THE
UNIVERSITY
OF RHODE ISLAND
COLLEGE OF
PHARMACY

2026 Research Showcase

Table of Contents

Graduate Students

Graduate Students

1st Graduate Students

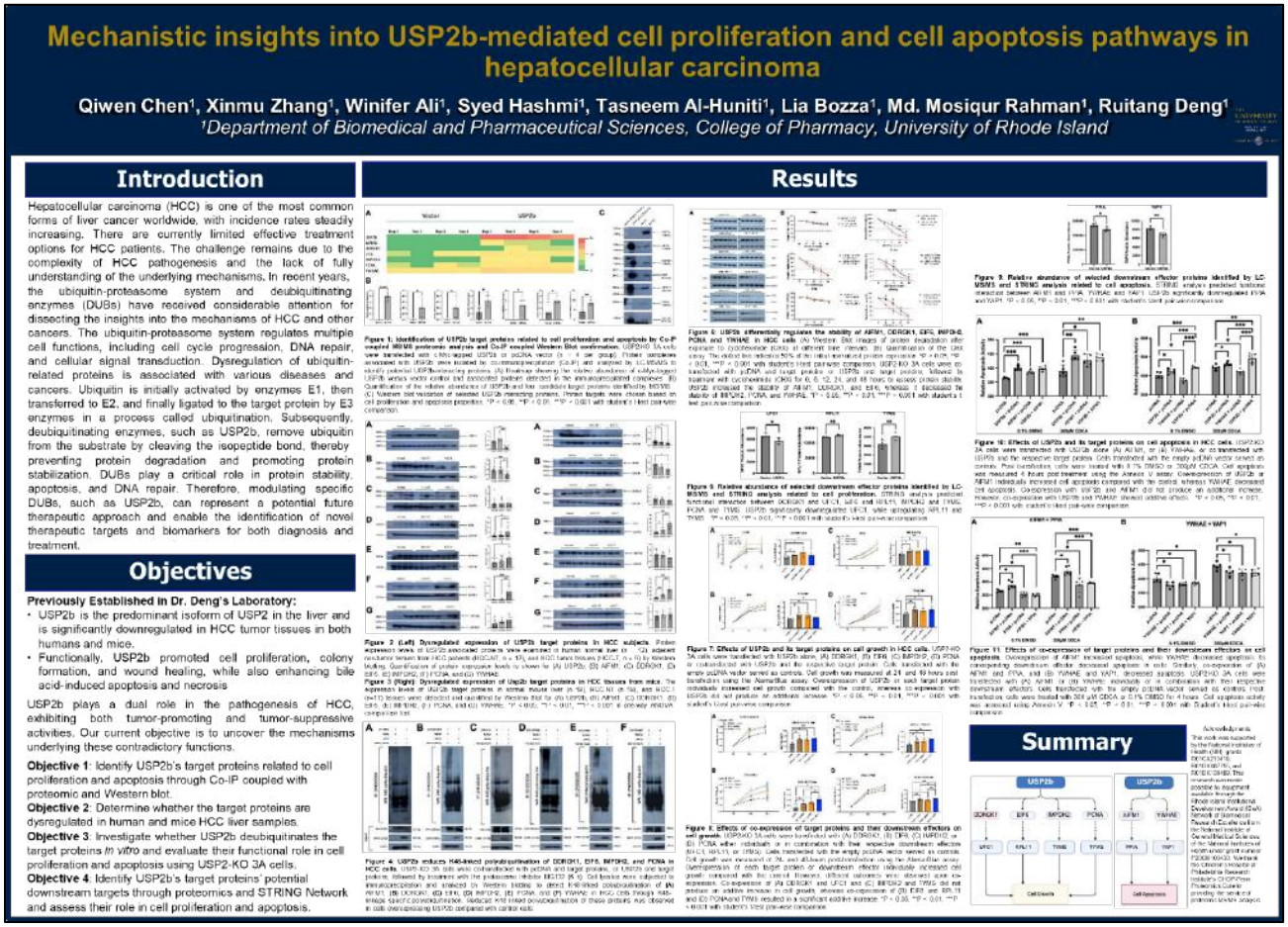
Dr. Deng accepting on behalf of the winning poster

2nd Graduate Students

Ololade Gbadebo accepting on behalf of the second placed poster

3rd Graduate Students

Evans Boateng Boakye Gbadebo accepting on behalf of the third placed poster

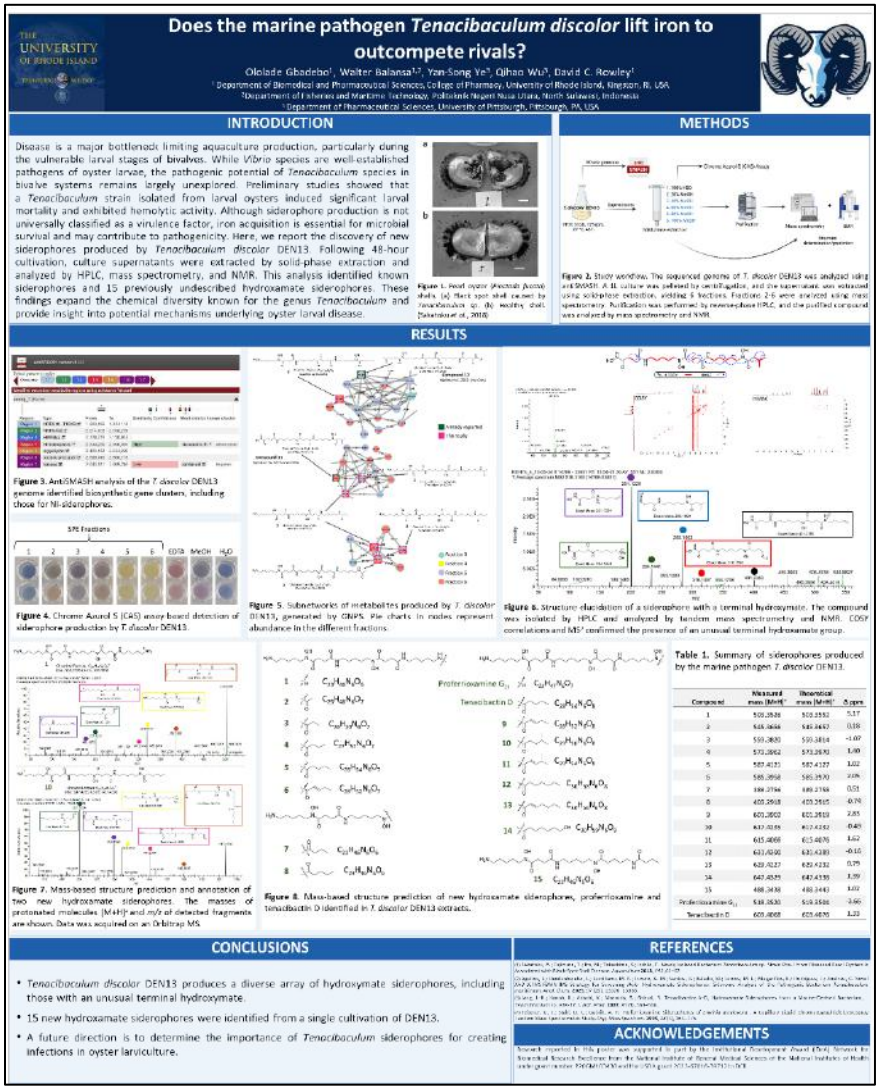


1st Graduate Students

First Place - Mechanistic Insights into USP2b-Mediated Cell Proliferation and Cell Apoptosis Pathways in Hepatocellular Carcinoma

Qiwen Chen, Xinmu Zhang, Winifer Ali, Syed Hashmi, Tasneem Al-Huniti, Lia Bozza, Md. Mosiqur Rahman, Ruitang Deng

Hepatocellular carcinoma (HCC) is one of the most common forms of liver cancer worldwide and accounts for 90% of liver cancer cases. By 2025, it is estimated to have more than one million cases globally. Hepatitis B virus and hepatitis C virus are the main risk factors for HCC development. Early-stage HCC patients may profit from multiple treatment options, including surgical resection, liver transplantation, arterial embolization, radioembolization, or systemic targeted agents. Currently, there is a limited effective option in treating HCC patients. There is an urge to develop more effective therapies for HCC. However, the challenge remains due to the complexity of HCC pathogenesis and the lack of understanding of the complex mechanism. In recent years, the ubiquitin-proteasome system (UPS) and deubiquitinating enzymes (DUBs) have emerged as an important topic for understanding the mechanism of HCC and other cancers. The ubiquitin-proteasome system is one of the most important posttranslational modification pathways in eukaryotic cells that regulates cell functions, including cell cycle progression, DNA repair, and signal transduction. Ubiquitination can be reversed by deubiquitinating enzymes (DUBs) such as ubiquitin-specific peptidase 2 (USP2) that can cleave ubiquitin or ubiquitinated proteins from targeted proteins. In our previous study, we found that the overexpression of USP2b exhibited tumorigenic activities through promoting cell proliferation, colony formation, and wound healing in HepG2-WT and Huh 7 cells. Interestingly, overexpression of USP2b exhibited tumor suppressor characteristics through enhancing bile acid-induced apoptosis and necrosis in HepG2-WT and Huh7 cells upon bile acid treatment. Through a coimmunoprecipitated (Co-IP) – coupled proteomic analysis and western blot, novel USP2b-regulated downstream target proteins involved in the cell proliferation signaling pathway and the apoptosis signaling pathways have been identified. These newly identified USP2b target proteins were significantly upregulated or downregulated in HCC subjects. This finding reveals that USP2b exhibited both oncogenic and tumor- suppressing activities by regulating different signaling pathways. Therefore, delineating the novel mechanism in which USP2b promotes tumorigenesis while also expressing tumor-suppressing activities will provide the basis for developing more effective therapies by targeting USP2b or its downstream signaling pathways.

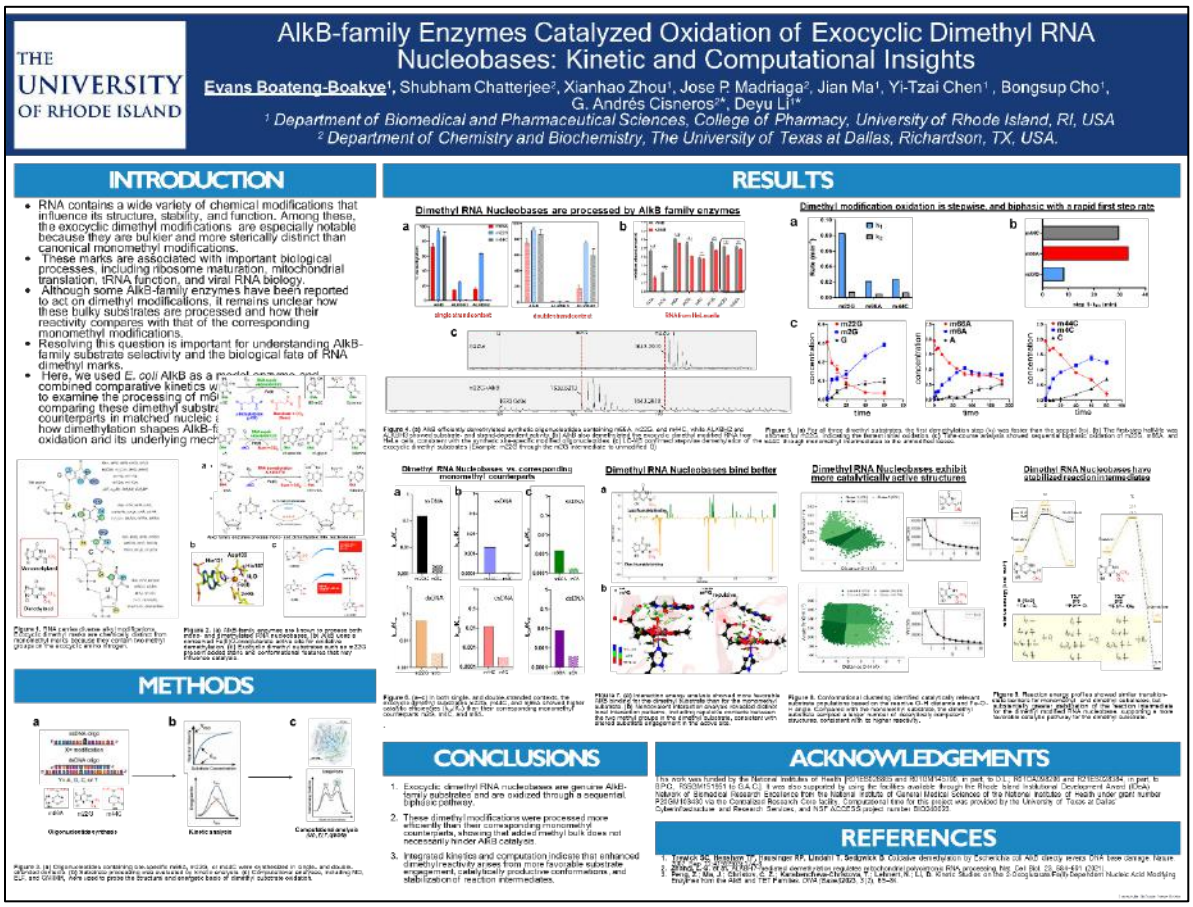


2nd Graduate Students

Second Place - Does the marine pathogen Tenacibaculum discolor lift iron to outcompete rivals?

Ololade Gbadebo, Walter Balansa, Yan-Song Ye, Qihao Wu, David Rowley

Disease is a major bottleneck limiting aquaculture production, particularly during the vulnerable larval stages of bivalves. While Vibrio species are well-established pathogens of oyster larvae, the pathogenic potential of Tenacibaculum species in bivalve systems remains largely unexplored. Preliminary studies showed that a Tenacibaculum strain isolated from larval oysters induced significant larval mortality and exhibited hemolytic activity. Although siderophore production is not universally classified as a virulence factor, iron acquisition is essential for microbial survival and may contribute to pathogenicity. We hypothesized that siderophore production contributes to the pathogenicity of T. discolor in oyster larvae. Here, we report the discovery of new siderophores produced by Tenacibaculum discolor DEN13. The bacterial whole genome was sequenced and annotated. The genome was analyzed using antiSMASH to identify biosynthetic gene clusters, including that of NRPS-independent siderophores. Following 48-hour cultivation, culture supernatants were extracted by solid-phase extraction using 20%, 40%, 60%, 80% methanol/water, and 100% methanol. Extracts were fractionated and purified using reverse-phase MPLC followed by reverse-phase HPLC. Extracts and isolates were analyzed by reverse-phase HPLC, mass spectrometry, and NMR spectroscopy, followed by metabolomics analysis. Iron-binding activity was determined using the Chrome Azurol S (CAS) assay. These analyses identified known siderophores and 15 new hydroxamate siderophores. These findings expand the chemical diversity known for the genus Tenacibaculum and provide insight into potential mechanisms underlying oyster larval disease.



3rd Graduate Students

Third Place - AlkB-family Enzymes Catalyzed Oxidation of Exocyclic Dimethyl RNA Nucleobases: Kinetic and Computational Insights

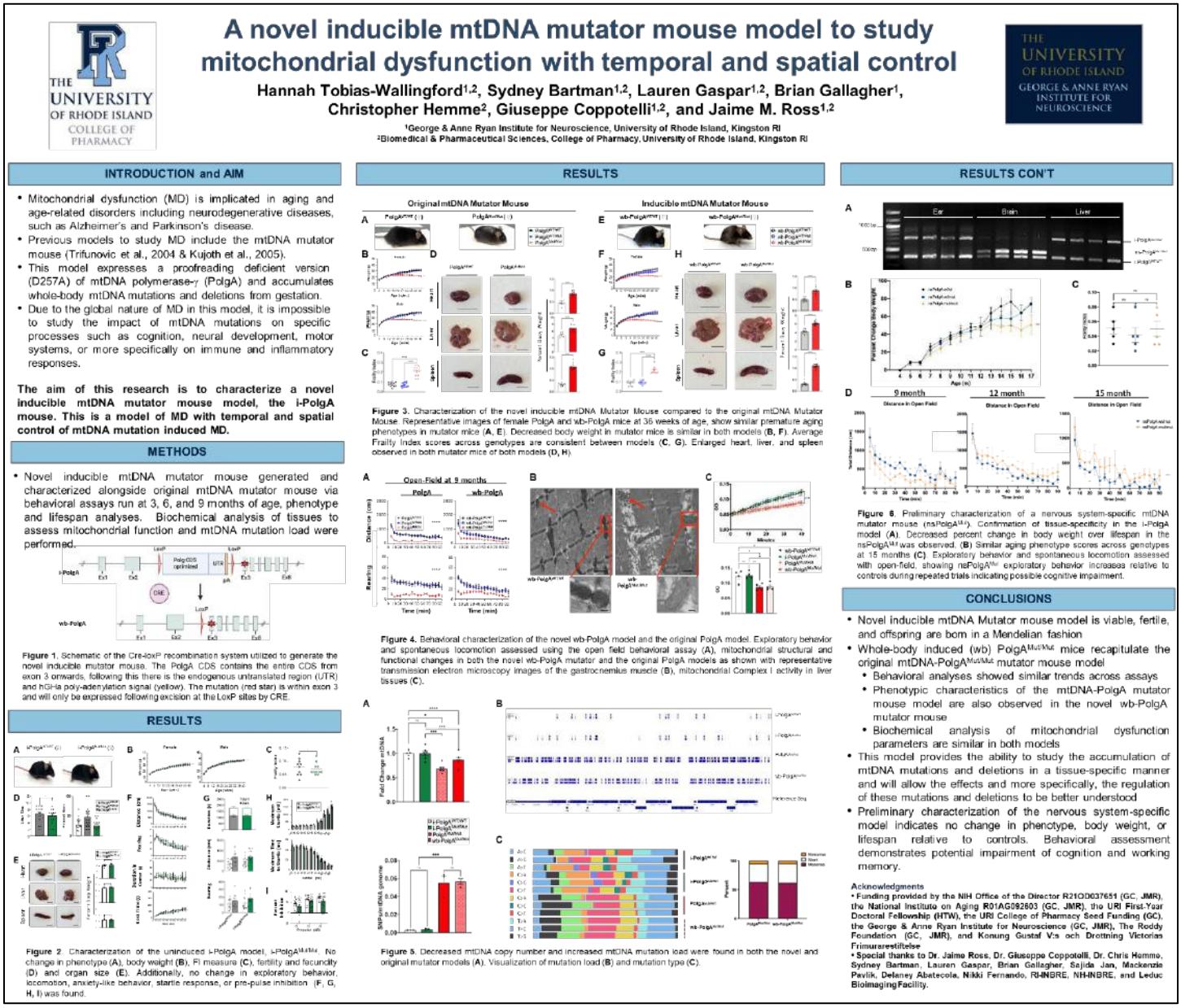
Evans Boateng-Boakye, Shubham Chatterjee, Xianhao Zhou, Jose P. Madriaga, Jian Ma, Yi-Tzai Chen, Bongsup Cho, G. Andrés Cisneros, Deyu Li

Exocyclic dimethyl modifications of RNA nucleobases, including N6,N6-dimethyladenosine (m66A), N2,N2-dimethylguanosine (m22G), and N4,N4-dimethylcytidine (m44C), are biologically important marks associated with ribosome maturation, mitochondrial translation, tRNA function, and viral RNA biology. Although some AlkB-family Fe(II)/2-oxoglutarate-dependent dioxygenases have been reported to act on di-methylated nucleobases, how these bulky and sterically distinct substrates are processed, and how their reactivity compares with corresponding monomethyl modifications, remain unclear. Here, we used Escherichia coli AlkB as a model enzyme and integrated comparative kinetics with computational analysis to define the oxidation behavior of exocyclic dimethyl nucleobases.

Site-specifically modified oligonucleotides containing m6,6A, m2,2G, or m4,4C were synthesized and examined in matched single-stranded and double-stranded contexts. In vitro assays showed that AlkB efficiently oxidizes all three dimethyl substrates, whereas some mammalian homologs showed substrate- and strand-dependent activity on selected dimethyl modifications. Time-course analyses revealed that their oxidation proceeds through a sequential biphasic pathway, with a rapid first demethylation step to the corresponding monomethyl intermediate followed by a slower second demethylation step to the unmodified base. Surprisingly, all three dimethyl substrates were processed more efficiently than their corresponding monomethyl counterparts in both strand contexts.

To explain this unexpected behavior, we performed computational analyses on the mono-and dimethyl substrates. Molecular interaction and conformational analyses showed that the dimethyl RNA nucleobases bind more favorably in the enzyme active site and samples a larger population of catalytically competent structures. Reaction energy profiles also indicated that dimethylation of the RNA nucleobase enhances the stabilization of its reaction intermediate and not necessarily lower its transition state barrier.

Together, this work shows that exocyclic dimethyl RNA-type nucleobases are genuine and efficiently processed AlkB-family substrates. It provides a mechanistic framework for understanding dimethyl substrate selectivity and has implications for RNA modification biology, repair-dependent sequencing strategies, and future engineering of AlkB-family enzymes.



A novel inducible mtDNA mutator mouse model to study mitochondrial dysfunction with temporal and spatial control

Hannah Tobias-Wallin, Sydney Bartman, Lauren Gaspar, Brian Gallagher, Christopher Hemme, Giuseppe Coppotelli, Jaime M. Ross

Mitochondrial dysfunction is a hallmark of numerous age-related diseases including neurodegenerative diseases, such as Alzheimer's and Parkinson's disease. A wealth of studies supports the accumulation of mitochondrial DNA (mtDNA) mutations as a contributing factor of mitochondrial dysfunction in aging and disease. One of the best models to study the relationship between mtDNA mutations and mitochondrial dysfunction is the mtDNA mutator mouse, which expresses a proofreading-deficient version of mtDNA polymerase-gamma (PolgA), resulting in accelerated accumulation of mtDNA mutations and aging-like mitochondrial dysfunction. Despite its groundbreaking contributions to mitochondrial biology and aging research, this model is limited by the whole-body accumulation of mtDNA mutations, which prevents the investigation of tissue-specific differences in mitochondrial dysfunction. To overcome this limitation, we developed a novel inducible knock-in mtDNA mutator mouse model (iPolgA) that allows spatial and temporal control of mtDNA mutations, enabling the precise study of mitochondrial dysfunction in a tissue- and time-specific manner. Here, we report the generation and validation of this novel model through whole-body induction via Cre recombinase. Our data demonstrate that, upon induction, this model recapitulates the phenotype of the original mtDNA mutator mouse manifesting the same behavioral and biochemical alterations. Additionally, we are working towards demonstrating functionality of the novel iPolgA model and are generating a nervous system-specific mtDNA mutator mouse to evaluate the effects of mitochondrial dysfunction specifically in brain. This work highlights the iPolgA model as a powerful tool for studying the impact of mtDNA mutations on aging and neurodegenerative disorders with enhanced specificity and control

THE UNIVERSITY OF RHODE ISLAND COLLEGE OF PHARMACY

Activity of USP2b in Cellular Senescence

Lia Bozza*, Tasneem Al-Huniti, Qiwen Chen, Md. Mosiqur Rahman, Xinmu Zhang, Winifer Ali, Syed Hashmi, Ruitang Deng
University of Rhode Island, College of Pharmacy

Introduction

Cellular senescence is a state of permanent, stress-induced cell cycle arrest first described by Hayflick and Moorhead (1961). While senescent cells remain metabolically active, they are resistant to apoptosis and secrete pro-inflammatory cytokines. Senescence is beneficial for a short time, but chronic senescence drives inflammation. In hepatocytes, bile acid toxicity is a key senescence trigger, implicating protein homeostasis pathways in its regulation. The ubiquitin-proteasome system (UPS) is a primary way of controlled protein degradation, with deubiquitinating enzymes (DUBs) regulating this process by removing ubiquitin tags and preventing premature protein degradation. Among liver-enriched DUBs, USP2b is the predominant isoform expressed in liver tissue (Nadolny et al., 2021), yet its role in hepatocyte senescence remains unknown.

