, MS
Institution: UT Health San Antonio
Category: Student

Inhibiting PELP1 signaling enhances the therapeutic effectiveness of topoisomerase inhibitors in triple-negative breast cancer

Khaled Mohamed Nassar, John R Sanchez, Durga Meenakshi Panneerdoss, Behnam Ebrahimi, Xue Yang, Uday P. Pratap, Megharani Mahajan, Salvador Cardenas Alejo, Abhi Katabathina, Panneerdoss Subbarayalu, Daohong Zhou, Rajeshwar R. Tekmal, Gangadhara Reddy Sareddy, Manjeet K. Rao, Suryavathi Viswanadhapalli, and Ratna K. Vadlamudi

Background: Triple-negative breast cancers (TNBCs) are aggressive with poor prognosis and high metastasis, accounting for 15-24% of breast cancer deaths. Proline-, glutamic acid-, and leucine-rich protein 1 (PELP1), an oncogene, are commonly deregulated in TNBC and serve as a poor survival marker. The objective of this study is to establish the molecular mechanism of action of PELP1 in the progression of TNBC using IPTG-inducible PELP1 knockdown (PELP1-iKD) models and develop a novel combination therapy targeting PELP1.

Methods: TNBC models (MDA-MB-231, BT-549, HCC-1806, SUM-149) with PELP1-iKD were generated through lentiviral transduction. PELP1 signaling was further inhibited with the pharmacological inhibitor SMIP34. SMIP34's effectiveness was tested with 140 FDA-approved drugs using an MTT-based screen, and combination therapy was evaluated using colony formation and Annexin V/PI apoptosis assays. Mechanistic studies were conducted using RT-qPCR, Western blotting, Traffic light assay, comet assays, and confocal microscopy. The utility of SMIP34 + Topoisomerase inhibitors (TIs) combination therapy was assessed in cell line-derived xenografts (CDXs), patient-derived organoids (PDOs), and patient-derived xenografts (PDXs).

Results: Western blotting analysis confirmed that the addition of IPTG reduced PELP1 expression in a dose-dependent manner in all four TNBC PELP1-iKD cells. PELP1 KD significantly decreased cell survival and colony formation in TNBC cells while enhancing apoptosis. PELP1-iKD cells showed a delayed DNA damage response, characterized by elevated γ-H2AX levels and impaired activation of phospho-ATM, ATR, and DNA-PKcs following DNA damage. Treatment with SMIP34 also resulted in a delayed DNA damage response and accumulation of γ-H2AX, similar to the genetic approach. In an MTT-based screen, SMIP34 enhanced the sensitivity of TNBC cells to TIs. These results were validated in PELP1-iKD cells, where PELP1-iKD further increased sensitivity to TIs, providing genetic evidence of PELP1's role in the synergy between SMIP34 and TIs. The ability of SMIP34 to enhance the efficacy of TIs was confirmed in additional TNBC cell lines, with synergistic effects observed in cell survival, colony formation, and apoptosis assays. Mechanistic investigations demonstrated elevated levels of γ-H2AX in cells treated with the PELP1-iKD+TIs and SMIP34+TIs combinations, compared to monotherapy with TIs. Comet assay results indicated heightened DNA damage with these combination treatments. Furthermore, combined treatment with SMIP34 and Mitoxantrone significantly inhibited the proliferation of PDOs in vitro and reduced the growth of CDX and PDX tumors compared to vehicle or monotherapy treatments.

Conclusion: Collectively, these findings establish a robust preclinical foundation for the development of PELP1-targeted combination strategies for the treatment of TNBC.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 39

Presenter: Dena Norouzi, PhD student
Institution: UT Health San Antonio
Category: Student

Improving Procurement-to-Transplantation Timeline via Hemoglobin Based Oxygen Carriers (HBOC)-Enhanced Machine Perfusion for Optimal Trauma Care

Dena Norouzi MS1,2, Braden Miller MD1, Manuela Gaviria MD1, Jennifer Cox-Hinshaw1, Cody Hinshaw1, Jorge Pena1, Diandra Wood1, Shauna Hill, PhD1, Charles Fries MD, PhD2

Hemoglobin-Based Oxygen Carriers (HBOCs) present a promising solution by mimicking red blood cells'oxygen-transport functions and maintaining oxygen and nutrient supply to the tissues. This could significantlyprolong the viability window, enhancing the prospects for successful transplantation. Preliminary findings froma small-scale preclinical study utilizing HBOC-enhanced machine perfusion have shown promising results,achieving 100% viability in a porcine semitendinosus muscle flap (SMF) model for up to 24 hours. In thesestudies, we harvested SMF from porcine, subjected them to 24-hour subnormothermic machine perfusion usingHBOC solution, then autotransplanted them back onto the porcine model, monitoring for viability. Our techniqueshowed no signs of tissue degradation in ex vivo and in vivo analyses up to 14 days. These results highlight ourmethod's potential to extend preservation times and boost transplantation success. Building on the success ofachieving 24-hour tissue preservation with HBOC in a preliminary pilot study, we hypothesize that combiningHBOC with our advanced machine perfusion technique extends tissue preservation to an unprecedented 24-hourduration, thereby enhancing transplantation success rates.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 40

Presenter: Alex Nunnery, BA, BS
Institution: UT Health San Antonio
Category: Student

Assessing Potential Adjunct Medications such as Hydroxocobalamin and Methylene Blue, with REBOA, in the Management of Hemorrhage in a Large Animal (Sus scrofa) Model of Polytrauma

Dena Norouzi, Maria Castaneda, Jae Choi PhD, Kaysie Sachs, Katie Boutin, R. Madelaine Paredes PhD, Denise Manfrini MD, Mark Foster MD, CPT Aaron Alindogan MD, Col Joseph Maddry MD, Patrick C Ng MD, Alex Nunnery BA,BS

Background: Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) is a lifesaving intervention for severe hemorrhagic shock. However, balloon deflation often results in cardiovascular collapse due to ischemia-reperfusion injury. Hydroxocobalamin (HOC) and Methylene Blue (MB) are potential adjunct therapies that may mitigate these effects by modulating nitric oxide and improving vascular and metabolic function.