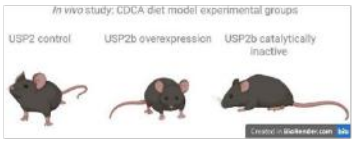
Research question

We propose that USP2b dysregulation impairs endoplasmic reticulum (ER) protein homeostasis, thereby promoting bile acid-induced hepatocyte senescence. In this project, we will address the question: How does USP2b expression modulate bile acid-induced senescence?

Methods

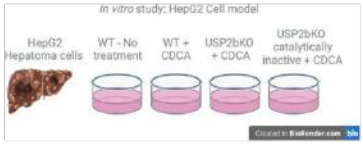
In vivo — chenodeoxycholic acid (CDCA) diet mouse model

Experimental groups: USP2b knockout control, USP2b overexpression, and catalytic inactive mutant (C276A), all on CDCA diet. Endpoint: liver tissue harvest. Readouts: SA-β-galactosidase staining, p21/p16/GRP78 western blot (cell cycle exit and ER stress)



In vitro — HepG2 cell model

Experimental groups: wild-type no treatment, wild-type + CDCA, USP2bKO + CDCA, and catalytic inactive mutant + CDCA. Readouts: SA-β-galactosidase staining, p21/p16/GRP78 western blot



Tool – Catalytic mutant C276A substitution

Active site Cys→Ala eliminates hydrolysis activity. This controls for protein expression vs. enzymatic function of USP2b.

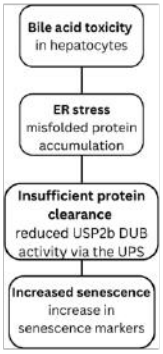
AAAACGGTGTATAAAGAAGTTC
AAAACGGGCTATAAAGAAGTTC

Ongoing Work

(1) Does USP2b expression alter cell cycle progression?

(2) Does the overexpression of USP2b reduce ER stress through activation of ER protein homeostasis machinery in hepatocytes?

Proposed pathway of USP2b activity in bile acid induced senescence



Understanding this pathway may reveal new therapeutic targets in cholestatic liver disease.

References

Hayflick et al (1961) Exp Cell Res 25:3

Nadolny C et al (2021) Am J Cancer Res 11:10

Images created in https://BioRender.com and Canva.com

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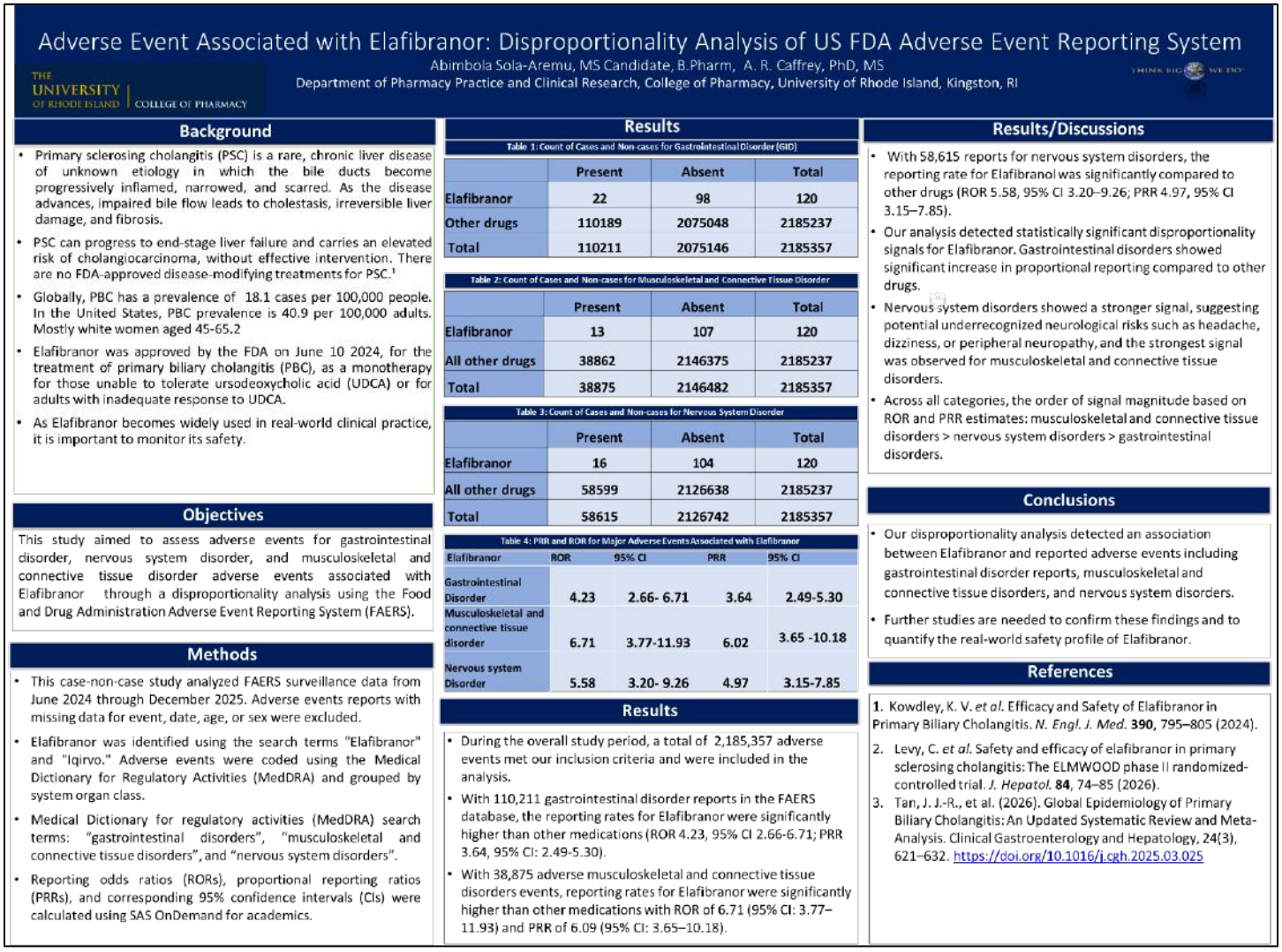
Activity of USP2b in Cellular Senescence

Lia Bozza, Tasneem Al-Huniti, Qiwen Chen, Md. Mosiqur Rahman, Xinmu Zhang, Winifer Ali, Syed Hashmi, Ruitang Deng

Cellular senescence is characterized by terminal cell cycle arrest coupled with sustained metabolic function. Under liver injury conditions, elevated bile acid levels can induce cellular senescence, but whether senescence contributes to disease or is a result of it remains an open question. Addressing this requires an understanding of the molecular regulators involved in senescence in the liver: among them is ubiquitin-specific peptidase isoform 2 (USP2b), an enzyme that deubiquitinates proteins tagged for proteasome-mediated degradation. Previous work in the lab of Dr. Deng has shown that USP2b is highly expressed in the liver tissue and it exhibits anti-senescence functions in both mouse and cell models. When USP2b was overexpressed in HepG2 cells and treated with bile acid to induce cellular stress, the number of senescent cells was significantly reduced compared to the control. These findings suggest that USP2b has anti-senescence activity, and this project aims to investigate the mechanisms responsible.



Adverse Event Associated with Elafibranor: Disproportionality Analysis of US FDA Adverse Event Reporting System

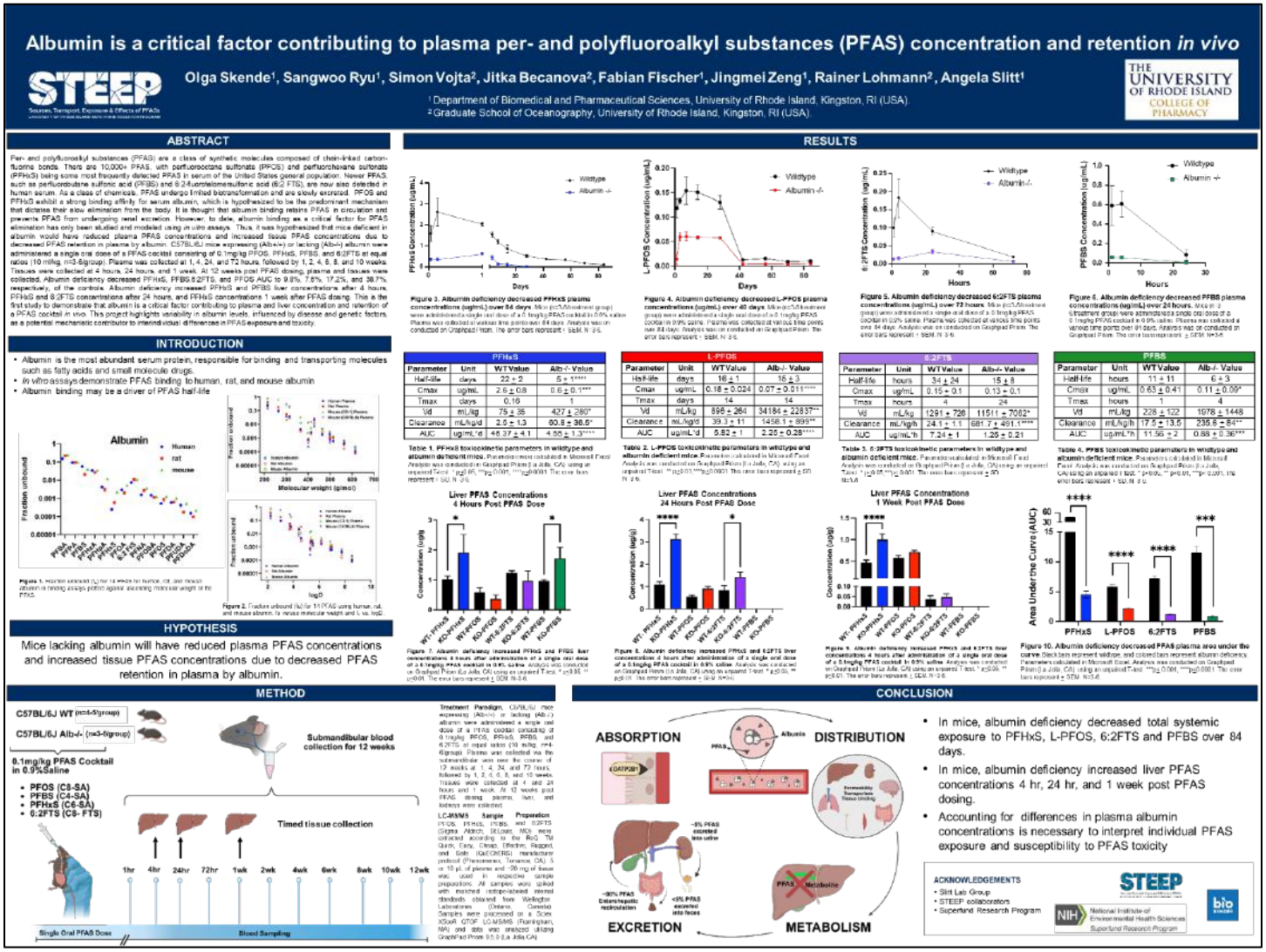
Abimbola Sola-Aremu, A. R. Caffrey

Background: Elafibranor, approved by the U.S. Food and Drug Administration (FDA) in June 2024 for the treatment of primary biliary cholangitis (PBC), represents a novel therapeutic option for patients who are intolerant to or inadequately responsive to ursodeoxycholic acid. As its use expands in real-world clinical practice, comprehensive safety evaluation is essential. This study aimed to assess adverse event (AE) signals associated with Elafibranor using post-marketing surveillance data.

Methods: A retrospective disproportionality analysis was conducted using the FDA Adverse Event Reporting System (FAERS) database from June 2024 through December 2025. Reports with missing key variables were excluded. Elafibranor-related AEs were identified using standardized drug names and coded based on the Medical Dictionary for Regulatory Activities (MedDRA). Adverse events were grouped into system organ classes, including gastrointestinal, musculoskeletal and connective tissue, and nervous system disorders. Reporting odds ratios (RORs), proportional reporting ratios (PRRs), and 95% confidence intervals (CIs) were calculated to detect safety signals.

Results: A total of 2,185,357 AE reports met inclusion criteria. Elafibranor demonstrated statistically significant disproportionality signals across all evaluated categories. Gastrointestinal disorders showed elevated reporting (ROR 4.23, 95% CI 2.66–6.71; PRR 3.64, 95% CI 2.49–5.30). Musculoskeletal and connective tissue disorders exhibited the strongest signal (ROR 6.71, 95% CI 3.77–11.93; PRR 6.02, 95% CI 3.65–10.18). Nervous system disorders also showed a significant association (ROR 5.58, 95% CI 3.20–9.26; PRR 4.97, 95% CI 3.15–7.85), suggesting potential underrecognized neurological risks.

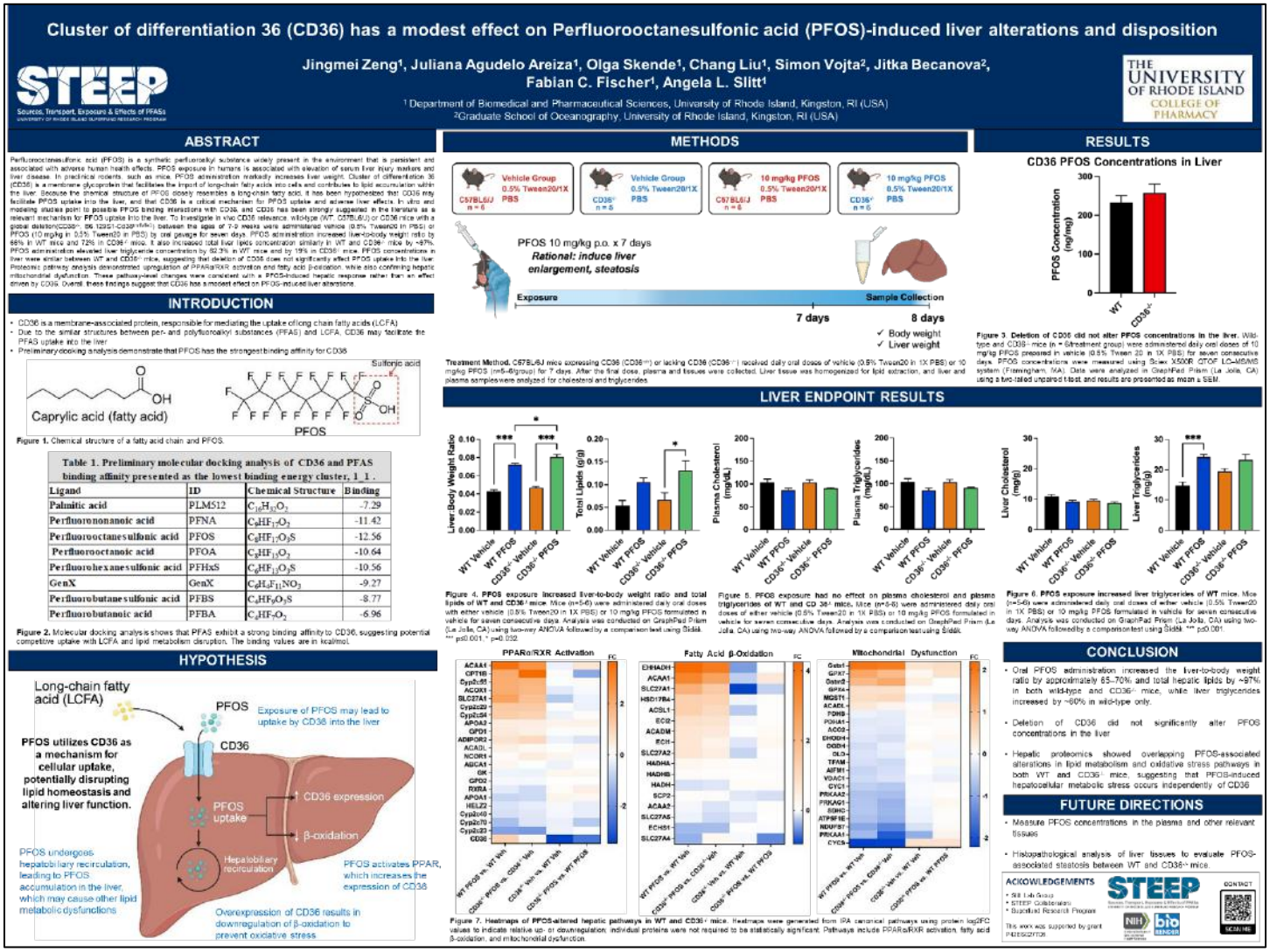
Conclusions: This analysis identified significant safety signals associated with Elafibranor across multiple organ systems. These findings highlight the importance of continued pharmacovigilance and may inform clinicians and regulators regarding potential risks. Further studies are warranted to validate these signals and better characterize the real-world safety profile of Elafibranor



Albumin is a critical factor contributing to plasma per- and polyfluoroalkyl substances (PFAS) concentration and retention in vivo

Olga Skende, Sangwoo Ryu, Simon Vojta, Jitka Becanova, Fabian Fischer, Jingmei Zeng, Rainer Lohmann, Angela Slitt

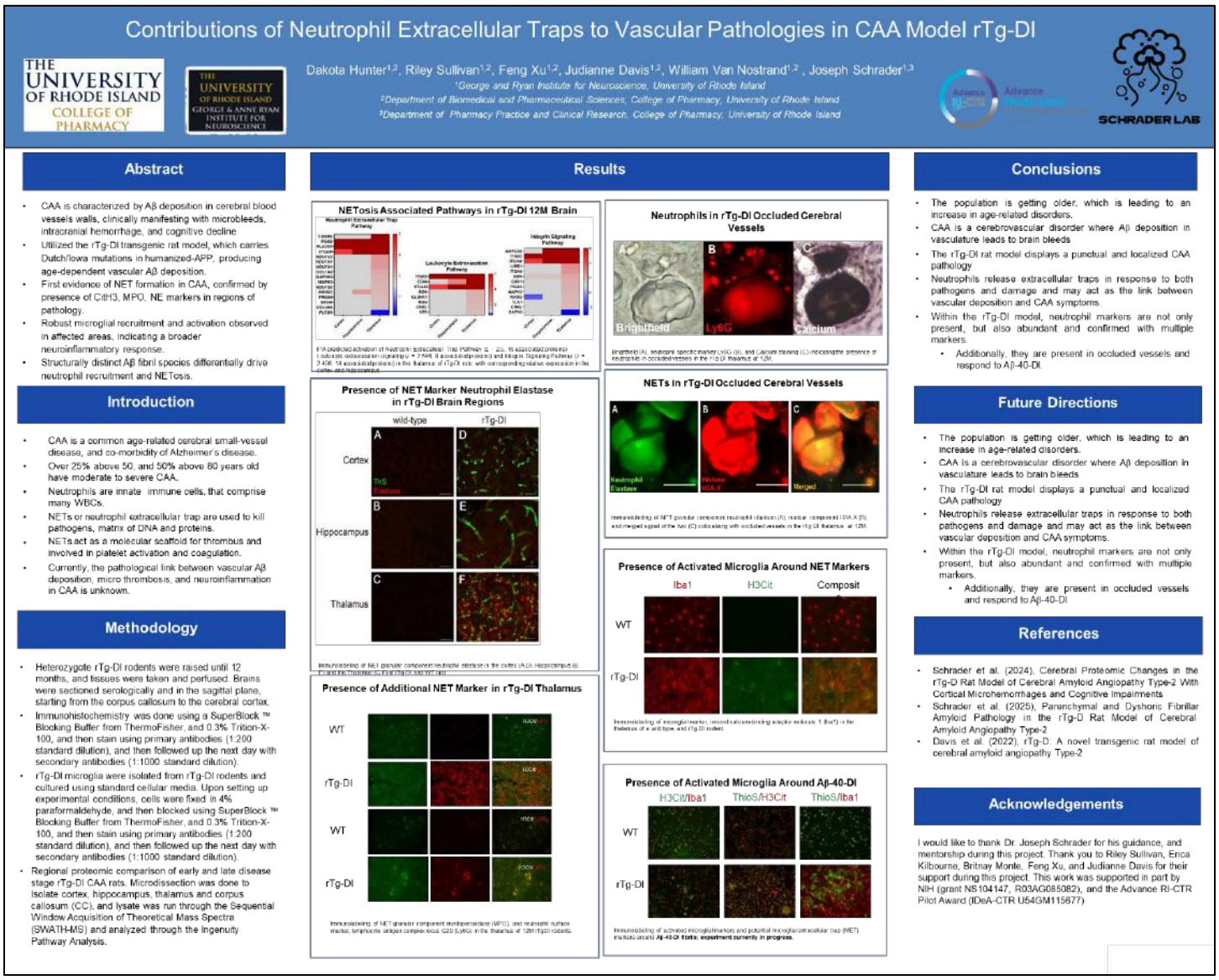
Per- and polyfluoroalkyl substances (PFAS) are a class of synthetic molecules composed of chain-linked carbon-fluorine bonds. There are 10,000+ PFAS, with perfluorooctane sulfonate (PFOS) and perfluorohexane sulfonate (PFHxS) being some most frequently detected PFAS in serum of the United States general population. Newer PFAS, such as perfluorobutane sulfonic acid (PFBS) and 6:2-fluorotelomersulfonic acid (6:2 FTS), are now also detected in human serum. As a class of chemicals, PFAS undergo limited biotransformation and are slowly excreted. PFOS and PFHxS exhibit a strong binding affinity for serum albumin, which is hypothesized to be the predominant mechanism that dictates their slow elimination from the body. It is thought that albumin binding retains PFAS in circulation and prevents PFAS from undergoing renal excretion. However, to date, albumin binding as a critical factor for PFAS elimination has only been studied and modeled using in vitro assays. Thus, it was hypothesized that mice deficient in albumin would have reduced plasma PFAS concentrations and increased tissue PFAS concentrations due to decreased PFAS retention in plasma by albumin. C57BL/6J mice expressing (Alb+/+) or lacking (Alb-/-) albumin were administered a single oral dose of a PFAS cocktail consisting of 0.1mg/kg PFOS, PFHxS, PFBS, and 6:2FTS at equal ratios (10 ml/kg, n=3-6/group). Plasma was collected at 1, 4, 24, and 72 hours, followed by 1, 2, 4, 6, 8, and 10 weeks. Tissues were collected at 4 hours, 24 hours, and 1 week. At 12 weeks post PFAS dosing, plasma and tissues were collected. Albumin deficiency decreased PFHxS, PFBS,6:2FTS, and PFOS AUC to 9.8%, 7.6%, 17.2%, and 38.7%, respectively, of the controls. Albumin deficiency increased PFHxS and PFBS liver concentrations after 4 hours, PFHxS and 6:2FTS concentrations after 24 hours, and PFHxS concentrations 1 week after PFAS dosing. This is the first study to demonstrate that albumin is a critical factor contributing to plasma and liver concentration and retention of a PFAS cocktail in vivo. This project highlights variability in albumin levels, influenced by disease and genetic factors, as a potential mechanistic contributor to inter-individual differences in PFAS exposure and toxicity.



Cluster of differentiation 36 (CD36) has a modest effect on Perfluorooctanesulfonic acid (PFOS)-induced liver alterations and deposition

Jingmei Zeng, Juliana Agudelo Areiza, Olga Skende, Chang Liu, Simon Vojta, Jitka Becanova, Fabian C. Fischer, Angela L. Slitt

Perfluorooctanesulfonic acid (PFOS) is a synthetic per- and polyfluoroalkyl substance that is environmentally persistent and associated with adverse health effects. In humans, PFOS exposure has been linked to elevated serum liver injury markers and liver disease, while in mice, PFOS administration markedly increases liver weight. Cluster of differentiation 36 (CD36) is a membrane glycoprotein that facilitates long-chain fatty acid uptake into cells and contributes to hepatic lipid accumulation. Because PFOS structurally resembles a long-chain fatty acid, CD36 has been proposed as a potential mediator of PFOS uptake into the liver and a contributor to PFOS-induced hepatotoxicity. To investigate the in vivo relevance of CD36, wild-type (WT, C57BL/6J) and global CD36 knockout (CD36-/-, B6.129S1-Cd36tm1Mfe/J) mice aged 7–9 weeks were administered vehicle (0.5% Tween 20 in PBS) or PFOS (10 mg/kg in 0.5% Tween 20 in PBS) by oral gavage for seven days. PFOS increased liver-to-body weight ratio by 66% in WT mice and 72% in CD36-/- mice. Total liver lipid concentration increased by approximately 97% in both genotypes. Liver triglycerides increased by 62.3% in WT mice and 19% in CD36-/- mice. However, PFOS concentrations in liver were similar between WT and CD36-/- mice, suggesting that CD36 deletion does not significantly alter PFOS hepatic deposition. Proteomic pathway analysis demonstrated upregulation of PPARα/RXR activation and fatty acid β-oxidation, while also confirming hepatic mitochondrial dysfunction. These pathway-level changes were consistent with a PFOS-induced hepatic response rather than an effect driven by CD36. Overall, these findings suggest that CD36 has a modest effect on PFOS-induced liver alterations.



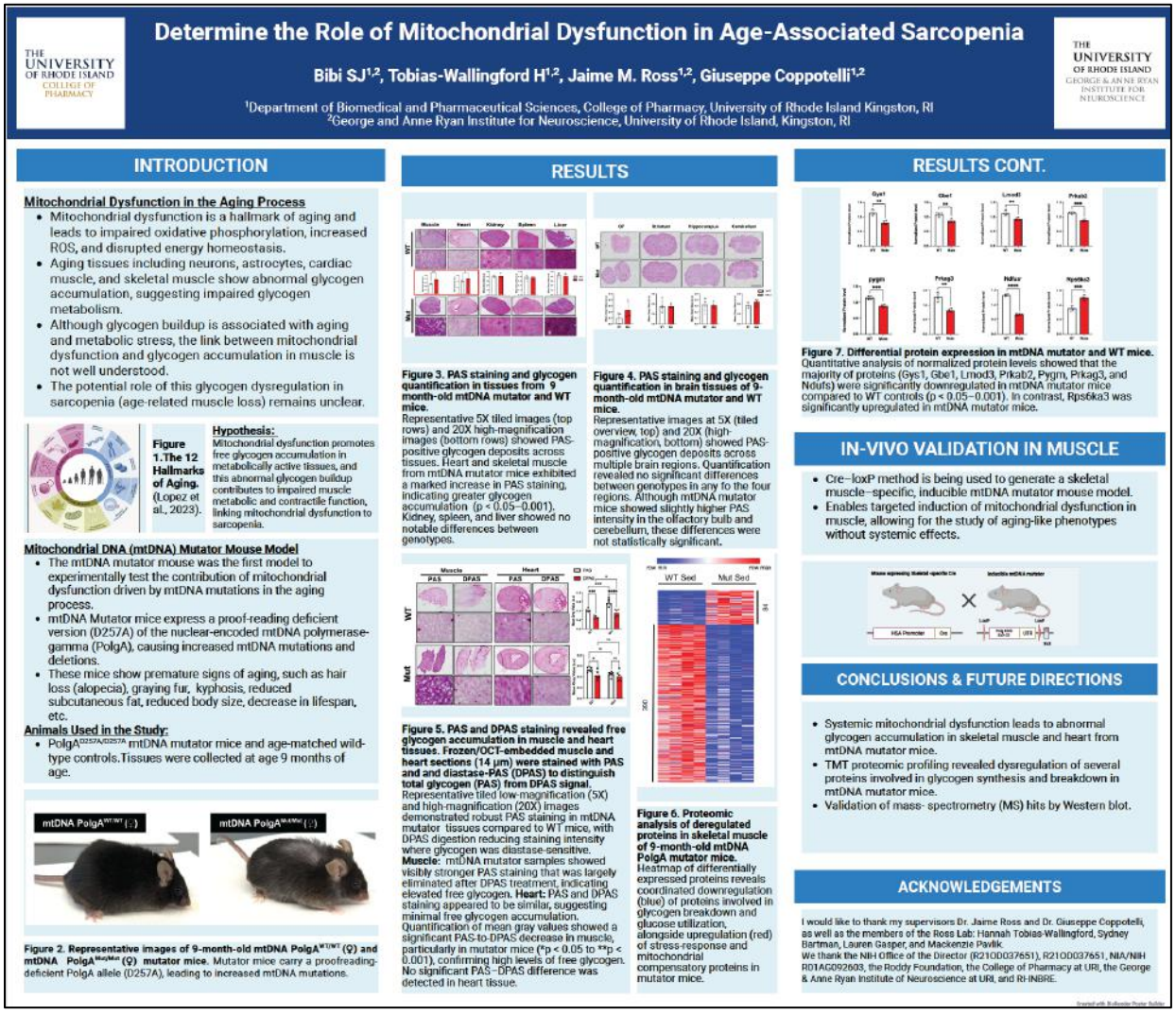
Contributions of Neutrophil Extracellular Traps to Vascular Pathologies in CAA Model rTg-DI

Dakota Hunter, Riley Sullivan, Feng Xu, Judianne Davis, William Van Nostrand, Joseph Schrader

Cerebral amyloid angiopathy (CAA) is a cerebrovascular disorder characterized by progressive deposition of amyloid-β (Aβ) peptides within cerebral blood vessel walls, affecting an estimated 60% of individuals over 85. CAA is strongly associated with microbleeds, intracranial hemorrhage, and cognitive decline, yet its neuroimmune mechanisms remain poorly understood.

Using the preclinical rTg-DI transgenic rat model, we investigated the role of neutrophils and neutrophil extracellular traps (NETs) in CAA pathology. NETs are web-like structures released during innate immune responses that promote thrombus formation and sterile inflammation. Immunohistochemical analyses revealed NET markers, such as citrullinated histone H3 (H3Cit), myeloperoxidase (MPO), and neutrophil elastase (NE), within regions of active vascular Aβ deposition, alongside robust microglial activation. This represents the first evidence of NET formation in CAA.

We hypothesize that distinct Aβ fibril species differentially modulate NETosis, driving vascular deterioration. Future work will characterize fibril-neutrophil interactions in vitro and evaluate pharmacological NETosis inhibition as a therapeutic strategy.

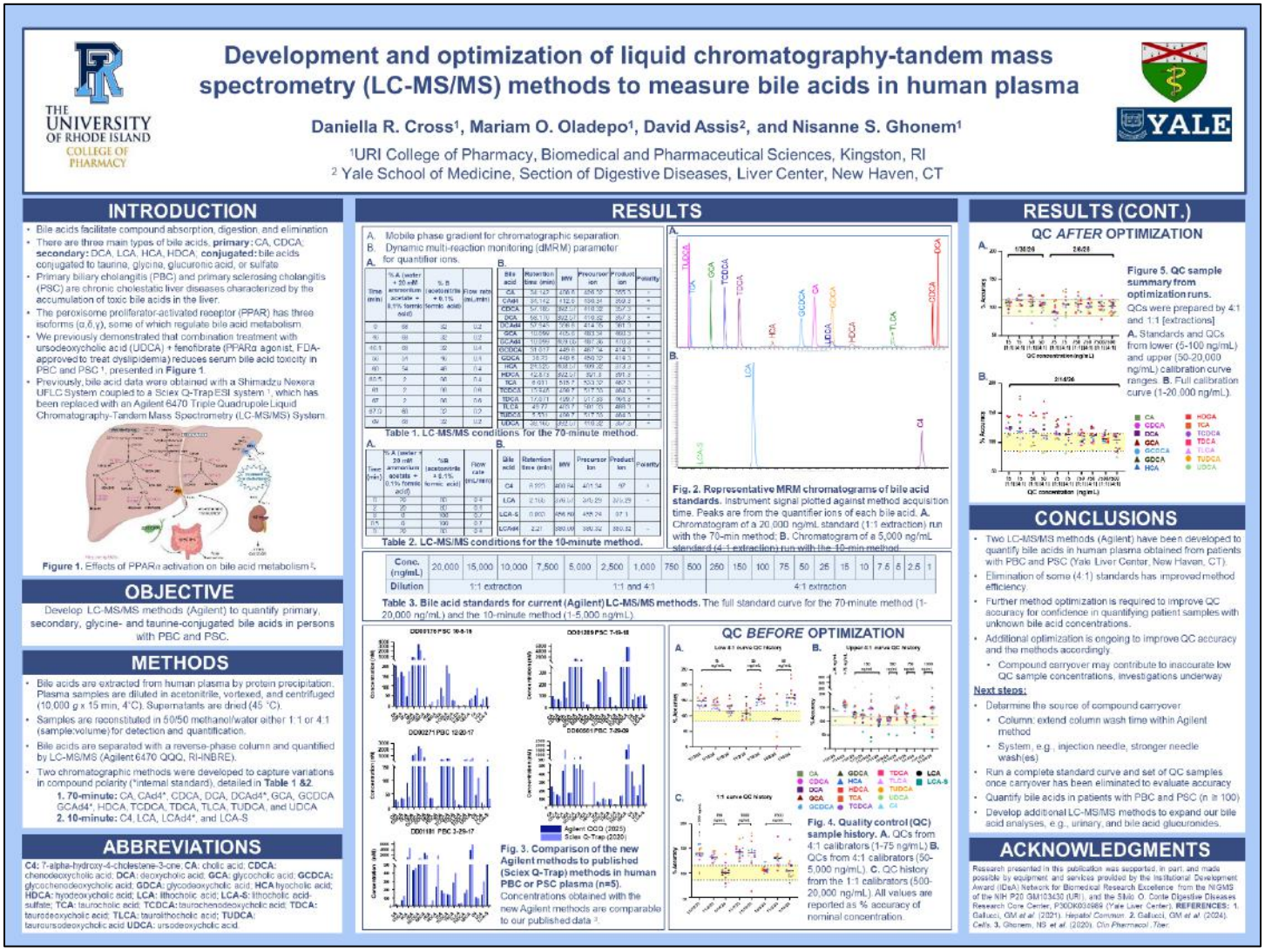


Determining the Role of Mitochondrial Dysfunction in Age-Associated Sarcopenia

Bibi SJ, Tobias-Wallingford H, Jaime M. Ross, Giuseppe Coppotelli

As global life expectancy increases, the prevalence of age-related diseases such as sarcopenia continues to rise. Although the cellular mechanism of aging is not fully understood, gerontologists have identified several major hallmarks of aging including epigenetic alteration, chronic inflammation and mitochondrial dysfunction. Among these, mitochondrial dysfunction is a key hallmark of aging, characterized by cellular and tissue damage, increased reactive oxygen species, and impaired glucose metabolism. Age-associated glycogen accumulation has been observed in various aging cell types, including neurons, astrocytes, and muscle cells. In this study, we investigated glycogen accumulation in association with mitochondrial impairment using the mtDNA mutator (PolgAD257A/D257A) mouse, a model of accelerated aging caused by systemic mitochondrial dysfunction due to increased mitochondrial DNA (mtDNA) mutations and deletions. Histological analyses with Periodic Acid–Schiff (PAS), diastase–PAS (dPAS) staining and colorimetric glycogen quantification analyses revealed that mitochondrial dysfunction promotes free glycogen deposition in skeletal muscle and to some extent cardiac tissue. These findings suggest that mitochondrial dysfunction disrupts glycogen metabolism, leading to abnormal glycogen processing and free glycogen accumulation in metabolically active tissues. We propose that this glycogen buildup may impair contractile and metabolic functions, thereby contributing to sarcopenia, the age-related loss of muscle mass and strength. Future studies will further investigate the relationship between glycogen accumulation and age-associated sarcopenia using a muscle-specific mitochondrial dysfunction mouse model, as well as determine whether interventions such as exercise can mitigate these effects by enhancing oxidative metabolism and promoting efficient glycogen utilization. Together, these findings identify disrupted glycogen metabolism as a potential biochemical hallmark linking mitochondrial dysfunction to systemic aging and muscle decline.

Keywords: Mitochondrial dysfunction, Glycogen metabolism, Sarcopenia, PAS staining, Aging

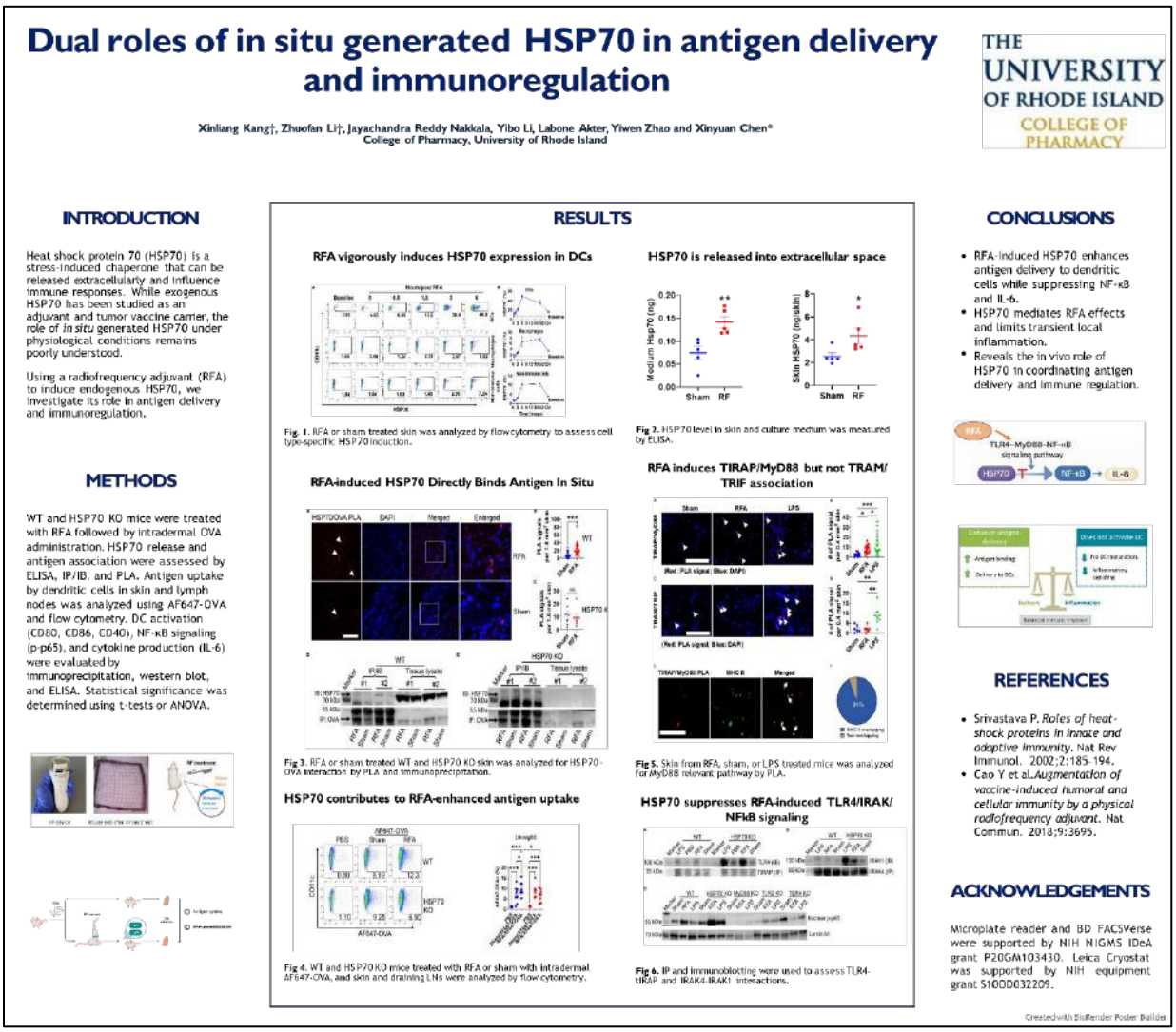


Development and optimization of liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods to measure bile acids in human plasma

Daniella R. Cross, Mariam O. Oladepo, David Assis, Nisanne S. Ghonem

The liver is a major excretory organ in the body, and bile acids, which are produced by the liver, are important endogenous regulators of compound absorption and excretion. However, bile acids are also hydrophobic molecules that become toxic at elevated concentrations. Primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) are chronic cholestatic liver diseases, characterized by an accumulation of bile acids, i.e.,

bile acid-induced liver injury. Left untreated, PBC and PSC often progress to cirrhosis and liver failure. Until recently, ursodeoxycholic acid (UDCA) was the only FDA-approved treatment for cholestasis. Recently, two peroxisome proliferator-activated receptor (PPAR) agonists received accelerated FDA approval for second-line treatment of PBC. Notably, PPAR regulates bile acid synthesis, metabolism, and detoxification pathways. Our lab has previously demonstrated that adjunct fenofibrate, a PPARα agonist, in combination with UDCA, reduces bile acid-induced liver injury in patients with PBC and PSC. New analytical methods are needed to determine the effects of adjunct fenofibrate therapy on bile acid levels and composition for patients with PBC and PSC. We recently developed two liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods to quantify 17 primary, secondary, and glycine- and taurine-conjugated bile acids. While individual bile acids may vary, the full range of quantification is from 1 – 20,000 ng/mL. Despite preliminary results that demonstrate our LC-MS/MS methods quantify bile acids in human plasma, further optimization is underway to improve efficiency and accuracy, e.g., quality control, of the methods, including elimination of analyte carryover following the injection of highly concentrated standards. Additional LC-MS/MS methods are in development to expand our research and quantify the effect of PPAR agonist therapy on bile acid metabolism and excretion in PBC and PSC.