Objective: This study aimed to evaluate the efficacy of HOC and MB, each in combination with whole blood (WB), as adjunct resuscitative therapies to prevent cardiovascular collapse after Zone I REBOA deflation in a polytrauma model using Sus scrofa. Methods: Seventeen Yorkshire swine underwent a standardized polytrauma model, including traumatic brain injury, tibia fracture, and controlled hemorrhage, leading to a mean arterial pressure (MAP) below 30 mmHg. After ten minutes of shock, Zone I REBOA was inflated for one hour, followed by a controlled five-minute deflation. Animals were randomized into three groups: (1) WB alone, (2) WB with HOC, and (3) WB with MB. Physiological parameters (blood pressure, heart rate) and laboratory markers (lactate, pH) were monitored for two hours post-deflation. Survival analysis was conducted using Kaplan-Meier curves, and data were analyzed via linear mixed models.

Results: Baseline characteristics were comparable across groups. MB-treated animals exhibited significantly lower lactate levels compared to WB alone at 15 minutes post-deflation and sustained reductions at 90 and 120 minutes. Additionally, MB-treated animals showed higher pH values at 15 and 30 minutes post-deflation, suggesting a reduction in ischemia-reperfusion injury and enhanced metabolic recovery. Kaplan-Meier survival analysis revealed no significant differences between groups.

Conclusion: Methylene Blue demonstrated potential in mitigating metabolic dysfunction following REBOA deflation by reducing lactate levels and maintaining pH. While survival differences were not observed, MB may enhance post-deflation recovery. Future research will focus on organ preservation and long-term outcomes, with potential applications in prehospital and battlefield trauma care.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 41

Presenter: Durga Meenakshi Panneerdoss
Institution: University of Texas at San Antonio
Category: Student

Combining LIPA inhibitor ERX-208 with DNA-damaging agents as a novel strategy to enhance ovarian cancer treatment

Durga Meenakshi Panneerdoss, Khaled Mohamed Nassar, William Cole Arnold, Suryavathi Viswanadhapalli, Edward Kost, Jung-Mo Ahn, Ganesh V. Raj, Ratna K. Vadlamudi

Background: Ovarian cancer (OCa) is the most lethal primary gynecologic malignancy in the United States. Lack of effective early detection strategies results in delayed diagnosis. Despite initially responding to chemotherapy treatment, a significant number of OCa patients eventually develop resistance, which ultimately leads to patient mortality. Early identification and improved therapy are necessary for OCa patients. Our team identified ERX-208 as a potent oligo-benzamide molecule (IC50 ~100 nM) with a high level of activity against OCa cells after screening more than 2,000 compounds. ERX-208's targeting of lysosomal acid lipase A (LIPA) results in endoplasmic reticulum stress, protein synthesis disruption, and apoptosis. The objective of this project is to investigate the potential of ERX-208 to enhance FDA-approved chemotherapeutics.

Methods: In our study, we performed in vitro screening of 147 FDA-approved chemotherapy drugs in combination with ERX-208 to assess their effects on the viability of ovarian cancer (OCa) model cells. The drug combination dose-response data were analyzed using the SynergyFinder Plus software to calculate synergy and combination sensitivity scores. To validate the synergistic effects, we conducted several in vitro assays, including tests for cell proliferation, colony formation, cell cycle progression, DNA damage, apoptosis, and invasion. Furthermore, preclinical studies were carried out using patient-derived xenograft (PDX) models to evaluate the combination's efficacy in a more clinically relevant setting.

Results: We discovered that ERX-208 sensitizes ovarian cancer (OCa) cells to six FDA-approved chemotherapy medications through our in vitro screening and cell viability assays. These drugs-Mitomycin, Oxaliplatin, Trifluridine, Capecitabine, Epirubicin hydrochloride, and Bleomycin sulfate-were selected based on their highest synergy scores among the 147 compounds tested. All six drugs were shown to induce DNA damage and inhibit cell cycle progression. The study confirmed that ERX-208 enhances the therapeutic efficacy of these chemotherapeutic agents across multiple OCa cell lines. Specifically, ERX-208 treatment reduced cell viability, colony formation, and invasion, while enhancing DNA damage and apoptosis in combination with these drugs. RNA-seq studies investigating the underlying mechanisms of this synergy are in progress. Furthermore, combining ERX-208 with cisplatin significantly decreased tumor volume and weight in PDX models, compared to monotherapy with either agent alone.

Conclusions: In summary, our findings demonstrate that combining ERX-208 with DNA-damaging agents enhances their therapeutic effects, highlighting the potential of ERX-208 combination therapy as an effective treatment strategy for ovarian cancer (OCa).

Conflict: The patents surrounding ERX-208 are licensed to EtiraRx.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 42

Presenter: George Parra, MS
Institution: UT Health San Antonio
Category: Student

Proteomic and structural analysis of the oncogenic EWS::FLI1 spliceosomal interactome.

George L. Parra, Susan T. Weintraub, Bernard Fongang, David S. Libich

The EWS::FLI1 gene fusion is implicated as a source of oncogenic activity in the majority of Ewing sarcoma (EwS) cases (>70%). EWS::FLI1 is composed of RNA-binding protein EWS (EWS) and ETS transcription factor Friend leukemia integration 1 (FLI1). It is thought that EWS::FLI1 and EWS participate in mRNA processing and spliceosomal activities, however, the structural interaction mechanisms are unknown. Proteomic experiments show spliceosomal proteins are present in both EWS and EWS::FLI1 interactomes, including proline-rich-region-binding spliceosomal peptidyl-prolyl isomerases (PPIs). EWS::FLI1 contains a low complexity domain (LCD), enriched in proline residues, imparts intrinsic structural disorder and acts as a multivalent binding region. Here we used modern proximity labelling techniques that exploit a biotin ligase fused to EWS and EWS::FLI1 to identify their interactomes. This approach is particularly well suited for intrinsically disordered proteins since it does not rely on binding affinities but rather the physical distance between interacting proteins. From these experiments we identified specific and unique interactions between EWS and EWS::FLI1 and PPI proteins that we hypothesized were mediated by the LCD (EWSLCD) common to both proteins. We employed NMR to provide insight into the interaction between PPIL1 and the EWSLCD and identified the binding sites on both proteins. Specifically, our studies will yield actionable insights regarding the protein-protein interfaces in EWS::FLI1 that can be targeted to attenuate its oncogenic activity. Defining the interaction interfaces of EWS::FLI1 is central to understanding its pathophysiology and importantly, identification of potential therapeutic targets. Combining novel discovery proteomics with cutting-edge NMR approaches will provide unparalleled insight into the transformative mechanics of EWS::FLI1.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 43

Presenter: Mei Robson
Institution: Institute for Health Promotion Research
Category: Student

Translating Language into Quality: Investigating the Role of Preferred Language in Survivor-Reported Healthcare Satisfaction

Mei Robson, B.S. and Derek Rodriguez, PhD.

Background. Language barriers in healthcare can impact patient-provider communication, leading to disparities in care, particularly among Hispanic/Latino (H/L) cancer survivors. H/Ls experience the highest cancer rates and poorest outcomes, due to language barriers, lower income, lack of insurance, and educational disparities that limit access to quality care. Effective communication is essential for patient understanding, decision-making, and adherence to treatment. Despite increasing awareness, the impact of language preference on perceived healthcare quality among H/L cancer survivors remains unclear. Addressing these gaps is essential for improving healthcare equity.

Objective. This study aimed to assess whether Spanish-preferring H/L cancer survivors report lower healthcare satisfaction than English-preferring survivors. It also examined how demographic and non-medical drivers of health interact with language preference to influence patient satisfaction. We hypothesized that Spanish-preferring survivors would report lower satisfaction due to language-related challenges in healthcare settings. This study seeks to determine whether these challenges extend to H/L cancer survivors and impact their healthcare experiences. To our knowledge, this is the first study to examine language-related barriers specifically within the context of H/L cancer survivorship.

Methods. We analyzed data from the Avanzando Caminos: Cancer Survivorship Cohort Study, a prospective study of H/L cancer survivors in South Texas. A subset of 321 participants who had completed primary cancer treatment within the past ten years was included. Patient satisfaction was measured using self-reported ratings of six provider-related factors (courteousness, respect, helpfulness, attentiveness, explanation, and time spent) on a five-point Likert scale. Participants rating all six factors at the highest level (5/5) were classified as reporting "perfect" healthcare quality. This dichotomization allowed for a clearer distinction in perceived care experiences. Covariates included sex, age, race, religion, education, income, insurance status, marital status, having children, social support, cancer knowledge, and depression. Bivariate analyses and logistic regression were used to examine associations between language preference and healthcare satisfaction, adjusting for covariates.

Results. Of the 321 participants, 52% reported "perfect" healthcare quality. The logistic regression analysis revealed that Spanish-only speakers were 50% less likely to report "perfect" healthcare quality than English/bilingual speakers ($p = 0.05$, CI = 0.25, 1.01), adjusting for other covariates. Other factors were not significantly associated with healthcare quality.

Discussion. Spanish-only speakers had significantly lower odds of reporting "perfect" healthcare quality, emphasizing the role of language barriers in healthcare satisfaction. Our findings reinforce research on language barriers but contrast with studies linking income and education to healthcare quality, suggesting language may have a stronger impact on H/L cancer survivors' healthcare perceptions. These results underscore the need for language-concordant care (access to professional interpreters, bilingual providers/healthcare navigators, and linguistic competency training). Although this study identifies a meaningful trend, the borderline significance suggests further research with larger samples is needed.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 44

Presenter: Annie Smelter
Institution: UT Health San Antonio
Category: Student

Hepatic TBX3 Overexpression Disrupts Ammonia Detoxification in Mice

Annie Smelter, Iriscilla Ayala, Skanda Hebbale, Edgar Hinostroza, Marcel Fourcaudot, and Luke Norton

Background: The liver plays an essential metabolic role by regulating glucose, lipid, and amino acid metabolism, as well as detoxifying harmful substances in the body. The structural and functional unit of the liver is the liver lobule, consisting of a central vein surrounded by six portal triads. Hepatocytes can be divided into different zones, named based on their bordering structures: periportal (zone 1) and pericentral (zone 3). These zones are significant, as hepatocytes in different zones perform different metabolic functions. The transcriptional regulation of these zones is not well understood. In our recent studies, it appears that T-box transcription factor 3 (TBX3) cooperates with transcription factor 7-like 2 (TCF7L2) to regulate zone-specific gene expression. However, the metabolic function of TBX3 in the liver is poorly understood.

Methods: To determine the impact of TBX3 overexpression in wild-type mouse liver, we employed a liver specific adeno-associated virus 8 (AAV8) delivery of either Gfp or Tbx3 mRNA under a hepatocyte-specific promoter. Mice were treated with a single periorbital injection of either AAV8-GFP or AAV8-TBX3 and observed for 14 days. However, mice were sacrificed on day 13 due to rapid lethality in the final days of the experiment. Body weight, food intake, and plasma ammonia levels were tracked throughout the experiment. Endpoint analyses included gene expression via RT-qPCR, protein expression via western blotting, and histology.

Results: Mice treated with AAV8-TBX3 demonstrated robust mRNA and protein overexpression, as well as rapid and significant body weight reduction in the absence of a change in food intake when compared mice treated with AAV8-GFP. Zonal gene expression was altered, with greater effects on periportal gene expression compared to pericentral. Finally, we found significant changes in the gene expression of key ammonia detoxification genes that correlated with a significant elevation of plasma ammonia levels.