Dual roles of in situ generated HSP70 in antigen delivery and immunoregulation

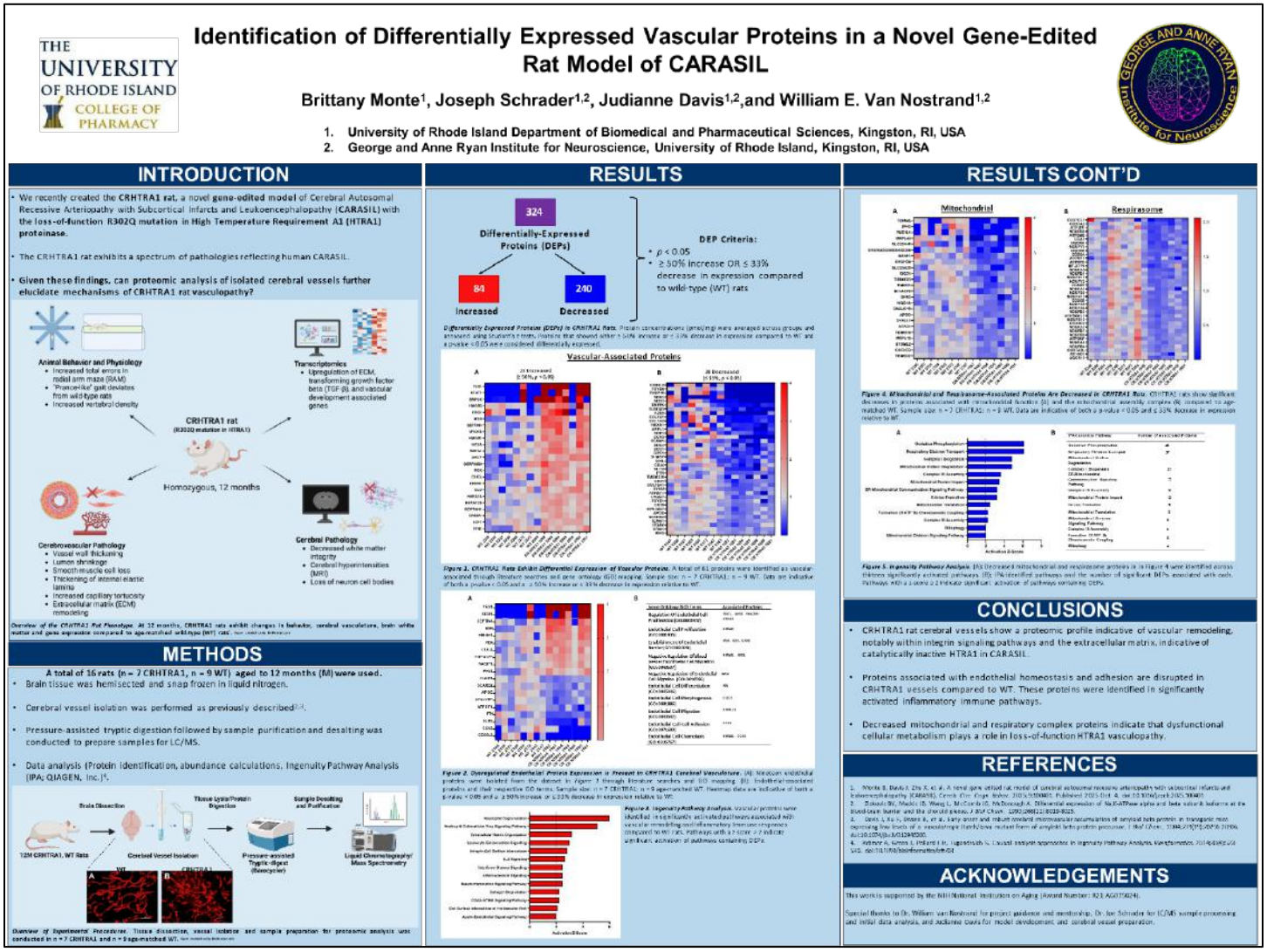
Xinliang Kang, Zhuofan Li, Jayachandra Reddy Nakkala, Yibo Li, Labone Akter, Yiwen Zhao, Xinyuan Chen

Introduction: Extracellular release of inducible HSP70 spurred interests to explore its potential interactions with innate immune systems. Both pro- and anti-inflammatory roles have been reported though the immunostimulatory roles were largely disputed due to the likely use of contaminated HSP70. The anti-inflammatory roles inspired the exploration of HSP70 to treat autoimmune diseases by suppressing pathological inflammatory responses. Besides immunomodulation, HSP70 has been explored as tumor vaccine carriers to elicit cytotoxic T lymphocyte responses due to its ability to deliver bound peptides to MHC I presentation pathway. With increasing understanding of the potential use of ex vivo prepared HSP70 in vaccination and therapy, the functions and potential applications of in situ induced HSP70 in antigen delivery and immunomodulation remain largely unexplored.

Methods: This study utilizes physical radiofrequency adjuvant (RFA) to induce HSP70 synthesis accompanied with mild inflammation followed by intradermal injection of vaccine antigens into RFA-treated skin in murine models to explore its potential roles in antigen delivery and immunomodulation.

Results: We found in situ induced HSP70 could bind intradermally injected model antigen ovalbumin and contribute to enhanced antigen uptake in skin and draining lymph nodes. HSP70 failed to induce dendritic cell maturation and rather suppressed RFA-induced TLR4/IRAK/NFkB activation and IL-6 expression.

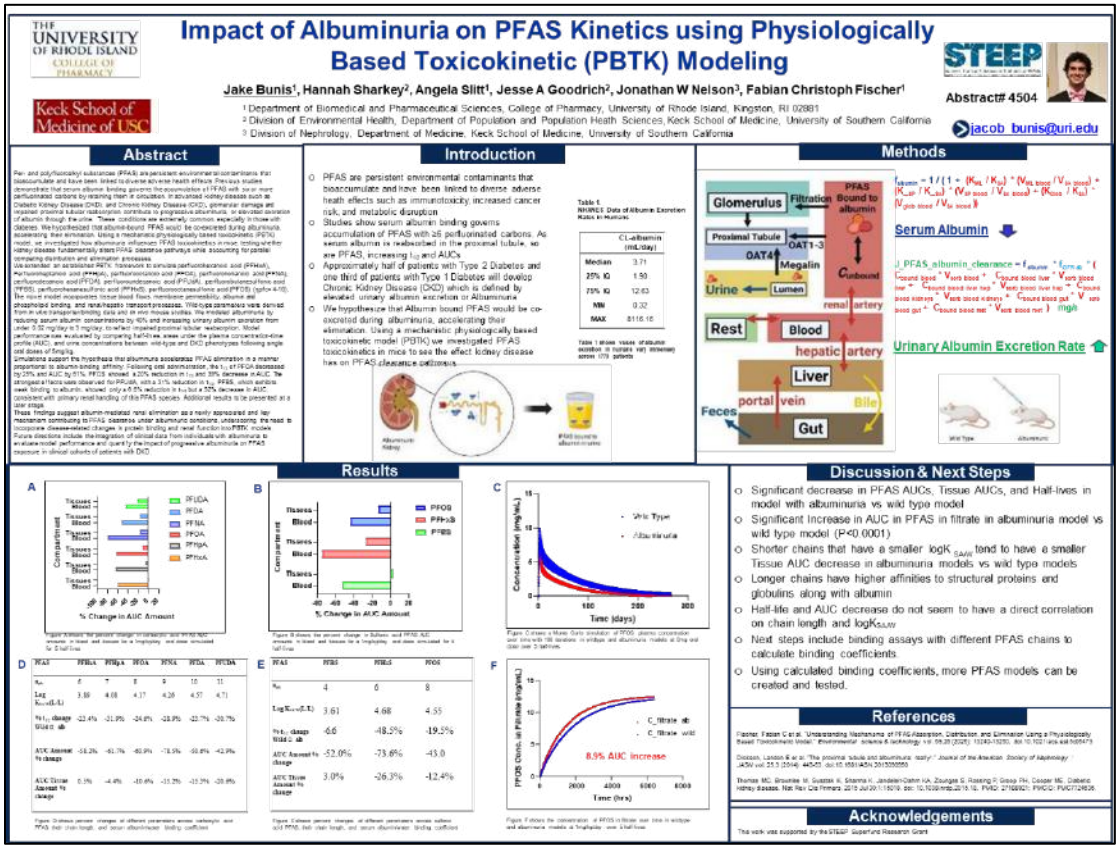
Discussion: These results indicate dual roles of in situ induced HSP70 in antigen delivery and immunoregulation at physiological conditions. These dual functions highlight opportunities to exploit endogenous HSP70 for both vaccine adjuvantation and immunomodulation.



Identification of Differentially Expressed Vascular Proteins in a Novel Gene-Edited Rat Model of CARASIL

Brittany Monte, Joseph Schrader, Judianne Davis, William E. Van Nostrand

Recently, we created the CRHTRA1 rat, a novel gene-edited model of Cerebral Autosomal Recessive Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CARASIL) harboring the homozygous R302Q mutation in the High Temperature Requirement A1 (HTRA1) serine proteinase. In 12 months (M) old CRHTRA1 animals, we identified several behavioral, cerebrovascular, brain white matter and cerebral transcriptomic alterations that reflect human CARASIL pathology. To further examine underlying mechanisms of the cerebral vasculopathy observed in CRHTRA1 rats, proteomic analysis was performed on isolated cerebral vessels. Analysis of vessel-enriched samples was conducted in 12M CRHTRA1 rats (n = 7) and age-matched wild-type (WT) rats (n = 9). We identified a total of 324 differentially expressed proteins (DEPs), 84 of which were significantly increased and 240 significantly decreased in CRHTRA1 rats. Further investigation of these DEPs resulted in the identification of multiple functional categories, including vascular associated, mitochondrial function, and respirasome-associated proteins. Using Ingenuity Pathway Analysis (IPA), we identified activated pathways associated with extracellular matrix (ECM) remodeling, atherosclerosis signaling, collagen degradation and integrin cell surface interactions. Proteins associated with the maintenance of the vascular endothelium and adherens junctions were identified in pathways of neuroinflammation and immune system activation. Respirasome and mitochondrial proteins were identified in pathways of respiratory complex formation, oxidative phosphorylation, and mitochondrial dysfunction. These findings provide new insight into how the R302Q HTRA1 mutation affects cerebral vessels contributing to the pathology of CARASIL.



Impact of Albuminuria on PFAS Kinetics using Physiologically Based Toxicokinetic (PBTK) Modeling

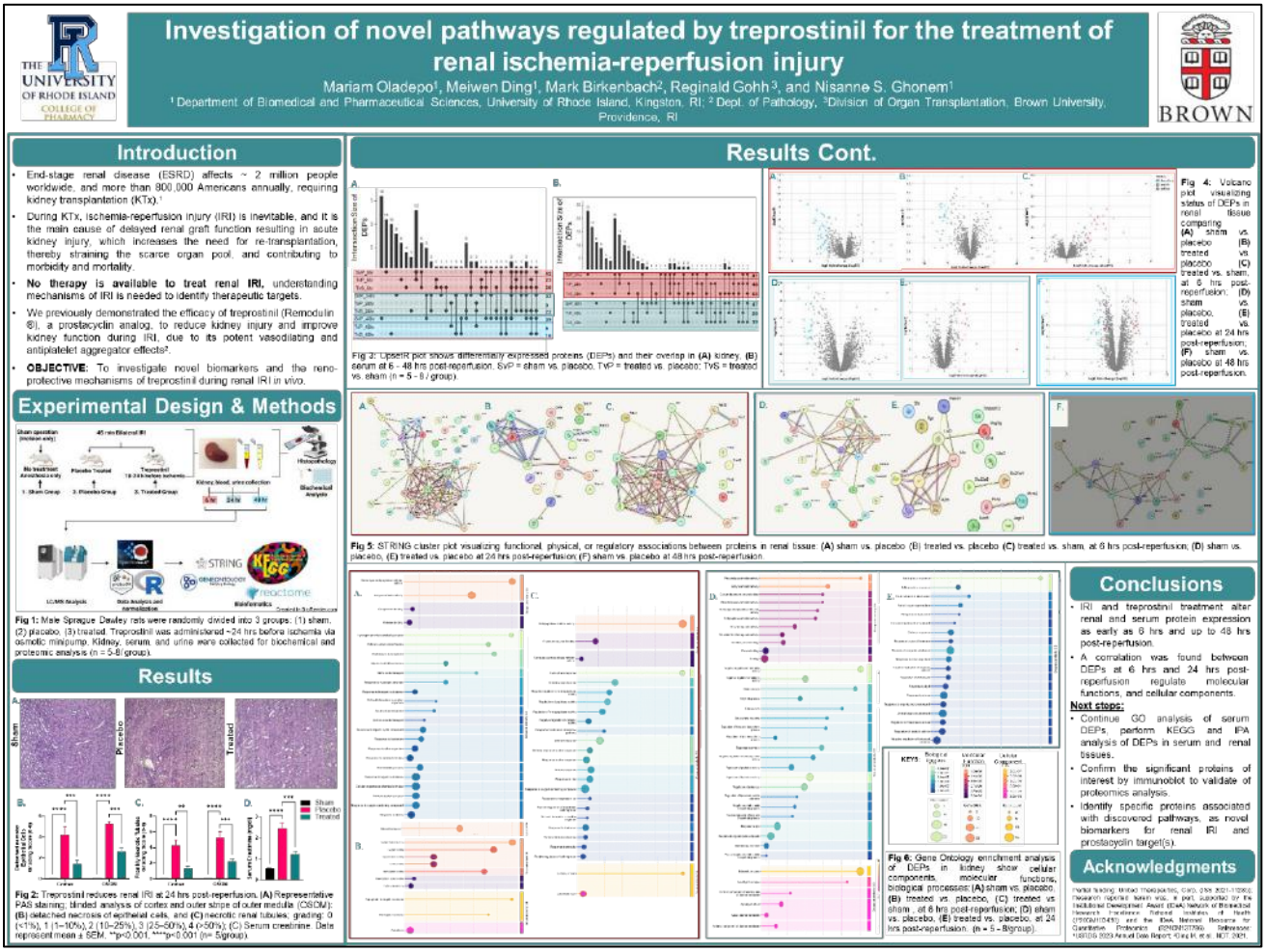
Jake Bunis, Hannah Sharkey, Angela Slitt, Jesse A. Goodrich, Jonathan W Nelson, Fabian C. Fischer

Per- and polyfluoroalkyl substances (PFAS) are persistent environmental contaminants that bioaccumulate and have been linked to diverse adverse health effects. Previous studies demonstrate that serum albumin binding governs the accumulation of PFAS with six or more perfluorinated carbons by retaining them in circulation. In advanced kidney disease such as Diabetic Kidney Disease (DKD), and Chronic Kidney Disease (CKD), glomerular damage and impaired proximal tubular reabsorption contribute to progressive albuminuria, or elevated excretion of albumin through the urine. These conditions are extremely common, especially in those with diabetes. We hypothesized that albumin-bound PFAS would be co-excreted during albuminuria, accelerating their elimination. Using a mechanistic physiologically based toxicokinetic (PBTK) model, we investigated how albuminuria influences PFAS toxicokinetics in mice, testing whether kidney disease fundamentally alters PFAS clearance pathways while accounting for parallel competing distribution and elimination processes.

We extended an established PBTK framework to simulate perfluorohexanoic acid (PFHxA), Perfluoroheptanoic acid (PFHpA), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUdA), perfluorobutanesulfonic acid (PFBS), perfluorohexanesulfonic acid (PFHxS), perfluorooctanesulfonic acid (PFOS) (ηpfc= 4-10). The novel model incorporates tissue blood flows, membrane permeability, albumin and phospholipid binding, and renal/hepatic transport processes. Wild-type parameters were derived from in vitro transporter/binding data and in vivo mouse studies. We modeled albuminuria by reducing serum albumin concentrations by 40% and increasing urinary albumin excretion from under 0.02 mg/day to 3 mg/day, to reflect impaired proximal tubular reabsorption. Model performance was evaluated by comparing half-lives, areas under the plasma concentration-time profile (AUC), and urine concentrations between wild-type and DKD phenotypes following single oral doses of 5mg/kg.

Results: Simulations support the hypothesis that albuminuria accelerates PFAS elimination in a manner proportional to albumin-binding affinity. Following oral administration, the t1/2 of PFOA decreased by 25% and AUC by 61%. PFOS showed a 20% reduction in t1/2 and 39% decrease in AUC. The strongest effects were observed for PFUdA, with a 31% reduction in t1/2. PFBS, which exhibits weak binding to albumin, showed only a 6.6% reduction in t1/2 but a 52% decrease in AUC, consistent with primary renal handling of this PFAS species.

These findings suggest albumin-mediated renal elimination as a newly appreciated and key mechanism contributing to PFAS clearance under albuminuric conditions, underscoring the need to incorporate disease-related changes in protein binding and renal function into PBTK models. Future directions include the integration of clinical data from individuals with albuminuria to evaluate model performance and quantify the impact of progressive albuminuria on PFAS exposure in clinical cohorts of patients with DKD.



Investigation of novel pathways regulated by treprostinil for the treatment of renal ischemia-reperfusion injury

Mariam Oladepo, Meiwen Ding, Mark Birkenbach, Reginald Gohh, Nisanne Ghonem

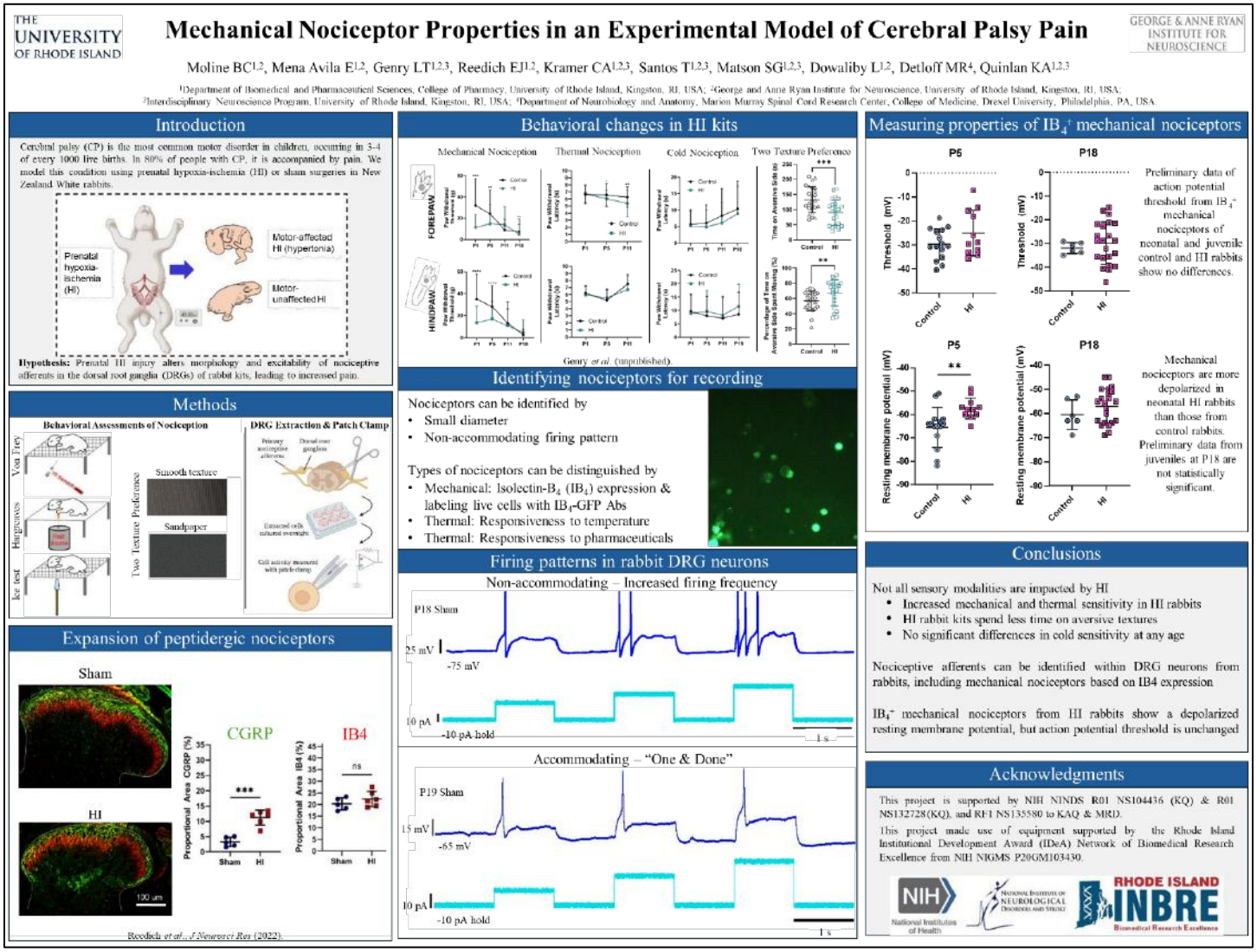
Renal ischemia-reperfusion injury (IRI) is a significant contributor to acute kidney injury and delayed graft function post-kidney transplantation, with no treatment available. We previously demonstrated the efficacy of treprostinil (Remodulin®), an FDA-approved prostacyclin (PGI2) analog, in reducing renal IRI in vivo. This study investigates novel biomarkers and reno-protective mechanisms of treprostinil during renal IRI in vivo.

Male Sprague Dawley rats were randomly divided into sham, placebo, treated groups, and subjected to bilateral renal IRI (45 mins) followed by reperfusion (1-48 hrs). Treprostinil was administered subcutaneously and serum and kidney tissue were collected for biochemical and proteomic analyses.

Treprostinil reduced peak serum creatinine levels by 52% ($P<0.05$), and histology data showed necrotic tubules of kidney tissues by ~50% vs. placebo ($P<0.01$) at 24 hrs post-reperfusion.

Proteomic profiling in renal tissues detected 2931 proteins, with a total of 91, 58 and 60 differentially expressed proteins (DEPs) at 6, 24, and 48 hrs post-reperfusion, respectively. Similarly, 806 proteins were detected in serum, with a total of 197 and 106 DEPs at 24 and 48 hrs, respectively (>1-fold at $p<0.05$) at 24 hrs post-reperfusion. A correlation was found using STRING and GO analysis between DEPs at 6 hrs and 24 hrs post-reperfusion, including proteins that regulate molecular functions, e.g., oxygen, heme, hemoglobin, protease and complement binding; biological processes, e.g., acute phase response, response to external stimulus and stress, as well as proteins involving cellular components of the extracellular space, cytoplasm and some apical parts of the cell.

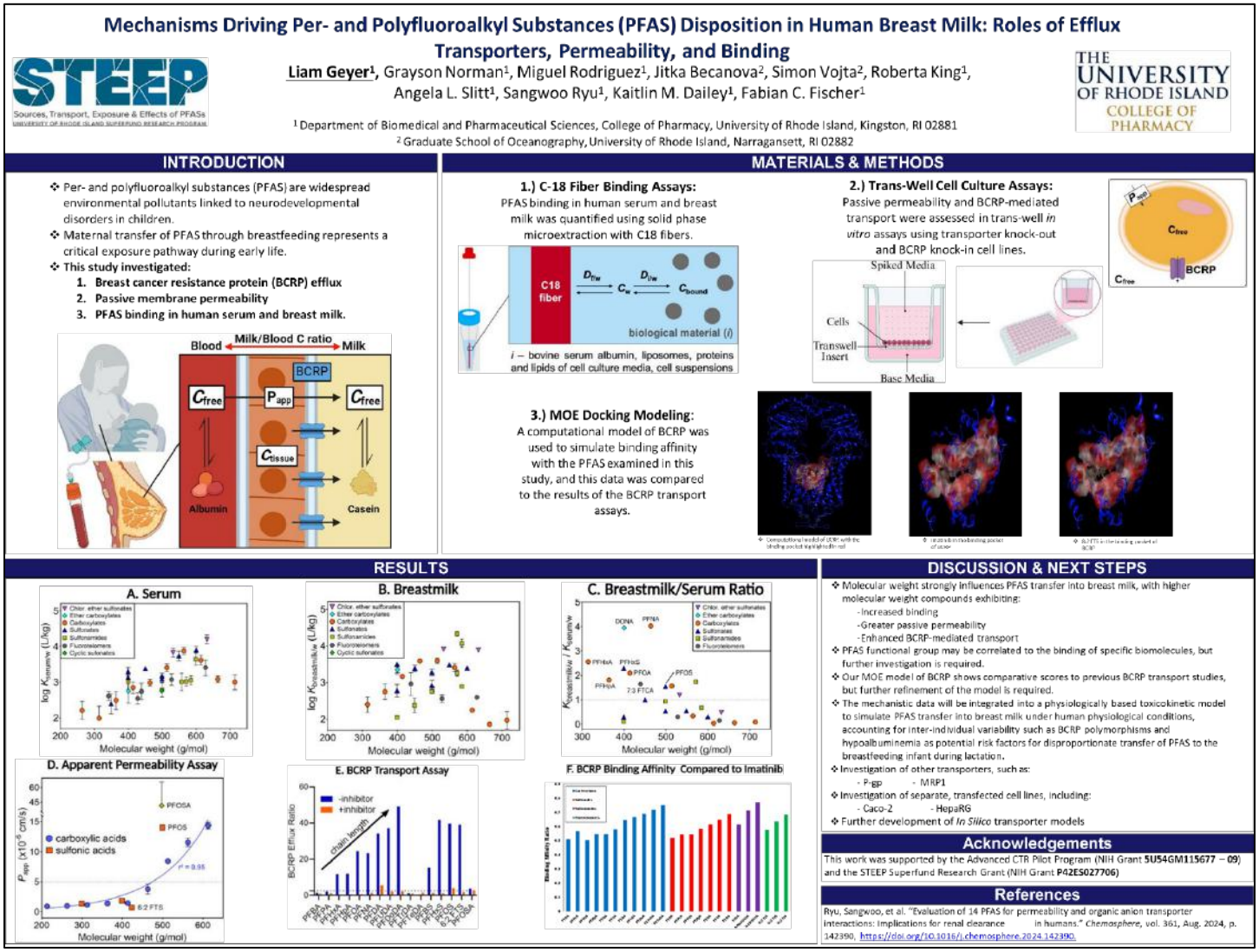
In conclusion, IRI and treprostinil therapy alter renal and serum protein expression as early as 6 hr and up to 48 hr post-reperfusion. These findings identify specific proteins regulated during renal IRI which provide mechanistic insight to identify novel biomarkers involved in IRI and therapeutic targets of treprostinil.