Conclusion: We found that hepatic TBX3 overexpression disrupts the expression of zonal genes, as well as those essential to ammonia detoxification. These changes, along with the significant elevation in plasma ammonia, suggest that the rapid weight loss and lethality observed in the final days of the experiment may have been due to ammonia toxicity. Future directions include chromatin immunoprecipitation sequencing to identify genes directly targeted by TBX3 and single nuclei RNA sequencing to further characterize the effects of TBX3 overexpression on zonation.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 45

Presenter: Kate Tuite
Institution: UT Health San Antonio
Category: Student

Sex differences in the effects of manipulating the paraventricular thalamus to orbitofrontal cortex pathway during reversal learning

Kathleen Tuite, Milena Girotti, David A. Morilak

Stress-related psychiatric disorders, such as major depressive disorder and anxiety disorders, have cognitive flexibility deficits that persist even after other symptoms go into remission. Reversal learning, a form of cognitive flexibility, is disrupted in stress-related psychiatric disorders. The orbitofrontal cortex (OFC) mediates reversal learning, and hyperactivity in the OFC is associated with psychiatric disorders in humans. We have previously reported that chronic stress impairs reversal learning and potentiates responses to excitatory input in the OFC, and that inducing long-term depression in the mediodorsal thalamus to OFC pathway reverses these deficits, indicating that increased activity in projections to the OFC is detrimental to reversal learning. However, the circuit-level mechanisms underlying stress-induced reversal learning deficits are not well established. The paraventricular thalamic nucleus (PVT) is highly stress responsive and is known to provide excitatory input to the OFC. Utilizing retrograde tracing from the OFC combined with ΔFosB immunohistochemistry we found that the PVT projects strongly to the OFC and this projection is repeatedly activated by chronic stress. Therefore, we next tested the hypothesis that increased input to the OFC from the PVT will disrupt reversal learning. We used an adeno-associated virus to deliver an excitatory (Gq) DREADD, an inhibitory (Gi) DREADD, or GFP control into the PVT under the control of the CaMKII promoter, and implanted guide cannulae into the lateral OFC for pathway specific in/activation. Activating the PVT-OFC pathway with the Gq DREADD significantly impaired reversal learning in non-stressed males, while inhibiting the PVT-OFC pathway with the Gi DREADD in chronically stressed animals reversed the stress-induced deficits in reversal learning only in males, with minimal or no effect of these manipulations in females. These results suggest that the PVT to OFC pathway is not as involved in the effects of stress on reversal learning in females as it is in males.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 46

Presenter: Varsha Venkatesh
Institution: UT Health San Antonio
Category: Student

Impact of Oral Antidiabetic Therapy on Hepatic and Whole-Body Insulin Sensitivity in Prediabetes

Varsha Venkatesh, Aurora Merovci, John Adams, Andrea Hansis-Diarte, Eugenio Cersosimo, Curtis Triplitt, Renata Belfort, Muhammad A. Abdul-Ghani, Ralph A. DeFronzo, Alberto O. Chavez

Introduction. Prediabetes (pre-DM) is highly prevalent in the general population, accounting for as many as 1 in 3 of the US adult population. Insulin resistance is a key pathophysiological defect that leads to the development of type 2 diabetes (T2DM). Both central (liver) and peripheral (muscle) insulin resistance affect glucose levels and, along with beta cell failure, are the main determinants of progression to diabetes. Finding effective and long-term interventions to prevent pre-DM progression into T2DM is the subject of intensive research.

Objective. To evaluate central and peripheral insulin sensitivity changes following early intervention with oral antidiabetics in subjects with pre-DM.

Methods. EPIC trial is evaluating beta cell preservation in individuals with pre-DM. Here we report a preliminary analysis of 56 individuals (age=50 yr ±1.6; A1c=5.8%±0.5; BMI=32.5±0.5; FPG=106 mg/dL ±1; 2hPG=163 mg±5) who have completed two years of treatment with either metformin (MET, n=12), pioglitazone (PIO, n=15), dapagliflozin (DAPA, n=15), or saxagliptin (SAXA,n=14). Participants received euglycemic insulin clamps to assess liver and muscle insulin sensitivity at baseline and following two years of intervention. Basal hepatic glucose production (bHGP) was measured by infusing [3-3H] glucose and analyzing its turnover rate in plasma during a 120 min equilibration period before the clamp. The liver insulin resistance index (LIRI) was calculated as bHGP x fasting plasma insulin (FPI) and peripheral insulin sensitivity as the rate of total glucose disposal during the clamp (TGD). The Adipose Insulin Resistance Index (AIRI) was calculated as the product of fasting free fatty acids (F-FFA) x FPI

Results. There was a decreased trend in FPG, 2hPG, and HgbA1c across groups (p=n.s). MET group had a significant decrease in BMI (33.1 to 30.9, p<0.01), and PIO was associated with a substantial increase in BMI (33.2 to 34.5, p<0.01); liver insulin resistance index (LIRI) showed a trend towards decrease with PIO (30.9 vs 25.6 , p=ns), along to a trend towards increase in whole insulin sensitivity (TGD 6.8 to 8.6 mg/kg.min, p=n.s). AIRI decreased with MET and PIO but did not reach statistical significance.

Conclusion. Early treatment with oral antidiabetics in pre-DM subjects has the potential to modify the progression to T2DM. Current findings and preliminary trends are consistent with literature on PIO, where liver, muscle, and adipose tissue markers show improvement despite weight gain.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 47

Presenter: Vanessa Young, MS
Institution: UT Health San Antonio
Category: Student

Sleep Duration and Fluid Biomarkers of Alzheimer's Disease: A Systematic Review and Meta-Analysis

Vanessa M. Young, Joy Zeynoun, Agustin Ruiz, Christine Gaspard, Christopher R. Frei, Tiffany Kautz, Arash Salardini, Jayandra Jung Himali, Antonio L. Teixeira, Sudha Seshadri, Andrée-Ann Baril

Introduction: Both short and long sleep duration have been increasingly recognized to be associated with Alzheimer's disease (AD) and other neurodegenerative diseases. Yet the mechanisms underlying this association remain poorly understood. This systematic review and meta-analysis investigated the relationship between sleep duration and fluid biomarkers of AD pathology, including amyloid-beta (Aβ), phosphorylated tau (p-tau), total tau (t-tau), and neurofilament light chain (NfL).

Methods: This systematic review protocol was registered in PROSPERO (CRD420246206360). We searched three electronic databases (PubMed, SCOPUS, and CINAHL) from inception to February 2024 and carried out a second search in September 2024. We included studies that examined self-reported or objective sleep duration continuously and/or categorically. The outcomes included levels of CSF and/or blood-based (serum or plasma) biomarkers of AD pathology and neurodegeneration: Aβ40, Aβ42, the Aβ42/40 ratio, p-tau217, p-tau181, t-tau, NfL, and GFAP. Risk of bias was assessed using Newcastle-Ottawa Scale.

Results: Twenty studies (n=12,238) met inclusion criteria, with 12 examining cerebrospinal fluid (CSF, n=2,686) and 8 investigating blood-based markers (n=9,552). Studies using objective sleep measures, particularly polysomnography (PSG), more frequently identified significant associations compared to subjective measures. CSF biomarkers demonstrated stronger associations with sleep duration than blood-based markers. Meta-analyses of CSF studies using PSG revealed a modest correlation between shorter sleep duration and lower Aβ42 (r=0.201, 95% CI [0.091, 0.305]), while associations with p-tau181 and t-tau were not significant. Several studies reported non-linear relationships, suggesting both short (≤5-6 hours) and long (≥8 hours) sleep durations may be associated with altered biomarker profiles. Blood-based p-tau 217 and GFAP were not investigated in any included study.

Conclusions: Methodological heterogeneity in sleep duration definitions and biomarker measurements limited cross-study comparisons. Current evidence is insufficient to determine whether sleep-targeted interventions can effectively modify disease trajectory, and reliable biomarkers are still needed to differentiate pathological sleep changes from normal aging patterns. Future research should focus on standardizing sleep measurements, investigating emerging and promising biomarkers like p-tau217 and GFAP, and conducting longitudinal studies between sleep duration and AD biomarker changes in different age groups.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 48

Presenter: Maritza Buendia, BSA
Institution: Mays Cancer Center UTHSA
Category: Other Research Assistant

Chromosome 9p deletions are associated with higher rates of R1 resection across GI cancers

Maritza Buendia BS, Madeline Silva MD, Candice Viera, MD, Sukeshi P. Arora MD, Neil B. Newman MD, Caitlin A. McIntyre MD, Mio Kitano MD MPH, Alexander A. Parikh MD MPH, Chun Liang Chen, PhD, Colin M. Court MD PhD

Introduction: Determining adequate surgical margins in gastrointestinal (GI) cancers remains imprecise due to the limitations of frozen section accuracy and the infiltrative nature of certain tumors. Chromosome 9p deletions, particularly involving the CDKN2A gene, are implicated in the dysregulation of cell cycle and tumor progression across multiple cancer types. These alterations are associated with worse prognoses and more aggressive tumor characteristics in both renal and gastrointestinal (GI) cancers. We investigated if the more aggressive and infiltrative biology of chromosome 9p deletions was associated with rates of microscopic margin positivity (R1 resection) across GI cancers.

Methods: The Cancer Genome Atlas (TCGA) was used to identify GI cancer patients who underwent primary tumor resection and had genomic information from the primary tumor available for analysis. Chromosome 9p deletions were identified from the arm_level copy number variation dataset and correlated with residual microscopic disease (R0 vs R1 resection) at primary tumor resection.

Results: A total of 1417 patients with 5 different GI cancers had clinical and genomic data available: hepatocellular carcinoma (n = 362), cholangiocarcinoma (n = 42), pancreas (n = 171), gastric (n = 368), colorectal (n = 477). Microscopically positive resection (R1 resection) occurred in 102 (7.2%) patients. Chromosome 9p deletions were associated with R1 resections for all GI cancers ($\chi 2 = 21.25$, $p = 0.000004$). R1 resection rates were higher in patients with chromosome 9p deletions for all GI cancers individually with the exception of cholangiocarcinoma in which the rate of R0 and R1 resections was the same for patients with and without chromosome 9p deletions (Fig 1).

Conclusions: This exploratory study revealed that the rate of R1 positivity in gastrointestinal cancers was higher in patients with chromosome 9p deletion. This suggests that 9p deletion may be associated with a more infiltrative cancer subtype, potentially impacting surgical management. Patients with known chromosome 9p deletions could benefit from resections with wider margins to reduce the risk of residual disease. This study has implications for pursuing a more precision medicine approach to surgical resection margins.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 49

Presenter: Samantha Gates
Institution: UT Health San Antonio
Category: Other Staff / Research Assistant

Characterizing the Biggs Biobank: Demographics, Biospecimens, and Biomarkers in a South Texas Cohort

Samantha N. Gates, Armaan S. Dhillon, Julia J. Mathews, Jazmyn A. Muhammad, Marco Boisselier, Amaya M. Seidl, Ashley LaRoche, Vanessa M. Young, Rosa P. Mavarez, Gabriel de Erausquin, A. Campbell Sullivan, Claudia L. Satizabal, Joanne Curran, Gladys Maestre, Sudha Seshadri, Tiffany F. Kautz

Background: The Biggs Biobank is a repository of biospecimens and associated data from participants located in South Texas. The Biggs Biobank primarily focuses upon neurodegenerative and age-related diseases affecting the central nervous system, but also co-enrolls from several community focused research studies, such as TARCC. Herein we report available demographics, biospecimen types, and biomarkers.