Mechanical Nociceptor Properties in an Experimental Model of Cerebral Palsy Pain

Brendan Moline, Elvia Mena Avila, Lauren T. Genry, Emily Reedich, Cassandra A. Kramer, Thais Santos, Sarah G. Matson, Laura Dowaliby, Mary R. Detloff, Katharina A. Quinlan

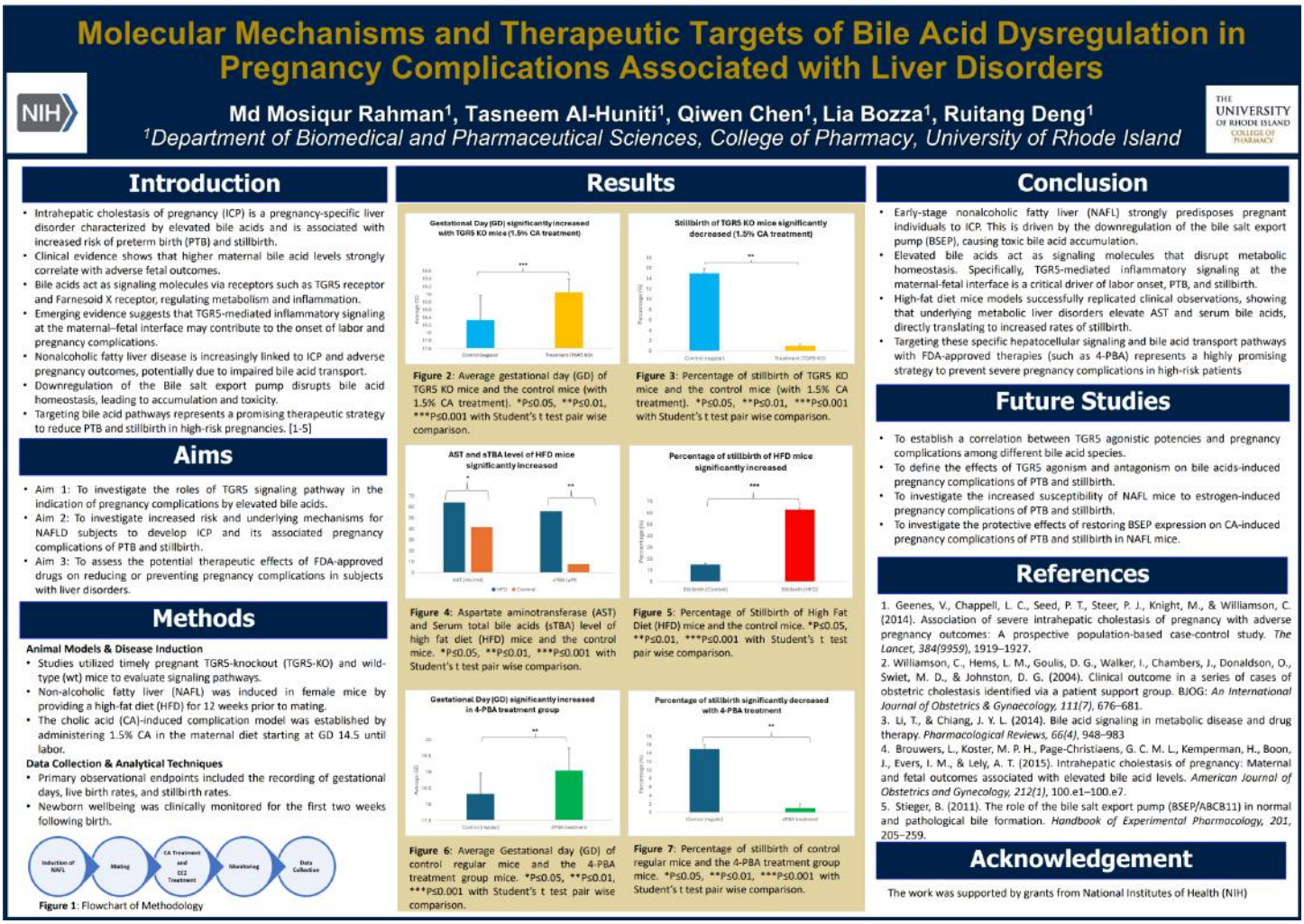
Cerebral palsy (CP) is a movement disorder typified by abnormalities in muscle tone, spasticity, and pain. Studies estimate that ~75% of people with CP experience pain, but the causes are understudied. Thus, we use an animal model of CP-related pain to evaluate changes in nociceptor excitability. In utero hypoxia-ischemia (HI) injury at 70-90% gestation in New Zealand White rabbits produces cell death in the brain and spinal cord, muscle stiffness like humans with CP, and behavior consistent with mechanical allodynia. To test if nociceptors (sensory neurons which detect and respond to noxious stimuli) in general, and more specifically the nociceptors responding to noxious mechanical stimuli are impacted by perinatal injuries, we measure neuron excitability in cells from dorsal root ganglia (DRGs) from rabbits exposed to prenatal HI, sham surgical procedure, or naïve controls. At postnatal day (P)1, rabbits undergo assessments of mechanical or thermal pain. At P5 & 18, DRGs are isolated, cultured, stained with fluorescent isolectin-B4 (IB4-GFP) a marker of mechanical nociceptors, and cellular electrical activity is recorded using whole-cell patch clamp. Preliminary findings indicate that rabbit DRG neurons exhibit firing patterns consistent with nociceptors and light touch sensory afferents, the former displaying repeated firing (non-accommodating) and the latter displaying singular firing (rapidly accommodating) when stimulated. Restricting our analysis to only mechanical nociceptors that expressed IB4, we found that mechanoreceptors from HI rabbits had a depolarized resting membrane potential at P5, but not P18 based on unpaired t-tests. This shift in membrane potential would allow these nociceptors to fire more readily than the equivalent neurons from control animals with the same stimuli. With a greater understanding of DRG neuron firing properties and excitability in HI rabbits, we can elucidate how perinatal injuries could impact pain in CP, allowing for development of safer and more efficacious treatments than currently available.



Mechanisms Driving Per- and Polyfluoroalkyl Substances (PFAS) Disposition in Human Breast Milk: Roles of Efflux Transporters, Permeability, and Binding

Liam Geyer, Grayson Norman, Miguel Rodriguez, Jitka Becanova, Simon Vojta, Roberta King, Angela L. Slitt, Sangwoo Ryu, Kaitlin M. Dailey, Fabian C. Fischer

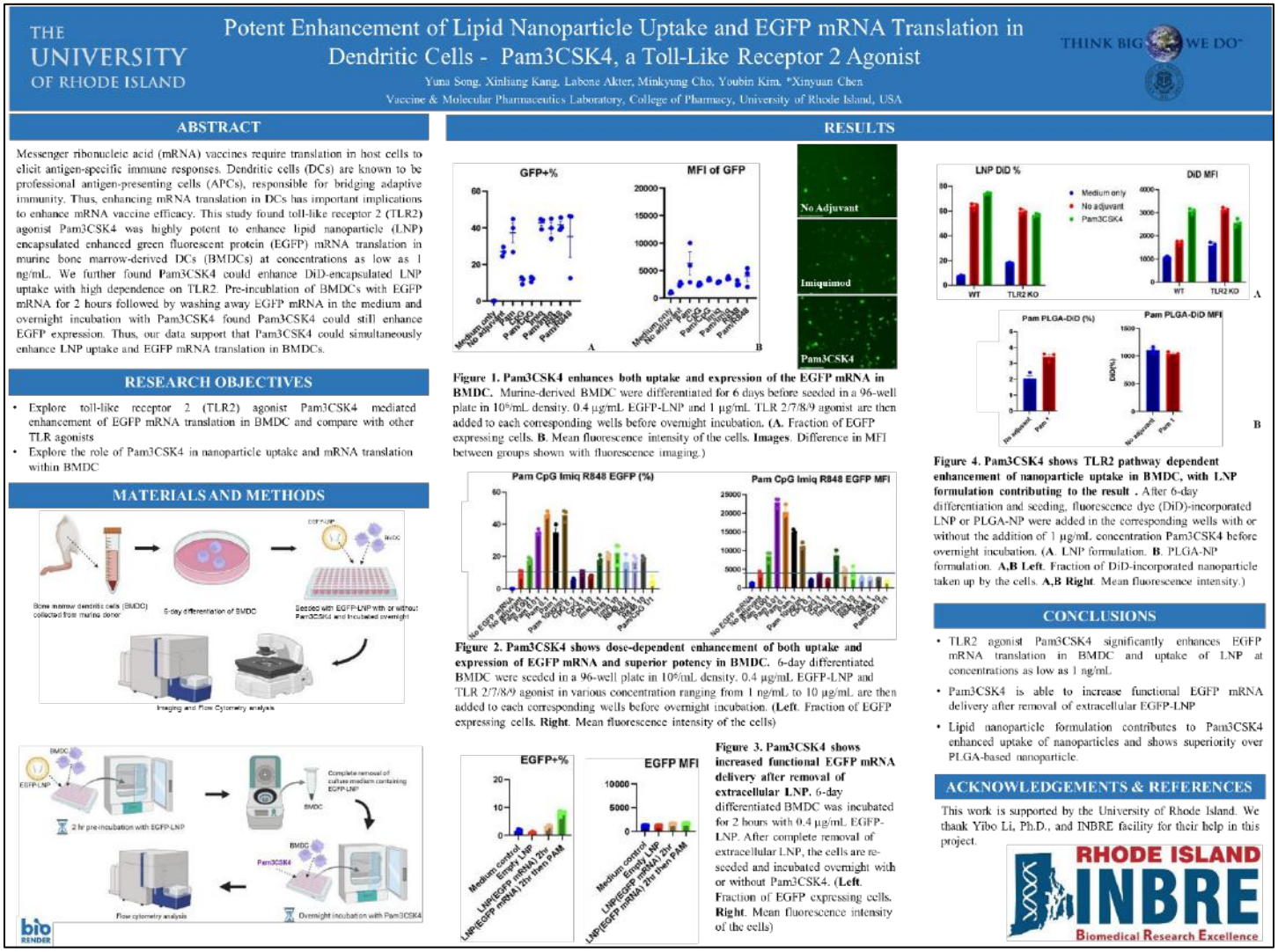
Per- and polyfluoroalkyl substances (PFAS) are widespread environmental pollutants linked to several disorders in children. Maternal transfer of PFAS through breastfeeding represents a critical exposure pathway during early life. This study investigated the toxicokinetic mechanisms driving PFAS transfer into breast milk by evaluating interactions with the efflux transporter Breast Cancer Resistance Protein (BCRP), passive membrane permeability, and PFAS binding in human serum and breast milk. PFAS binding in human serum and breast milk was quantified using solid-phase microextraction with C18 fibers. Passive permeability and BCRP-mediated transport were assessed in trans-well in vitro assays using transporter knock-out and BCRP knock-in cell lines and the results were compared to molecular docking simulations using the Molecular Operating Environment (MOE) software. PFAS binding in breast milk increased linearly with molecular weight for sulfonic acid and sulfonamide groups. In contrast, carboxyl and fluorotelomer PFAS followed this trend only up to 500 g/mol, after which binding declined. BCRP-mediated transport increased with molecular weight, with efflux ratios ranging from 10- to 50-fold higher in BCRP-expressing cells compared to inhibited controls, agreeing with molecular docking simulations. Similarly, passive permeability increased with molecular weight, with the highest permeability observed for PFAS above 500 g/mol. Our preliminary results show that molecular weight strongly influences PFAS transfer into breast milk, with higher molecular weight compounds exhibiting increased binding, greater passive permeability, and enhanced BCRP-mediated transport. The mechanistic data will be integrated into a physiologically based toxicokinetic model to simulate PFAS transfer into breast milk under human physiological conditions, accounting for inter-individual variability such as BCRP polymorphisms and hypoalbuminemia as potential risk factors for disproportionate transfer of PFAS to the breastfeeding infant during lactation.



Molecular Mechanisms and Therapeutic Targets of Bile Acid Dysregulation in Pregnancy Complications Associated with Liver Disorders

Md. Mosiqur Rahman, Tasneem Al-Huniti, Qiwen Chen, Lia Bozza, Ruitang Deng

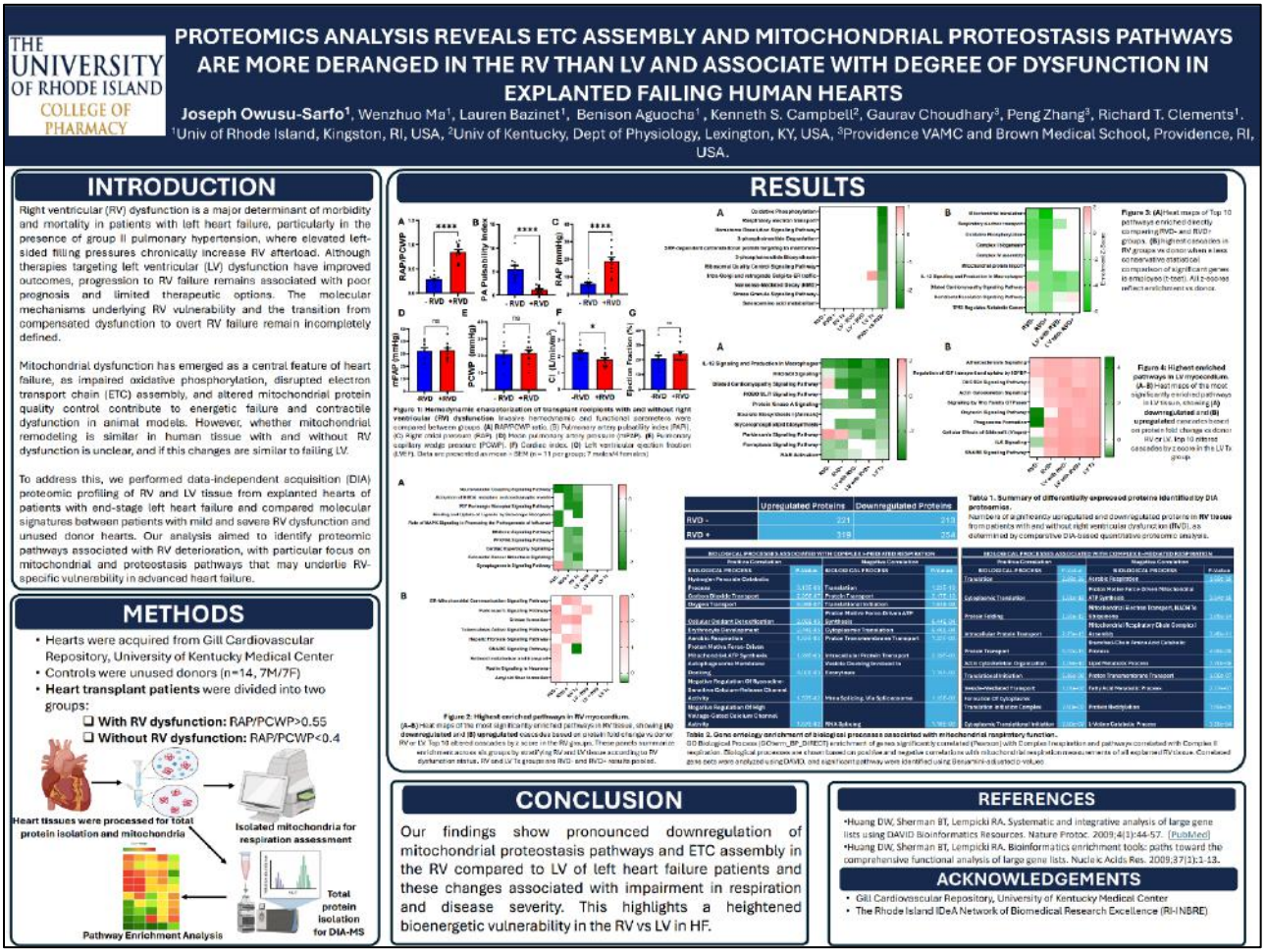
Nonalcoholic fatty liver disease (NAFLD) is an increasingly prevalent metabolic disorder that has recently been implicated in adverse pregnancy outcomes. Intrahepatic cholestasis of pregnancy (ICP) is a pregnancy-specific liver disorder characterized by impaired bile acid homeostasis and is strongly associated with preterm birth (PTB) and stillbirth. In our preliminary analysis of a cohort of 36,755 pregnant women, individuals with NAFLD demonstrated a markedly higher prevalence of ICP, with 14.1% of NAFLD patients developing ICP compared to the general population incidence of 1.37%. Moreover, women diagnosed with both NAFLD and ICP exhibited significantly elevated risks of PTB and stillbirth. Both NAFLD and ICP were associated with dysregulated bile acid metabolism, as indicated by increased serum total bile acid (sTBA) levels and reduced expression of the bile salt export pump (BSEP), a critical transporter responsible for bile acid excretion. Based on these observations, we hypothesize that early-stage NAFLD, specifically nonalcoholic fatty liver (NAFL), predisposes pregnant women to ICP and its associated complications through impaired BSEP-mediated bile acid clearance and subsequent bile acid accumulation. This study aims to elucidate the molecular mechanisms linking NAFL to ICP, with a particular focus on bile acid transport dysregulation and hepatocellular signaling pathways. Understanding these mechanisms may reveal novel therapeutic targets and inform preventive strategies for managing pregnancy complications in women with underlying liver disorders.



Potent Enhancement of Lipid Nanoparticle Uptake and EGFP mRNA Translation in Dendritic Cells - Pam3CSK4, a Toll-Like Receptor 2 Agonist

Yuna Song, Xinliang Kang, Labone Akter, Minkyung Cho, Youbin Kim, Xinyuan Chen

Messenger ribonucleic acid (mRNA) vaccines require translation in host cells to elicit antigen-specific immune responses. Dendritic cells (DCs) are known to be professional antigen-presenting cells (APCs), responsible for bridging adaptive immunity. Thus, enhancing mRNA translation in DCs has important implications to enhance mRNA vaccine efficacy. This study found toll-like receptor 2 (TLR2) agonist Pam3CSK4 was highly potent to enhance lipid nanoparticle (LNP) encapsulated enhanced green fluorescent protein (EGFP) mRNA translation in murine bone marrow-derived DCs (BMDCs) at concentrations as low as 1 ng/mL. We further found Pam3CSK4 could enhance DiD-encapsulated LNP uptake with high dependence on TLR2. Pre-incubation of BMDCs with EGFP mRNA for 2 hours followed by washing away EGFP mRNA in the medium and overnight incubation with Pam3CSK4 found Pam3CSK4 could still enhance EGFP expression. Thus, our data support that Pam3CSK4 could simultaneously enhance LNP uptake and EGFP mRNA translation in BMDCs.



Proteomics analysis reveals etc assembly and mitochondrial proteostasis pathways are more deranged in the RV than LV and associate with degree of dysfunction in explanted failing human hearts

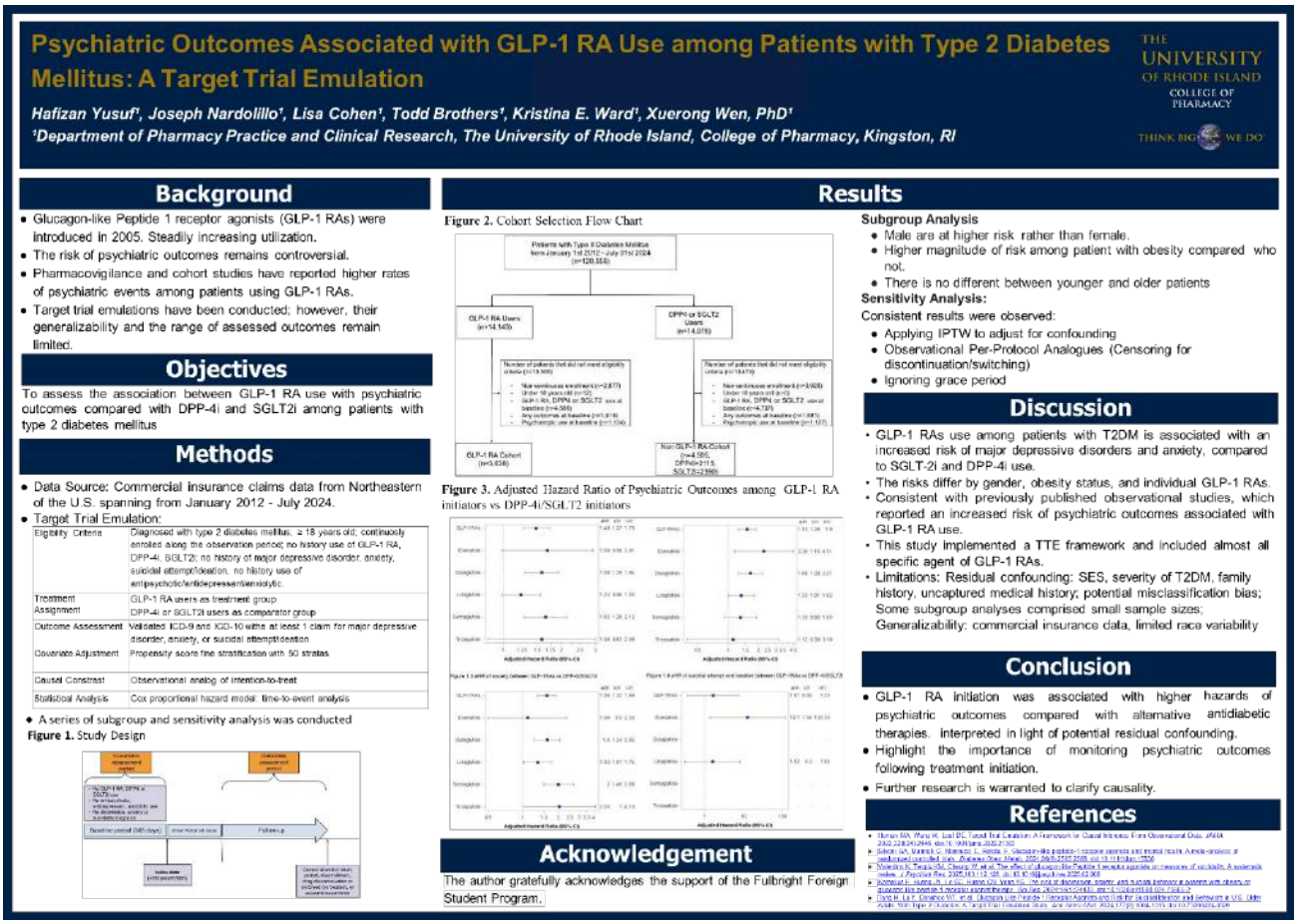
Joseph Owusu-Sarfo, Wenzhuo Ma, Lauren Bazinet, Benison Aguocha, Kenneth S. Campbell, Gaurav Choudhary, Peng Zhang, Richard T. Clements

RV dysfunction associated with group II pulmonary hypertension significantly increases mortality in left heart failure. However, signaling changes associated with progression of RV dysfunction remains poorly understood. We performed a DIA proteomic analysis of explanted left-heart failure patient RV and LV tissue and compared patients with mild and severe RV dysfunction to unused donor hearts.

Explanted transplant hearts (n=22) were obtained at transplant and unused donor hearts (controls) (n=16, 7M/7F) were provided by the Gill Cardiovascular Biorepository, University of Kentucky. All transplant patients exhibited left heart failure and pulmonary hypertension. Right atrial pressure to pulmonary wedge pressure ratio (RAP/PCWP) from right heart catheterization defined RV mild (RAP/PCWP<0.4, n=11, 7M/4F) and severe dysfunction (RAP/PCWP>0.55, n=11, 7M/4F). Total protein was isolated for DIA-MS analysis and mitochondria for isolated frozen mitochondrial respiration assessment.

DIA-MS analysis reliably measured ~4000 proteins/group. Mild RV dysfunction showed 221 up- and 213 downregulated proteins versus donors; severe dysfunction had 319 up- and 254 downregulated proteins (B-H adj P <0.05). LV changes were less pronounced. Enriched pathways downregulated in RV included mitochondrial translation, respiratory electron transport, oxidative phosphorylation, complex I biogenesis, and complex IV assembly, with greater enrichment in severe dysfunction. LV tissue showed minimal changes in these cascades but increased inflammatory signaling. 302 RV proteins correlated with CI-dependent and 532 with CII-dependent respiration, enriched for oxidative phosphorylation, RV cardiomyopathy, and mitochondrial disease signatures.

Our findings show significant downregulation of mitochondrial proteostasis pathways and ETC assembly in the RV compared to LV of left heart failure patients and these changes associated with impairment in respiration and disease severity. This highlights a heightened bioenergetic vulnerability in the RV vs LV in HF.



Psychiatric Outcomes Associated with GLP-1 RA Use among Patients with Type 2 Diabetes Mellitus: A Target Trial Emulation

Hafizan Yusuf, Joseph Nardolillo, Lisa Cohen, Todd Brothers, Kristina E. Ward, Xuerong Wen

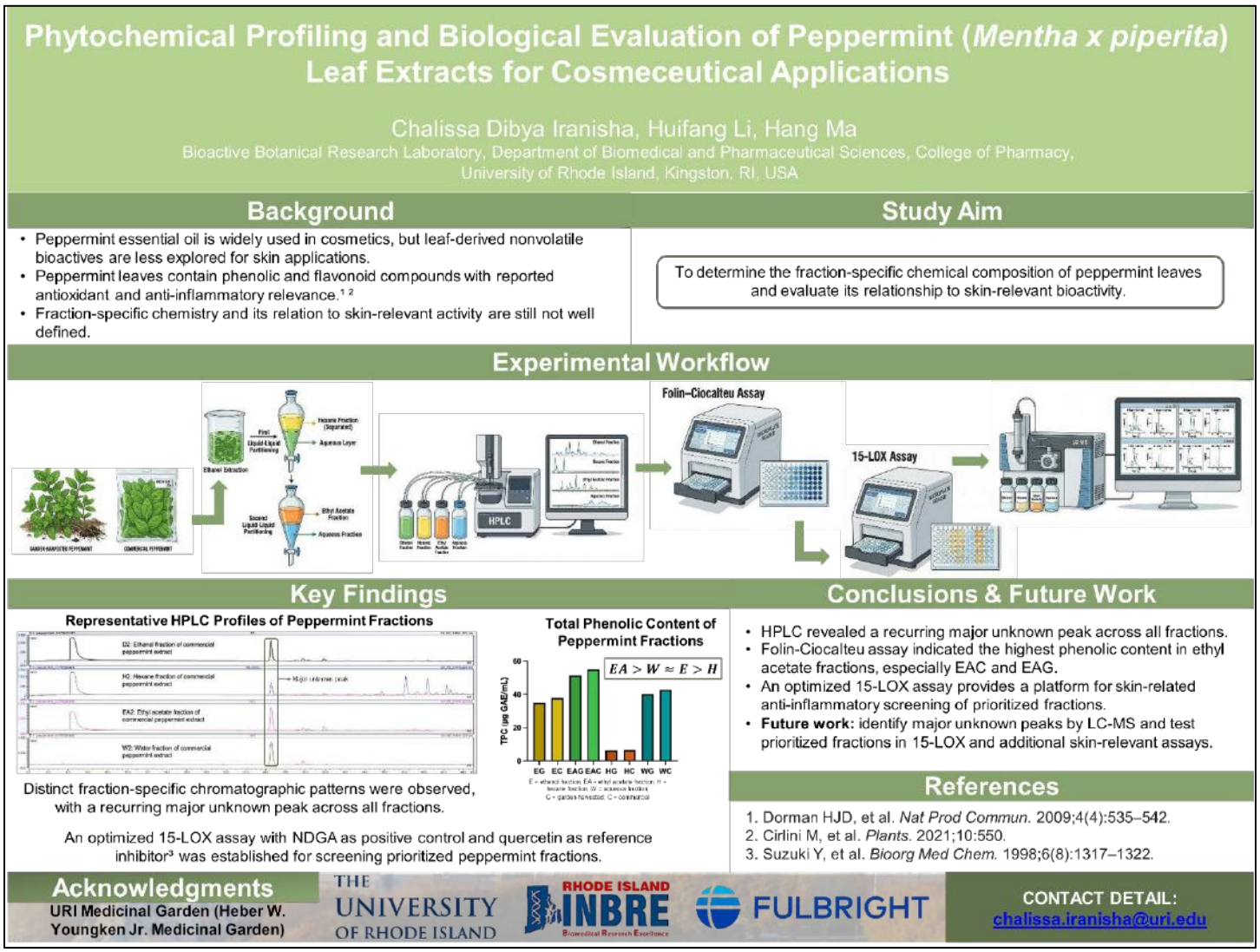
Background: The utilization of Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) has dramatically increased in the United States (U.S.) recently. However, the association between GLP-1 RAs use and psychiatric disorders, such as depression, anxiety, and suicidality, remains inconsistent.

Objective: To evaluate the association between GLP-1 RA and psychiatric outcomes compared with dipeptidyl peptidase-4 inhibitors (DPP-4i) or sodium–glucose cotransporter-2 inhibitors (SGLT2i) among patients with type 2 diabetes mellitus (T2DM) by implementing a target trial emulation framework.

Methods: Target trial emulations were conducted using a U.S. administrative claims database. The primary outcome was a composite of major depressive disorder, anxiety disorder, and suicide attempt or ideation. Propensity score fine stratification was applied to balance baseline covariates. Cox proportional hazards models with robust sandwich variance estimators were used to estimate adjusted hazard ratios (HRs) and 95% confidence intervals (CIs). Sensitivity and subgroup analyses were conducted to evaluate the robustness of the results.

Results: A total of 8,143 patients were included, of whom 3,638 were treated with GLP-1 RAs, 2,115 with DPP-4i, and 2,390 with SGLT2i. GLP-1 RAs initiation compared with DPP-4i or SGLT2i was associated with a higher risk of any psychiatric event (HR: 1.48; 95% CI 1.27-1.73), as well as major depressive disorder (HR:1.55; 95% CI 1.26-1.90) and anxiety (HR:1.58; 95% CI 1.32-1.89). In agent-specific analyses, dulaglutide and liraglutide were associated with elevated hazards of major depressive disorder and anxiety; exenatide with major depressive disorder and suicide attempt or ideation; and semaglutide with anxiety.

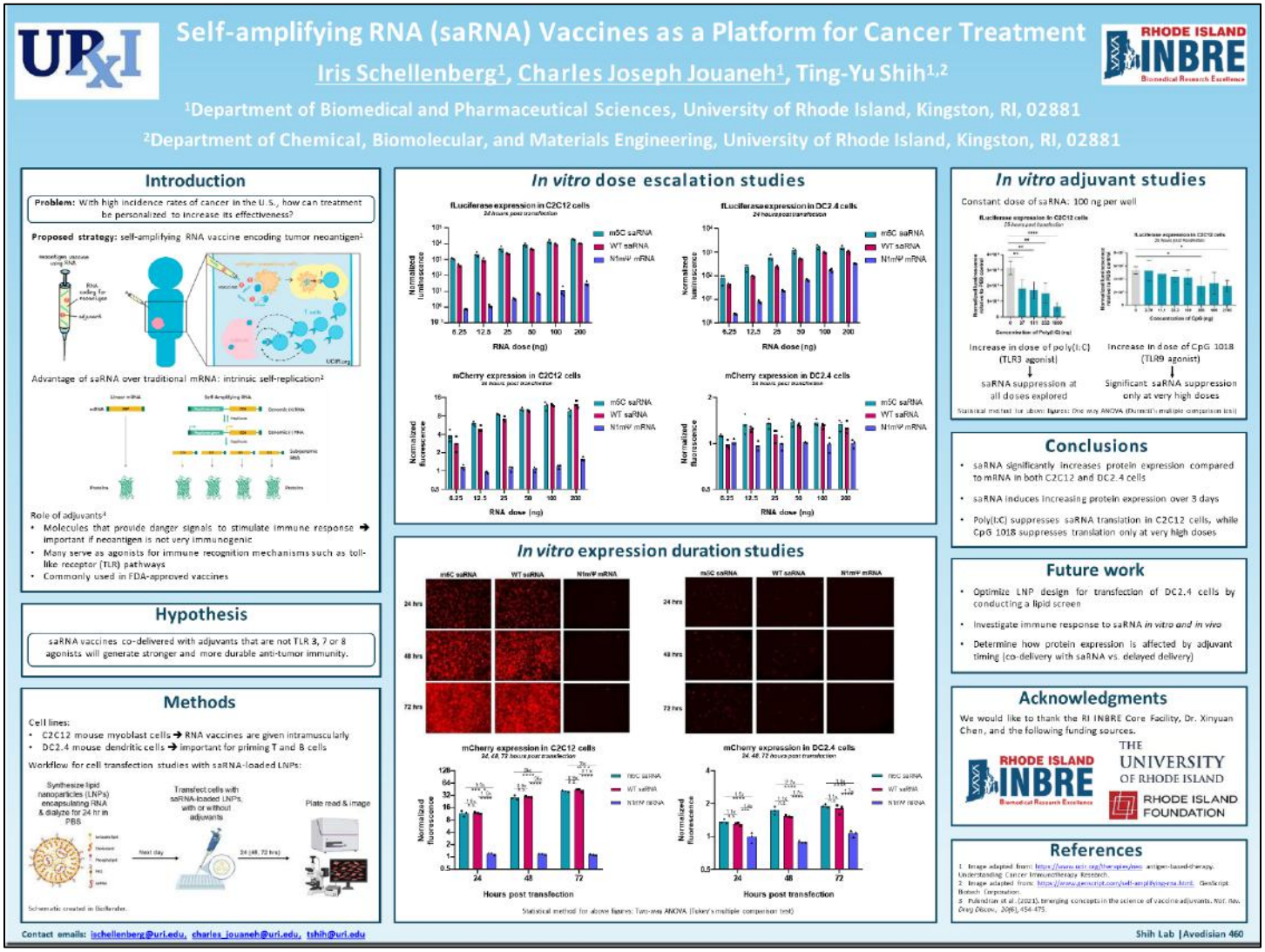
Conclusion: GLP-1 RA initiation was associated with higher hazards of psychiatric disorders compared with alternative antidiabetic therapies. These findings highlight the importance of monitoring psychiatric outcomes following treatment initiation, although the results should be interpreted in light of potential residual confounding. Further research is warranted to clarify causality and identify patients at greatest risk.



Phytochemical Profiling and Biological Evaluation of Peppermint (Mentha x piperita) Leaf Extracts for Cosmeceutical Applications

Chalissa Dibya Iranisha, Huifang Li, Hang Ma

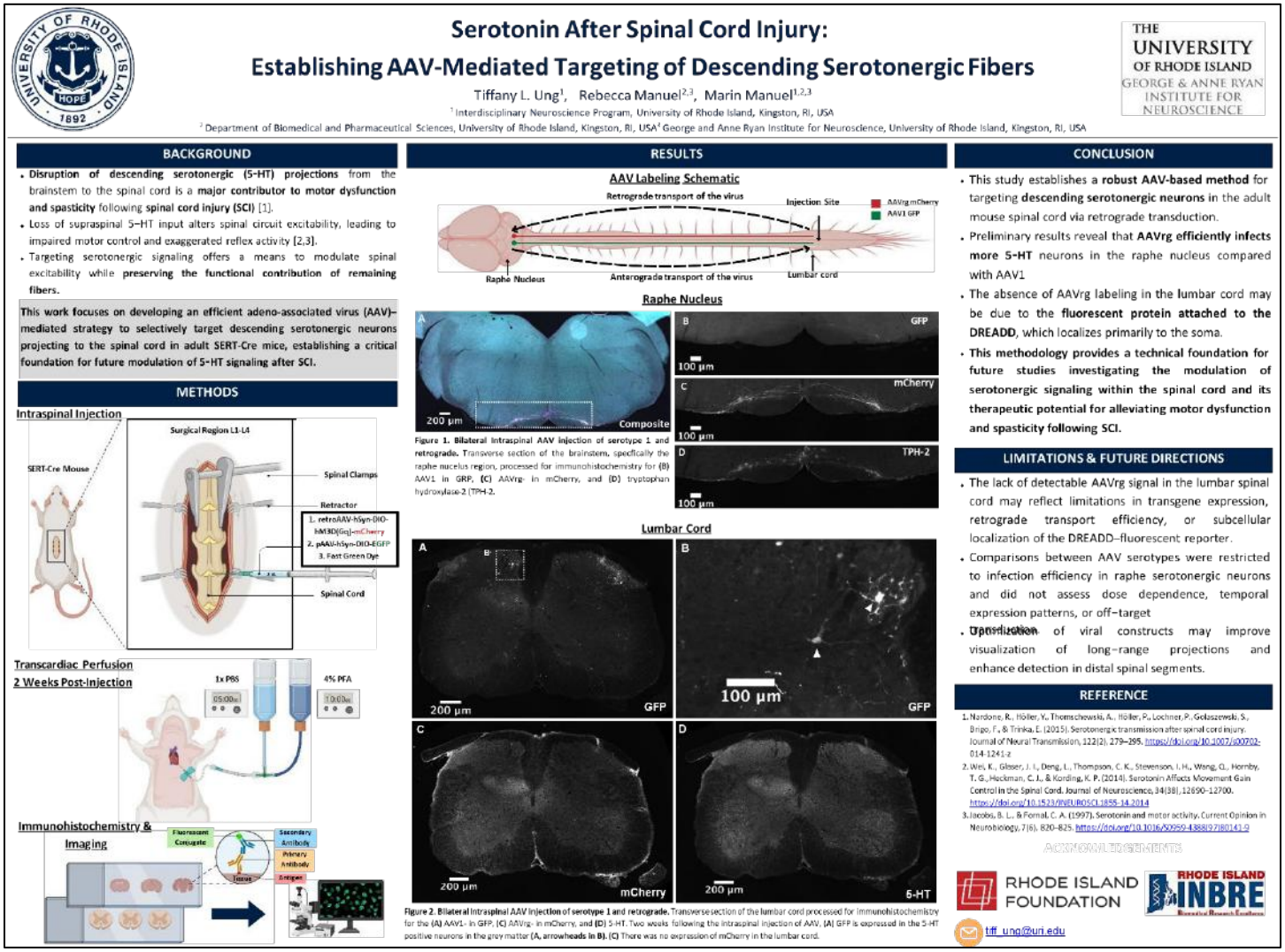
Peppermint (Mentha × piperita) is widely used in cosmetic formulations, primarily in the form of essential oils, while the bioactive potential of peppermint leaves remains comparatively underexplored. Leaf-derived extracts are rich in phenolic and flavonoid compounds with reported antioxidant and anti-inflammatory properties; however, their fraction-specific chemical composition and relationship to skin-relevant bioactivity are not well defined. In this study, peppermint leaves from garden-harvested and commercial sources were extracted and partitioned into ethanol, hexane, ethyl acetate, and aqueous fractions to obtain chemically distinct components. Phytochemical profiles of each fraction were analyzed by HPLC and compared against selected reference standards, including rosmarinic acid, pebrellin, gardenin B, wedelolactone, and eriodictyol-7-O-glucoside. Distinct chromatographic patterns were observed across fractions, with several peaks corresponding to putative phenolic markers such as rosmarinic acid and eriodictyol-7-O-glucoside. A major unknown constituent is being further characterized by LC–MS analysis. Preliminary Folin–Ciocalteu assay results showed that ethyl acetate fractions contained the highest phenolic content, followed by aqueous and ethanol fractions, compared to non-polar hexane fractions. The anti-inflammatory potential of each fraction and selected standards is being evaluated using an optimized lipoxygenase (15-LOX) inhibition assay with NDGA as positive control and quercetin as reference inhibitor. These findings highlight peppermint leaves as a promising and underutilized source of bioactive compounds and provide a phytochemical and functional basis for their development in cosmeceutical applications.



Self-amplifying RNA (saRNA) Vaccines as a Platform for Cancer Treatment

Iris Schellenberg, Charles Jouaneh, Ting-Yu Shih

Cancer is the second leading cause of death worldwide, demonstrating the need for more effective therapies. While existing cancer treatments can be successful, they are often limited by toxicity, tumor recurrence, and variable clinical efficacy. Cancer vaccines offer a promising alternative by harnessing the immune system to recognize and eliminate tumor cells. Recent advances in mRNA technology provide a versatile avenue for expressing tumor antigens and eliciting an anti-tumor immune response; however, they typically produce relatively transient antigen expression, limiting the effectiveness of this approach. To address this limitation, we propose using self-amplifying RNA (saRNA) augmented by immune adjuvants. The saRNA encodes viral replication machinery that enables self-replication of the RNA transcript, leading to stronger and more sustained protein production. Adjuvants are molecules commonly incorporated in vaccines, boosting immune activation through specific recognition mechanisms such as Toll-like receptor (TLR) pathways. However, several of these pathways, such as TLRs 3, 7, and 8, induce a type I interferon response that suppresses RNA translation. We hypothesized that saRNA vaccines co-delivered with adjuvants that are not TLR 3, 7, or 8 agonists will generate stronger and more durable anti-tumor immunity. Using firefly luciferase and mCherry reporter systems as the payload for the RNA, we compared protein expression from saRNA and mRNA with or without adjuvants. Our results demonstrated that saRNA drives significantly higher and longer-lasting protein expression in both reporter systems. Co-delivery with poly(I:C), a TLR3 agonist, suppresses saRNA translation compared to an saRNA control with no adjuvant. In contrast, CpG 1018, a TLR9 agonist, shows saRNA suppression only at very high doses. Taken together, our novel saRNA technology provides a promising platform for cancer vaccination.