Methods: The Biggs Biobank was created in January 2020 and collects biospecimens and data from consented research participants and clinic patients at the Glenn Biggs Institute, as well as the associated South Texas Alzheimer's Disease Research Center (STAC). In addition to data derived from electronic medical records (EMRs) and research records, the Biggs Biobank regularly stores blood products and cerebrospinal fluid (CSF). This report includes data from participants consented from January 2020 to October 2024 (n=1, 404 participants).

Results: Upon consent, Biggs Biobank participants had an average age of 71.0 (SD=9.98) and 61% identified as female. The sample was predominantly white (95.4%) with 50.9% self-identifying as Hispanic. Of participants with a cognitive diagnosis, 361 had confirmed normal cognition, while most of the remaining sample had a diagnosis of mild cognitive impairment (n=300) or dementia (n=316). Stored blood and CSF biospecimens include EDTA plasma (n=1,111), packed cells (n=1,111), DNA (n=936), serum (n=947), PBMCs (n=564), and CSF (n=382). 132 participants have matched plasma and CSF. We analyzed 7,946 data points across 21 selected biomarkers. These biomarkers included: PET Scan (n=120), MRI (n=509), APOE genotype (n=541), Aβ42 (CSF: n=242; plasma: n=400), t-Tau (CSF: n=384; plasma: n=320), p-Tau181 (CSF: n=242; plasma: n=165), NfL (CSF: n=103; plasma: n=760), GFAP (CSF: n=228; plasma: n=755), UCHL1 (CSF: n=142; plasma: n=242), HbA1c (whole blood: n=374), Cystatin C (plasma: n=113), C-Reactive Protein (plasma: n=155), Homocysteine (plasma: n=138), Aβ40 (plasma: n=400), p-Tau217 (plasma: n=264), p-Tau/Aβ42 (CSF: n=241), Total Protein (CSF: n=321), Glucose (CSF: n=347), WBC Count (CSF: n=198), RBC Count (CSF: n=240), and Myelin Basic Protein (CSF: n=2).

Conclusion: The Biggs Biobank provides a robust resource of data and biospecimens for researchers interested in testing hypotheses related to aging and neurodegeneration. We are actively seeking collaborators to maximize the research potential of our biobank and accelerate the neurodegenerative research discovery process.

15TH ANNUAL FRONTIERS OF TRANSLATIONAL SCIENCE RESEARCH DAY

Posterboard #: 50

Presenter: Krista Kilpadi, MD, PhD
Institution: UT Health San Antonio
Category: Other Staff

Inaugural Professional Development Program for Clinical Research Professionals: Key Insights and Outcomes

Krista L. Kilpadi, Danielle R. Gordon, Melanie M. Zuñiga-Rapp

Rationale. Clinical research professionals (CRPs) are critical to the development of new medical treatments. However, many early-career CRPs receive little to no training on how to conduct and manage clinical research. Often, they are recruited from other areas of clinical practice with no experience in research; while others have a limited understanding of human research. Nonetheless, CRPs often play a key role in the daily management of clinical research and serve as essential partners to principal investigators, ensuring data integrity and the ethical conduct of research.

Objectives. The objective of this program is to familiarize CRPs with regulations governing clinical research and best practices for conducting and managing research involving human participants thus improving the clinical research enterprise at UT Health San Antonio.

Methods. The two-day curriculum was designed and presented by representatives from UT Health San Antonio Research Operations. Recruitment for the workshop included university-wide email announcements and targeted notifications to select research teams. Participants were asked to complete a pre- and post-test to self-evaluate their skill level in performing 13 tasks typical of CRPs on a five-item ordinal scale. Results were compared pairwise, and the Wilcoxon Signed Rank test was used to determine whether differences between the pre- and post-workshop responses were statistically significant. Participants also responded to several questions about their satisfaction with the workshop.

Results. Nineteen individuals in the target population completed both the pre- and post-workshop surveys. They held a variety of job titles, including Research Coordinators, Clinical Research Nurses, Research Assistants, Research Area Specialists, and one Program Manager. Most attendees had less than three years of human research experience. Median skill scores increased after participation in the workshop for all 13 targeted tasks. The improvement in the median was 1 to 2 skill levels for every task except obtaining informed consent, a task which most participants felt skilled at before participating in the program. The difference between pre- and post-workshop skill assessments was statistically significant for all 13 tasks. Satisfaction feedback indicated that most participants found the material "very relevant" to their work, and all participants indicated that they would recommend the course to a colleague.

Conclusions. Participation in this two-day workshop significantly improved the confidence of early career clinical research professionals across all 13 skills targeted in the training program. These data suggest participation in the workshop can accelerate the understanding and competence of CRPs. We anticipate these outcomes will improve clinical research compliance, research data integrity, support for clinical investigators, and the recruitment and retention of CRPs. Such workforce development initiatives are crucial to increasing clinical research capacity at academic medical centers.

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Posterboard #: 51

Presenter: Alyssa Main, BS
Institution: UT Health San Antonio
Category: Other Staff Research Assistant

High intensity interval training and virtual reality-based games for improving balance in Parkinson's disease

Alyssa Main, Timothy Smith, Meenal Cascella, Camden Mooney, Michelle Aguirre, Abigail Moore, Okeanis Vaou, Daniel M. Corcos and Anjali Sivaramakrishnan

Background: Parkinson's Disease (PD) is a neurodegenerative disorder that can cause motor and cognitive impairments which can lead to falls. Previous research in older adults suggests that functional changes in the primary motor cortex, a key driver of movement, may underlie deficits in postural instability. Although this relationship is less clear in PD, some studies suggest that reduced inhibition of competing motor programs and reduced excitation in the motor cortex can affect movement selection, affecting balance. Priming is a novel concept in rehabilitation where an intervention's effects can be potentiated by another therapy. Few studies have shown that endurance exercise can modulate corticomotor excitability for improving task performance. This study aims to determine the clinical and neurophysiological effects of endurance exercise as a primer for virtual reality (VR)-based games on individuals with PD.