Serotonin After Spinal Cord Injury: Establishing AAV-Mediated Targeting of Descending Serotonergic Fibers

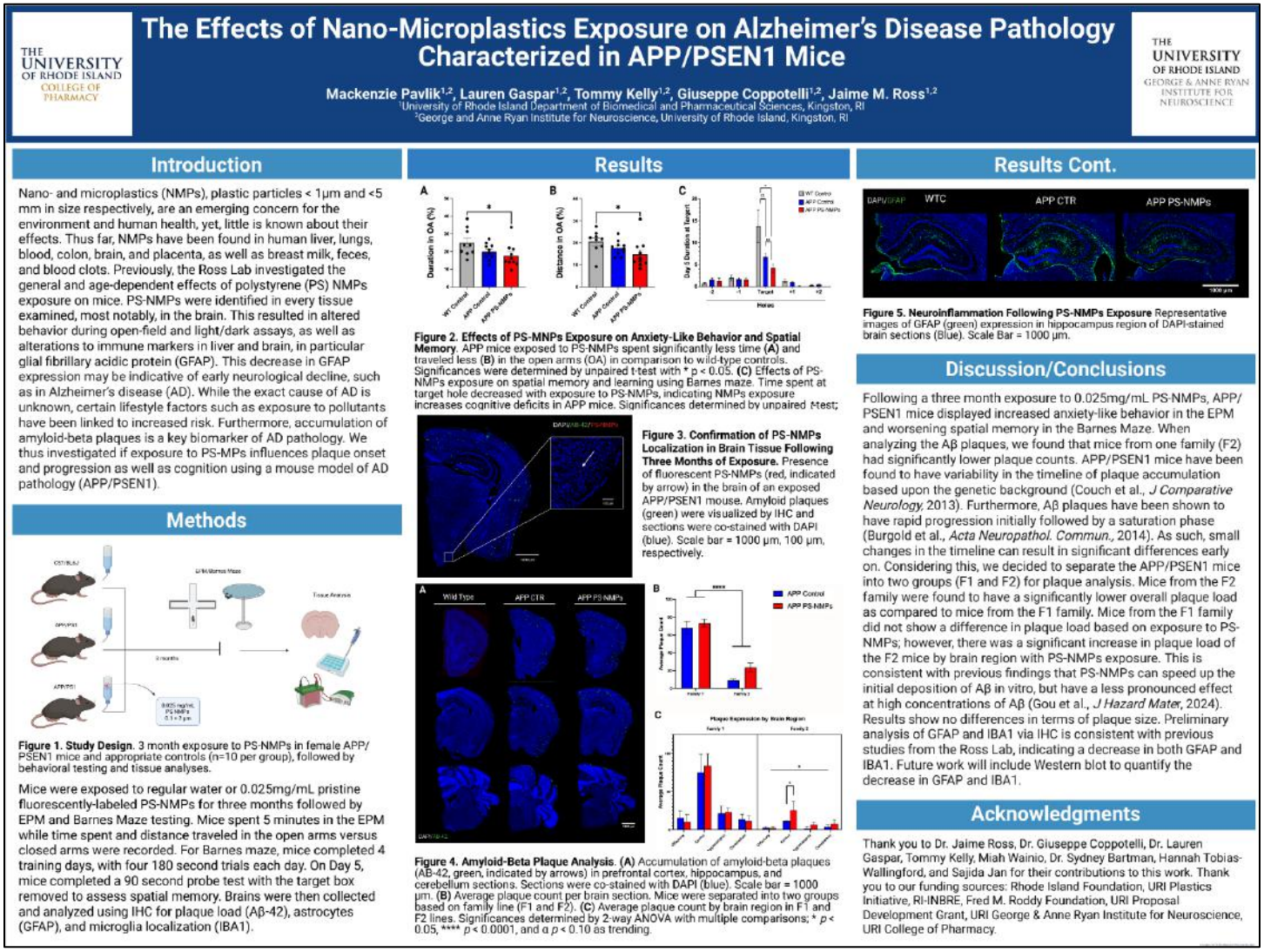
Tiffany Ung, Rebecca Manuel, Marin Manuel

Objective: Disruption of descending serotonergic (5-HT) projections from the brainstem to the spinal cord is a major contributor to motor dysfunction and spasticity following spinal cord injury (SCI). Loss of supraspinal 5-HT input alters spinal circuit excitability, leading to impaired motor control and exaggerated reflex activity. Targeting serotonergic signaling offers a means to modulate spinal excitability while preserving the functional contribution of remaining fibers. This work focuses on developing an efficient adeno-associated virus (AAV)–mediated strategy to selectively target descending serotonergic neurons projecting to the spinal cord in adult SERT-Cre mice, establishing a critical foundation for future modulation of 5-HT signaling after SCI.

Method: Cre-dependent adeno-associated viruses (AAV) were injected into SERT-Cre adult mice via intraspinal injection into the lumbar spinal cord. Two different AAV serotypes were compared for their ability to infect 5-HT neurons and be retrogradely transported to the raphe nucleus. Two weeks after injection, the brainstem and spinal cord tissues were collected and processed for immunohistochemistry. Tryptophan hydroxylase-2 (TPH-2) and 5-HT antibodies were used to confirm positive 5-HT neurons. Fluorescence imaging and manual cell counts were performed to quantify viral specificity and infection efficiency.

Results: Both viral strategies successfully labeled serotonergic neurons and their descending projections. Quantitative analysis revealed differences in the proportion of TPH-2-positive neurons infected by each AAV, indicating distinct efficiencies between approaches for targeting descending 5-HT.

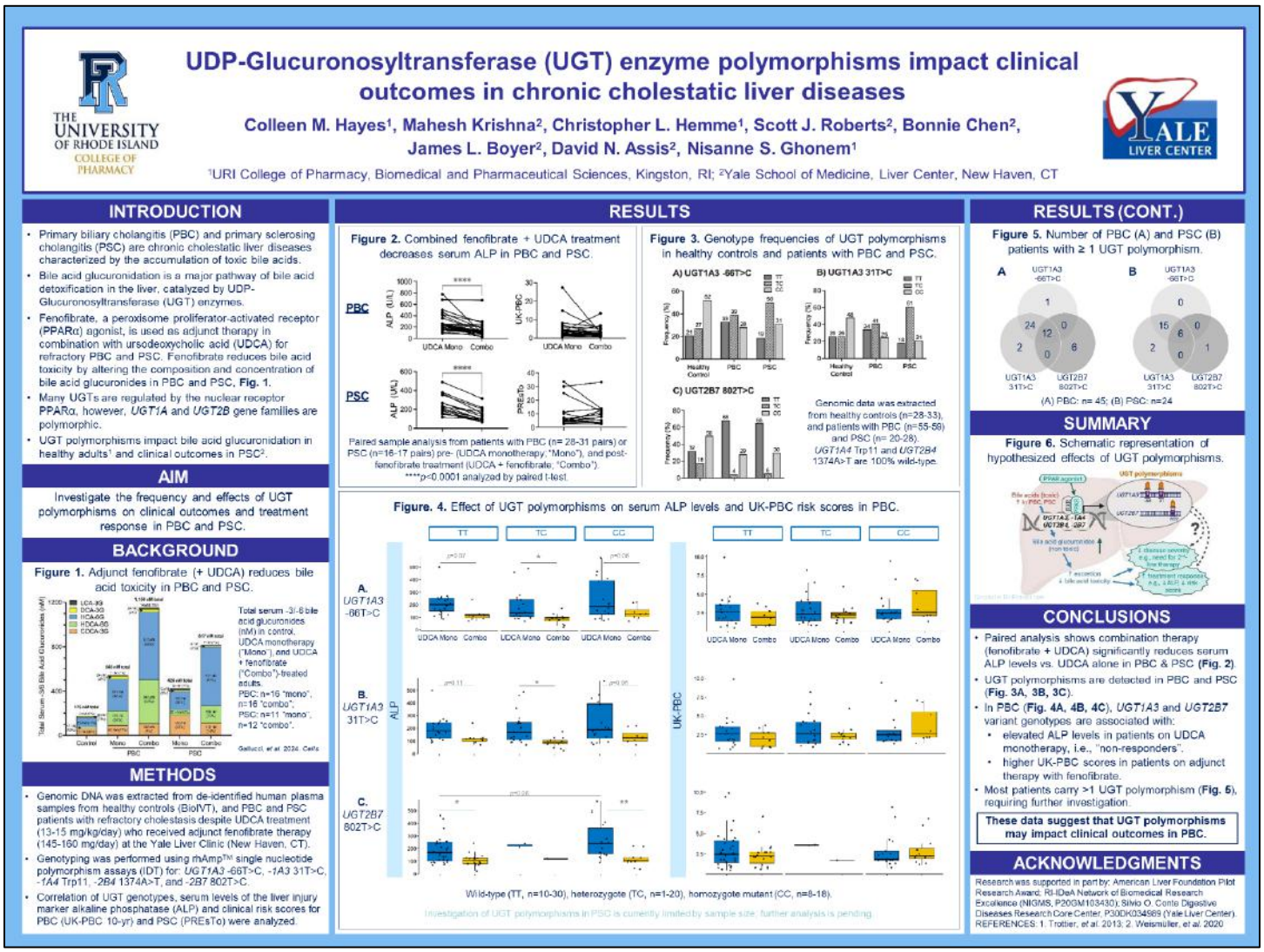
Conclusion: This study establishes a robust AAV-based method for targeting descending serotonergic neurons in the adult spinal cord. The methodology provides a critical technical foundation for future studies investigating modulation of serotonergic signaling within the spinal cord and its therapeutic potential in alleviating motor dysfunction and spasticity following SCI.



The Effects of Nano-Microplastics Exposure on Alzheimer's Disease Pathology Characterized in APP/PSEN1 Mice

Mackenzie Pavlik, Sydney Bartman, Lauren Gaspar, Giuseppe Coppotelli, Jaime M. Ross

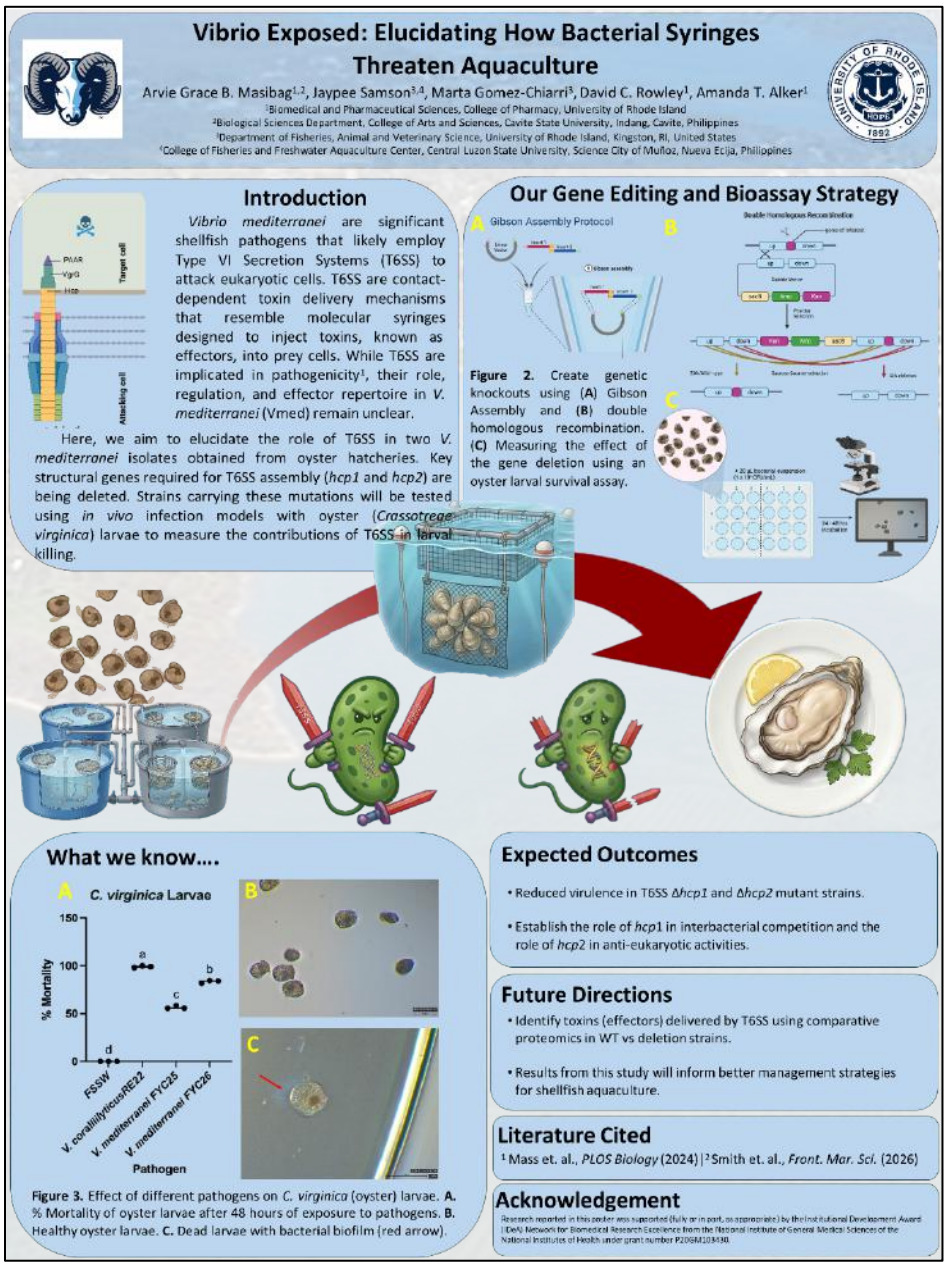
Alzheimer's disease and related dementias (AD/ADRD) are one of the most prevalent cognitive disorders, affecting more than 6 million Americans over the age of 65. While the exact cause of AD and ADRD is still unknown, several risk factors have been identified, including exposure to environmental toxins. In recent years, nano- and microplastics (NMPs), defined as particles ≤ 1 µm and ≤ 5 mm in size, respectively, have emerged as pervasive environmental pollutants. Previous studies have shown NMPs are able to accumulate in peripheral tissues throughout the body of both humans and mice, raising concerns regarding their potential health impacts. Furthermore, NMPs have been demonstrated to cross the blood-brain barrier to accumulate through the brain, resulting in alterations in cognitive behavior and immune markers consistent with neurological disease. We recently demonstrated that polystyrene (PS)-NMPs exposure in transgenic mice carrying the APOE4 variant, the largest known risk-factor for developing AD, resulted in marked sex-dependent alterations in locomotion and recognition memory, as well as changes to astrocytic and microglial markers in the brain. Building on these results, we are now examining the effects of NMPs exposure in a mouse model of Alzheimer's disease pathology (APP/PSEN1). Specifically, this study aims to determine whether chronic exposure to 0.1 µm and 2 µm polystyrene NMPs influences the onset and/or progression of amyloid-beta plaque deposition, alters neuroimmune markers, and affects cognitive function. Preliminary results indicate that chronic exposure to PS-NMPs in APP/PSEN1 mice worsens cognitive impairments, while plaque accumulation was observed to increase taking into account the plaque variability of the family line. Ongoing analyses are also investigating the histological, biochemical, and immunological changes resulting from PS-NMPs exposure.



UDP-Glucuronosyltransferase (UGT) enzyme polymorphisms impact clinical outcomes in chronic cholestatic liver diseases

Colleen M. Hayes, Mahesh Krishna, Christopher L. Hemme, Scott J. Roberts, Bonnie Chen, James L. Boyer, David N. Assis, Nisanne S. Ghonem

Primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) are chronic cholestatic liver diseases characterized by the accumulation of toxic bile acids in the liver. Glucuronidation is a major pathway of bile acid detoxification in which UDP-glucuronosyltransferase (UGT) enzymes conjugate glucuronic acid to bile acids, enhancing their elimination. In humans, bile acid glucuronidation is catalyzed by UGT1A1, -1A3, -1A4, -2B4, and -2B7 enzymes, which are regulated by the peroxisome proliferator-activated receptor alpha (PPARα). Importantly, two PPAR agonists received FDA-approval as second-line therapy for PBC, however, UGT enzymes are encoded by the polymorphic UGT1A and -2B genes, which can alter glucuronidation and, consequently, affect bile acid levels and subsequent liver injury. This study evaluates the frequency and clinical impact of UGT polymorphisms in people with PBC and PSC with refractory cholestasis requiring adjunct treatment of fenofibrate (a PPARα agonist) in combination with ursodeoxycholic acid. Genomic DNA was extracted from de-identified PBC and PSC plasma samples (Yale Liver Center Biorepository, New Haven, CT), and genotyping was performed for UGT1A3 -66T>C, -1A3 31T>C, -2B4 1374A>T, and -2B7 802T>C polymorphisms. The impact of UGT genotypes on clinical markers of liver injury, e.g., serum alkaline phosphatase (ALP), and clinical risk scores of end-stage liver disease (UK-PBC, PREsTo) was assessed. UGT polymorphisms were found in PBC and PSC patients, and all three genotypes (wild-type, heterozygous, homozygous mutant) were detected for UGT1A3 -66, -1A3 31, and -2B7 802. Notably, the UGT2B7 802T>C homozygous variant was associated with higher ALP levels in PBC patients receiving ursodeoxycholic acid therapy (p=0.06), suggesting a potential role of UGT polymorphisms in the treatment response to anti-cholestatic therapy. The data also show that many patients carry multiple UGT polymorphisms. These findings support further investigation into UGT polymorphisms as potential factors underlying clinical outcomes, and the response to anti-cholestatic therapy in PBC and PSC.

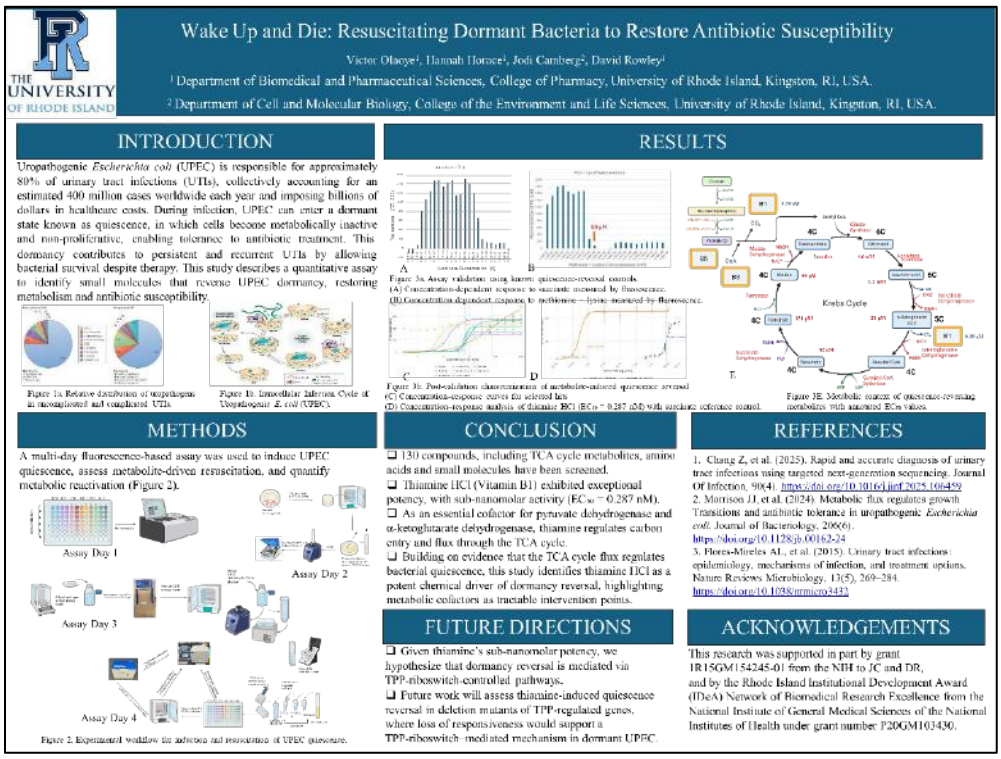


Vibrio Exposed: Elucidating How Bacterial Syringes Threaten Aquaculture

Arvie Grace Masibag, Jaypee Samson, Marta Gomez-Chiarri, David C. Rowley, Amanda T. Alker

Vibrio mediterranei are significant shellfish pathogens that likely employ Type VI Secretion Systems (T6SS) to attack eukaryotic cells. T6SS are contact-dependent toxin delivery mechanisms that resemble molecular syringes designed to inject toxins, known as effectors, into prey cells. While T6SS are implicated in pathogenicity, their role, regulation, and effector repertoire in V. mediterranei (Vmed) remain unclear.

Here, we aim to elucidate the role of T6SS in two V. mediterranei isolates obtained from oyster hatcheries. Key structural genes required for T6SS assembly (hcp1 and hcp2) are being deleted. Strains carrying these mutations will be tested using in vivo infection models with oyster (Crassotreae virginica) larvae to measure the contributions of T6SS in larval killing.



Wake Up and Die: Resuscitating Dormant Bacteria to Restore Antibiotic Susceptibility

Victor Olaoye, Hannah Horace, Jodi Camberg, David Rowley

Recurrent urinary tract infections (UTIs) are frequently caused by uropathogenic Escherichia coli (UPEC) that persist in a dormant, quiescent state. Quiescent bacteria exhibit reduced metabolic activity and antibiotic tolerance, contributing to treatment failure and infection recurrence. While prior studies have characterized mechanisms governing entry into and exit from bacterial quiescence, experimental approaches to identify dormancy-reversing molecules have relied largely on agar-plate assays. These platforms are inherently low throughput, limited in sensitivity, poorly suited for systematic small-molecule screening, and unable to efficiently generate quantitative dose–response relationships. To address this gap, we developed a novel, high-throughput, fluorescence-based quiescence reversal assay compatible with 96-well plate formats. This platform enables sensitive, quantitative measurement of metabolic reactivation, supports rapid determination of concentration-response relationships and EC_{50} values, and provides improved statistical power for compound screening. Using this assay, 130 compounds, including TCA cycle metabolites, amino acids, and small molecules, were screened for their ability to restore metabolic activity under quiescent conditions, with known quiescence-reversing metabolites validating assay performance. Thiamine (vitamin B1) exhibited exceptional potency, with sub-nanomolar activity (EC50 = 0.3 nM). Thiamine is an essential cofactor for pyruvate dehydrogenase and α-ketoglutarate dehydrogenase, enzymes that regulate carbon entry and flux through the TCA cycle. Consistent with prior evidence linking TCA cycle flux to bacterial exit from quiescence, these findings identify thiamine as a potent chemical driver of dormancy reversal and highlight metabolic cofactors as tractable intervention points for targeting dormancy-driven recurrent UTIs caused by UPEC.

To address this gap, we developed a novel, high-throughput, fluorescence-based quiescence reversal assay compatible with 96- and 384-well plate formats. This platform enables sensitive, quantitative measurement of metabolic reactivation, supports rapid determination of concentration-response relationships and EC_{50} values, and provides improved statistical power for compound screening. Using this assay, 130 compounds, including TCA cycle metabolites, amino acids, and small molecules, were screened for their ability to restore metabolic activity under quiescent conditions, with known quiescence-reversing metabolites validating assay performance.

A limited subset of screened metabolites induced reversal of quiescence, with activity observed predominantly at millimolar to micromolar concentrations. However, thiamine HCl (vitamin B1) exhibited exceptional potency, with sub-nanomolar activity (EC50 = 0.287 nM). Thiamine is an essential cofactor for pyruvate dehydrogenase and α-ketoglutarate dehydrogenase, enzymes that regulate carbon entry and flux through the TCA cycle. Consistent with prior evidence linking TCA cycle flux to bacterial exit from quiescence, these findings identify thiamine HCl as a highly potent chemical driver of dormancy reversal and highlight metabolic cofactors as tractable intervention points for targeting persistent UPEC. Ongoing work will investigate the contribution of TPP-riboswitch-regulated pathways to thiamine-induced resuscitation in dormant UPEC.