Methods: 8 individuals with PD (age range: 56 - 81 years, H&Y stages 2-3) were randomized to exercise (motor priming) and VR or stretching (control) and VR groups. The exercise group performed high intensity interval training which included warm-up, 20 minutes of exercise [interval bouts at 80% heart rate max (HRmax) and recovery bouts at 60% HRmax] and cooldown. The control group performed 30 minutes of whole body stretches. The VR-based exergames involved exercises that challenged the participants' balance such as dodging obstacles, reaching for kitchen shelves and playing seesaw with a monkey. Participants received the intervention for 24 sessions over 8 weeks. Outcomes included clinical and instrumented measures of balance i.e. the mini-Balance Evaluation Systems Test (miniBESTest), measures of postural sway as assessed by the Biodex BioSway, 6-minute walk distance, cognition (PD cognition rating scale) and corticomotor excitability as measured by transcranial magnetic stimulation (TMS). TMS measures included cortical silent period and short-interval intracortical inhibition. Outcomes were assessed at baseline, post intervention and at 6-week follow-up.

Results: We observed positive trends in balance, postural sway, six-minute walk distance and cognition in the experimental group, but these changes were not statistically significant ($p > 0.05$). Changes in cortical silent period and intracortical inhibition did not reach statistical significance.

Conclusion: Exercise priming with virtual reality did not seem to be superior to stretching and virtual reality-based games for improving balance, endurance, cognition and corticomotor excitability. The small sample size may explain these findings, and larger studies are needed to better understand the effects of exercise priming.

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Posterboard #: 52

Presenter: Jo Schultz
Institution: UT Health San Antonio
Category: Other Visiting Student (High School)

Berberine and Metformin Inhibit Caterpillar Growth and Chrysalis Development

Jo Schultz

The anti-diabetic drug metformin and herbal supplement berberine are reported to mimic diet restriction and extend the life and health span. Invertebrates such as nematodes, fruit flies, or crickets are commonly used to study such geroprotective properties because of their short lifespans. Butterflies also have short lifespans, but are less often used in pharmacology, toxicology or aging research. Painted lady caterpillars take roughly two weeks to reach the chrysalis stage, metamorphosis takes another week or so, and then the butterflies live on average up to a month or more to fly and find mates and start the next generation. The hypothesis of this study was that dietary administration of metformin and/or berberine to caterpillars would dose-dependently extend the lifespan of painted lady butterflies. To test this, caterpillars (3rd instar) were weighed and placed 5 per cup on diets spiked with 0, 0.1, 1 or 10 mg/g metformin or berberine, and monitored for weight, metamorphosis, butterfly size and lifespan. Some of the 10 mg/g metformin and all the 10 mg/g berberine-exposed caterpillars either failed to form chrysalises or never emerged as butterflies. With exposure to sunlight most of the 1 mg/g berberine fed caterpillars failed to molt and died, but this did not occur when shielded from sunlight. Caterpillars treated with 10 mg/g metformin and 1 mg/kg berberine emerged as smaller butterflies than control ones. Treatments of 0.1 mg/g metformin and berberine had no impact on caterpillar development or butterfly size. The lifespan of the butterflies was not increased by either metformin or berberine treatments, so the hypothesis they would extend the life span was not supported. However, these findings reveal that 1-10 mg/g metformin and berberine can inhibit lepidopteran metamorphosis. In parallel studies melatonin had similar effects and inhibited the molting hormone 20-hydroxyecdysone (20-E). Future studies will determine if metformin or berberine also inhibit 20E to slow metamorphosis.

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Posterboard #: 53

Presenter: Morgan Smith, M.S.
Institution: UT Health San Antonio
Category: Other Staff

Python-Based Machine Learning for Three-Dimensional Human Brain Model Segmentation and Analysis

Morgan Mekale Smith, MS, Elizabeth Ochoa, PhD, Mallory Keating, HT (ASCP), Margaret E. Flanagan, MD, and Kevin F. Bieniek, PhD

Pathology and cell loss in neurodegenerative diseases results in brain atrophy of specific neuroanatomical structures. Atrophy can be quantitatively assessed using neuroimaging techniques, but these methods can be costly. We seek to use three-dimensional (3D) modeling technologies and machine learning (ML) to permit visualization and quantitative analysis approaches, including model segmentation.

Python and Blender are specialized for analysis and 3D model manipulation, respectively. By utilizing these applications, we aim to apply these techniques to automate analysis of neuroanatomical structures to quantitatively measure atrophy using ML. Via structured-light scanning, 3D models of postmortem brain tissue were obtained. The 3D data was imported as .obj files and simplified using mesh decimation via Python. These decimated files were then imported into Blender for manual segmentation based on readily identifiable gyri and sulci. Segmented models were exported from Blender as .csv files into a Python-based ML pipeline for algorithm training. The performance of each model was assessed by obtaining the following evaluation metrics: accuracy, precision, recall, F1-score, and loss.

Our methods demonstrated that of the sci-kit learn models, the Random Forest and Decision Tree classifiers generated predictions with the highest accuracy, average precision, and recall scores when assigning labels to unannotated data. In addition, these algorithms demonstrated the lowest hamming loss scores compared to the other ML models. Our custom sequential Tensorflow model demonstrated improved accuracy scores, lower precision and recall, and slightly elevated binary cross entropy loss measurements. Our pipeline suggests that predictive modeling can be used to segment multiple 3D models using multi-label classification techniques with accuracy and precision scores of 60-89%. For 2D images, we expect annotation performed by ML techniques will be comparable to cortical atrophy measurements obtained using MRI neuroimaging.

Our findings provide support for the utilization of ML techniques to identify specific neuroanatomical sub-regions and measure atrophy from 3D brain models. Future validation against other neuroimaging modalities is necessary to confirm model consistency of surface mesh segmentation and cortical atrophy measurements.

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Posterboard #: 54

Presenter: Roslyn Valdespino, MPH
Institution: Biggs Institute
Category: Other Research Associate

Plasma Biomarker Associations with Cognition and HIV in Uganda

Roslyn Valdespino, MPH , Tiffany F. Kautz, PhD , Godfrey Masette, Gabrielle Hromas, PhD , Chen-Pin Wang, PhD , Jayandra J. Himali, PhD , Robert Paul, PhD , Noeline Nakasujja, MD, PHD , Zahra Reynolds, MPH , Flavia Atwine, BS., MPH , Edna Tindimwebwa, BPH., DCM , Meredith Greene, MD , Eliza Passell, MPH , Christine S Ritchie, MD, MSPH , Susanne S Hoeppner, PhD , Alexander C Tsai, MD , Janet Seeley, PhD , Lawren VandeVrede, MD, PhD , Amy Werry, PsyD , Elena Tsoy, PhD , Katherine L. Possin, PhD , Josephine E Prynn, MbChB MRCP MSc , Suzanne E. Schindler, MD, PhD , Sudha Seshadri, MD , Samson Okello , Stephen Asiimwe, MBChB, MS, DrPH , Deanna Saylor, MD, Mark J Siedner, MD, Jeremy A Tanner, MD, MPH

Background: In the coming decades, sub-Saharan Africa (SSA) is projected to have the fastest global growth in older adults, a >250% increase in Alzheimer's Disease (AD), and a >200% increase in older people living with HIV (PLWH). In the Global North, HIV infection has been associated with neuroinflammation, accelerated brain aging, cognitive impairment, and AD pathology. In SSA, data about the intersections of aging, AD, and HIV are lacking. We estimated associations between ADRD (AD and Related Dementias) plasma biomarkers and cognition in the Uganda Aging Cohort Study (UACS), a prospective cohort of PLWH well-treated on antiretroviral therapy (ART) and demographically similar HIV-negative individuals recruited via population sampling approaches.

Method: Blood samples were collected in EDTA tubes, centrifuged, aliquoted, and frozen at -80°C at semi-urban (n=320) and rural (n=330) sites. Plasma was shipped to the UTHSA Biggs Biobank Laboratory. Plasma p-tau217, Aβ42/40, and p-tau217/Aβ42 were measured on Fujirebio Lumipulse, and GFAP and NfL on Quanterix Simoa. Rural site Aβ42/40 and p-tau217/Aβ42 did not pass quality control due to cold-chain storage complications and were excluded from this analysis. Cognitive testing was conducted using locally validated reference-standard tests. Z-scores for each test were created using a regression-based normative approach with adjustment for age, sex, and education. Composite scores were created from mean Z-scores for global cognition and each cognitive domain. The presence/absence of cognitive impairment was defined using Jak/Bondi criteria. Multivariable regression models estimated associations between log-transformed ADRD biomarkers and cognitive outcomes, adjusting for age, sex, education, site, renal function via eGFR, and depression, and stratified by HIV serostatus. A sensitivity analysis restricted to the subsample of PLWH also adjusted for duration on ART.

Results: 560 total participants (49% PLWH, mean age 60.3 years, 50% female) were included. Elevated plasma NfL was associated with worse overall cognition, learning/memory, attention, executive function, and motor performance in the total cohort. In stratified analyses, elevated NfL was associated with overall cognition, attention, executive function, and motor performance in PLWH, whereas NfL was only associated with motor performance among HIV-negative individuals. Elevated plasma GFAP was associated with 62% higher odds of cognitive impairment in the total cohort and worsened executive function in PLWH. Plasma p-tau217, Aβ42/40, and p-tau217/Aβ42 were not associated with cognitive performance. Results were consistent in sensitivity analyses adjusting for ART duration among PLWH.

Conclusion: Plasma NfL and GFAP are associated with cognition among older adults in Uganda, particularly PLWH. The lack of association between plasma p-tau217 and cognition contrasts with findings from studies conducted in the Global North and may suggest that cognitive impairment is driven by non-Alzheimer Disease etiologies in this younger cohort. Further studies in diverse global populations are needed to inform appropriate use of new biology-based diagnostic criteria for ADRDs.

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Posterboard #: 55

Presenter: Zhimin Yang, MD
Institution: UT Health San Antonio
Category: Other Visiting Student

Retinoic acid boosts the IgA response by amplifying "TGF-β pathway" to enhance CSR to IgA and by promoting plasma cell differentiation

Zhimin Yang, Bhuwaneswor P. Kandel, Shili Li, Funan He, Carlos Rivera and Paolo Casali

Retinoic acid (RA), the active metabolite of vitamin A, plays important roles in multiple physiological functions, including immune homeostasis and immune responses. Using mouse immunization models, we show that RA boosts the T-dependent and T-independent IgA antibody responses. RA directly acts on B cells to integrate and amplify the "TGF-β pathway", thereby increasing class-switch recombination (CSR) to IgA. In addition, it promotes Prdm1/Blimp-1 expression and plasma cell differentiation, leading to greater overall IgA antibody response. RA, increases, through its receptor RARα, transcription of key TGF-β pathway genes Tgfb1, Tgfb3, Tgfbr1, Smad3, Runx2 and Igha as well as Prdm1, all of which contain RA-responsive elements (RAREs) within their promoters. The activity of RA in mediating gene transcription and amplification of IgA antibody response is further supported by RARα reverse agonist BMS493, which abolishes RA impact on B cells in vivo and in vitro. By inducing conformation change of RARα, RA increases recruitment of Smad3 and Runx2 to the promoters of Tgfb1 and Igha, which contain Smad-binding elements (SBEs) and Runx-binding elements (RBEs), forming a novel complex that drives target gene transcription activation. Thus, RA amplifies the TGF-β pathway to enhance CSR to IgA and promotes plasma cell differentiation, thereby boosting overall IgA antibody response.