BPS / Neuro / PharmD

BPS / Neuro / PharmD

1st BPS / Neuro / Pharmd

Delaney Abatecola accepting on behalf of the winning poster

2nd BPS / Neuro / Pharmd

Anna Schumacher accepting on behalf of the second placed poster

3rd BPS / Neuro / Pharmd

Camila Quiroga accepting on behalf of the third placed poster

Validation of the Inducible mtDNA Mutator Model of Mitochondrial Dysfunction

Delaney Abatecola[1,2,†], Nikki Fernando[1,2,†], Hannah Tobias-Wallingford[1,2], Giuseppe Coppotelli[1,2], and Jaime M. Ross[1,2]

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[2]Biomedical & Pharmaceutical Sciences, College of Pharmacy, University of Rhode Island, Kingston RI
[†]these authors contributed equally to this work

INTRODUCTION and AIM

- Mitochondrial dysfunction (MD) is a hallmark of aging and has been involved in many neurodegenerative diseases, such as Alzheimer's and Parkinson's disease, and in furthering neurocognitive deficits.
- Many previous models that study MD include the mtDNA mutator mouse (Trifunovic et al., 2004 & Kujoth et al., 2005). The model expresses a proofreading deficient version (D257A) of mtDNA polymerase-γ (PolgA) and gathering whole-body mtDNA mutations and deletions from gestation.
- As a result of the global nature of MD in this model, it has been challenging to study the impact of mtDNA mutations on specific processes such as cognition, neural development, motor systems, or particularly on inflammatory and immune responses. Additionally, it is impossible to study the impact of mutations occurring at different time points during development.
- A novel inducible knock-in mtDNA mutator mouse model, i-PolgA, has been developed to study MD with greater tissue and temporal specificity.

The aim of this research is to characterize a novel inducible mtDNA mutator mouse model, the i-PolgA mouse. This is a model of MD with temporal and spatial control of mtDNA. This work aims to validate the temporal control of the model via induction of the mutation and assessment of recombination across tissues.

METHODS

- Novel inducible mtDNA mutator mouse generated and induced via five consecutive days of intraperitoneal Tamoxifen injections (75 mg/kg) at one month of age. Following induction and tamoxifen washout period, tissues were obtained.
- Western blot, immunohistochemistry, and cell analyses were performed to assess recombination efficiency and specificity.
- Fibroblasts from untreated mice were cultured followed by 4-OHT treatment for 48 hours prior to imaging.

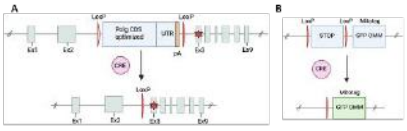

Figure 1. (A) Schematic of the Cre-LoxP recombination system utilized to generate the novel inducible mutator mouse. The PolgA CDS contains the entire CDS from exon 3 onwards, following this there is the endogenous untranslated region (UTR) and hGHa poly-adenylation signal (yellow). The mutation (red star) is within exon 3 and will only be expressed following excision at the LoxP sites by CRE. **(B)** Schematic of Mitotag reporter mouse being used in conjunction to assess CRE recombination. Following tamoxifen treatment, CRE will recombine, removing the STOP cassette and allowing for expression of GFP localized to the outer mitochondrial membrane.

RESULTS

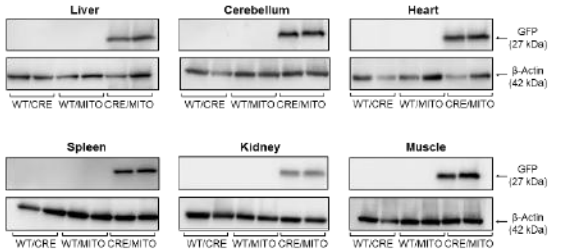

Figure 2. Validation of CRE recombination in the i-PolgA model via Western blot analyses. Detection of GFP expression across various tissues following tamoxifen treatment in i-PolgA mice expressing both CRE and Mitotag, confirming GFP in the Mitotag reporter mouse is appropriately expressed and tamoxifen treatments are sufficient to induce recombination.

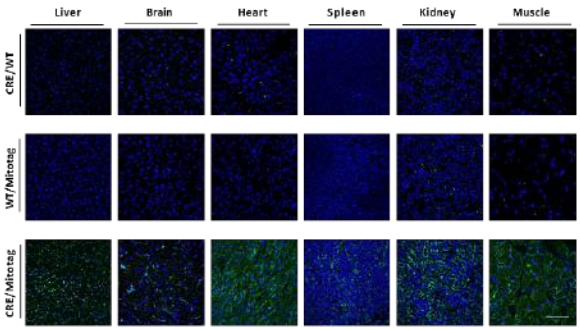

Figure 3. Validation of CRE recombination following Tamoxifen treatment in i-PolgA mice assessed via immunohistochemistry analyses of GFP. Representative images of GFP expression (green) in various Hoescht-stained (blue) tissue samples. Expression of GFP is limited to CRE/Mitotag in i-PolgA animals, confirming that GFP expression in the Mitotag reporter mouse is appropriately expressed and tamoxifen treatments are sufficient to induce CRE recombination. Scale bar 100 um.

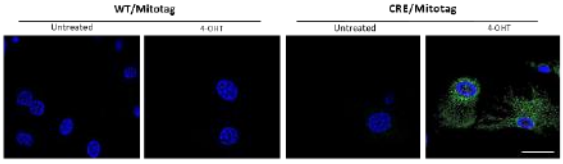

Figure 4. iPolgA/Fibroblasts treated with control or 4-OHT (tamoxifen) validate Cre recombination, with Mitotag GFP expression (green) observed in 4-OHT–treated cells. Nuclei are stained with Hoechst (blue). Scale bar 200 um.

CONCLUSIONS

- Tamoxifen induction of the i-PolgA model produces consistent CRE recombination across tissues, confirmed by GFP expression from the Mitotag reporter as assessed by both Western blot and immunohistochemistry analyses.
- These findings demonstrate consistent and reliable recombination efficiency across multiple tissue types.
- This work provides the first validation of temporal control in the novel i-PolgA model, establishing its utility for inducible, time-specific genetic manipulation *in vivo*.
- Validation and systematic assessment of CRE recombination following tamoxifen treatment establish a strong experimental foundation for future studies aimed at understanding the impacts of development of mitochondrial mutations at different stages of development.

NEXT STEPS

- Quantify recombination efficiency by measuring residual CDS abundance via qPCR following tamoxifen induction to further validate recombination completeness.
- Characterize the temporal progression and severity of mitochondrial dysfunction following induction using a cell-based model.
- Utilize this model to address long-standing questions regarding the impact of mitochondrial mutations that arise post-embryogenesis and at distinct developmental or aging time points, with a focus on tissue-specific outcomes.

Acknowledgments
•Special thanks to Dr. Jaime Ross, Dr. Giuseppe Coppotelli, Sajida Jan-Bibi, and Mackenzie Pavlik.

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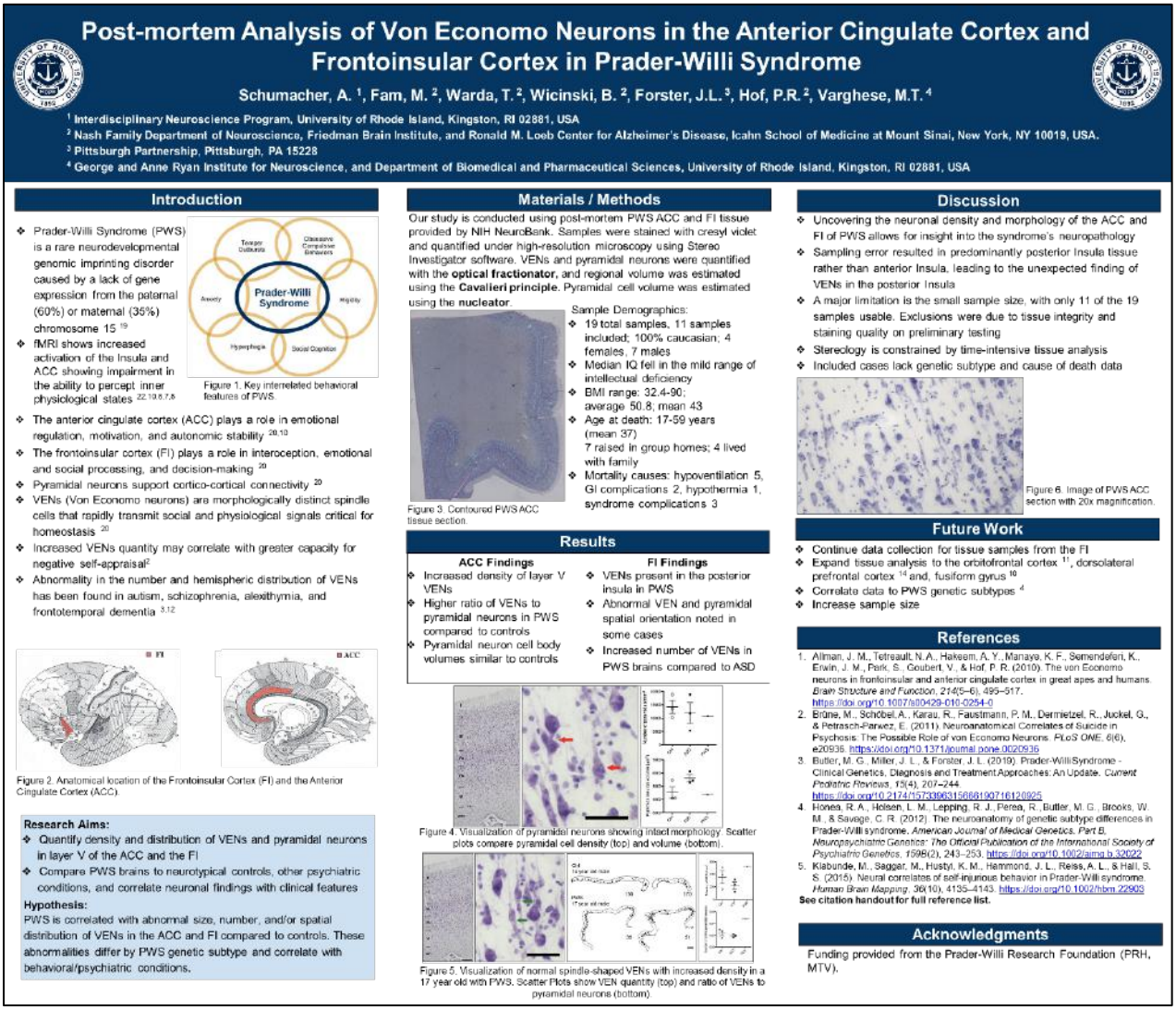
1st
BPS / Neuro / Pharmd

First Place - Validation of the Inducible mtDNA Mutator Model of Mitochondrial Dysfunction

Delaney Abatecola, Nikki Fernando, Hannah Tobias-Wallingford, Giuseppe Coppotelli, Jaime M. Ross

Mitochondrial dysfunction is a central feature of aging and many age-related diseases, and although the exact molecular mechanisms leading to the decline of mitochondrial function with aging remains to be elucidated, the accumulation of mitochondrial DNA (mtDNA) mutations is thought to play a major role in this decline. In this regard, various studies have demonstrated a dramatic increase in mtDNA mutations with aging not only in human tissues but also in experimental animal models. To better understand the link between mtDNA mutations and mitochondrial dysfunction in aging and diseases, Nils-Göran Larsson's group generated the original mtDNA mutator mouse. This model expresses a proofreading-deficient version of mtDNA polymerase-gamma (PolgA), resulting in an accelerated accumulation of mtDNA mutations and aging-like mitochondrial dysfunction. Although this model has significantly advanced research in mitochondrial biology and aging, it is limited by the whole-body accumulation of mtDNA mutations occurring from gestation. Given this, it is impossible to understand tissue-specific-and temporal differences in mtDNA mutations and to investigate the impact of mutations occurring at different times during development. To overcome this limitation, we developed a novel inducible knock-in mtDNA model (iPolgA). Here, we validate this system by inducing expression of the deficient polymerase and assessing recombination across multiple tissues using Western blotting, immunohistochemistry, and cell-based assays. Our results confirm induction and temporal control, establishing the functionality of the model and providing a framework for investigating future questions about mitochondrial biology and aging.



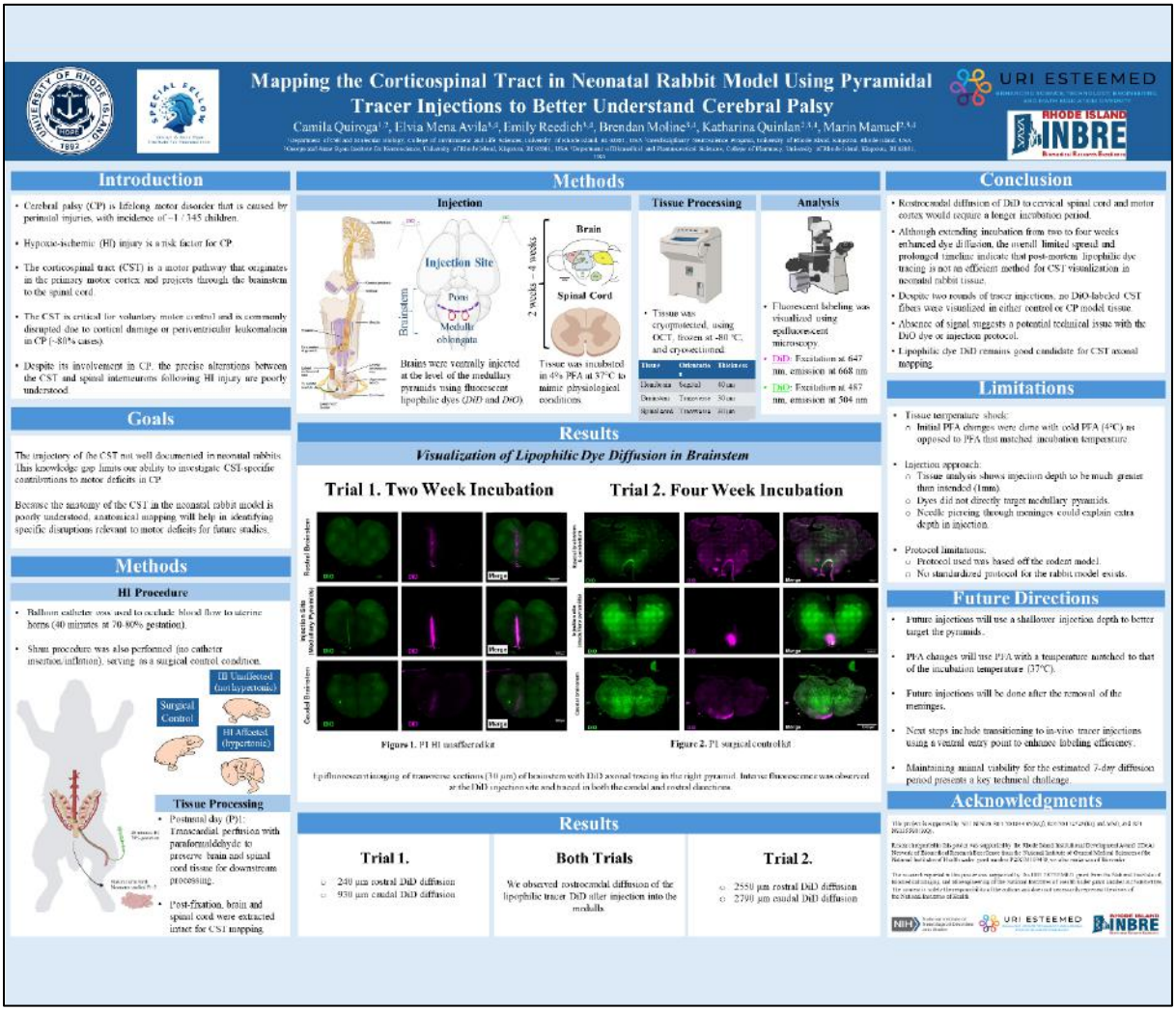
2nd

BPS / Neuro / Pharmd

Post-mortem Analysis of Von Economo Neurons in the Anterior Cingulate Cortex and Frontoinsular Cortex in Prader-Willi Syndrome

Schumacher, A., Fam, M., Warda, T., Wicinski, B., Forster, J.L., Hof, P.R., Varghese, M.T.

Prader-Willi syndrome (PWS) is a neurodevelopmental genomic imprinting disorder causing a lack of gene expression from the paternal (60%) or, less commonly, the maternal (35%) chromosome 15. PWS is characterized by hypotonia, poor suck, and failure to thrive in infancy, followed by hypogonadism, hyperphagia, obesity, and behavioral problems, including skin picking and tantrums. The anterior cingulate cortex (ACC) plays a role in emotional regulation, motivation, and error detection. The frontoinsular cortex (FI) plays a role in interoception, emotional and social processing, and decision-making. In these regions, pyramidal neurons support the computational output functions of these regions. Von Economo neurons (VENs) in these regions are morphologically distinct neurons associated with controlling homeostasis, behavior, and social behavior. Those with PWS exhibit neurobehavioral phenotypes, such as cognitive deficit and emotional instability, suggesting potential connectivity and molecular differences in these neurons. We aim to identify the number and distribution of VENs and pyramidal neurons in layer V of the anterior cingulate cortex (ACC) and the frontoinsular cortex (FI). We hypothesize that VENs will be abnormal in distribution and/or number in those with PWS compared to controls. Post-mortem PWS ACC and FI specimens provided by NIH NeuroBank were stained with cresyl violet and quantified under high-resolution microscopy using Stereo Investigator software. VENs and pyramidal neurons were quantified using the optical fractionator, and regional volume was estimated using the Cavalieri principle. Preliminary results confirm the presence of increased density of VENs in layer V of the ACC. The ratio of VENs to pyramidal neurons in the ACC was higher in PWS compared to controls. The pyramidal cell bodies of the ACC had volumes similar to those of controls. Preliminary results in the ACC show abnormal proliferation and migration of VENs in PWS development. The data collection of the FI is ongoing. Uncovering the neuronal density and morphology of the ACC and FI of those with PWS allows for a view into the neuropathology of the syndrome.



3rd

BPS / Neuro / Pharmd

Third Place - Mapping the Corticospinal Tract in a Neonatal Rabbit Using Pyramidal Tracer Injections for a Better Understanding of Cerebral Palsy

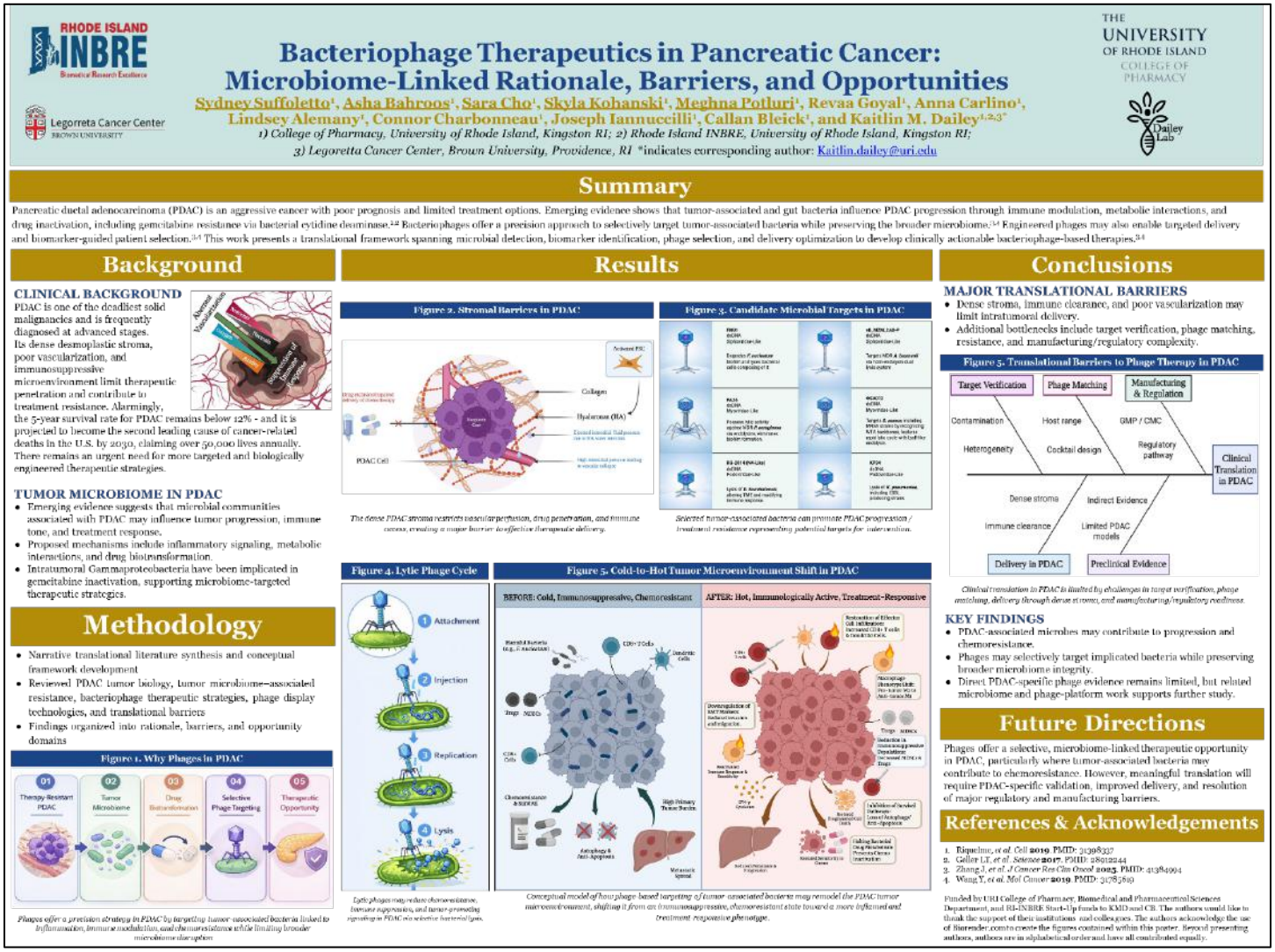
Camila Quiroga, Elvia Mena Avila, Emily Reedich, Brendan Moline, Katharina Quinlan, Marin Manuel

Cerebral palsy (CP) is a common motor disorder in children, with approximately 1 in 345 children diagnosed in the United States. Hypoxic ischemic injury (HI) during the perinatal period is a major risk factor and can disrupt the development of descending motor pathways, particularly the corticospinal tract (CST).

The CST originates in the primary motor cortex and projects through the brainstem to the spinal cord, playing a critical role in voluntary motor control. Despite its involvement in CP, the precise relationship between the CST and spinal interneurons following HI injury remains poorly understood. We use a neonatal HI rabbit model, which recapitulates key features of human CP, to investigate these changes. However, the trajectory and cortical origins of the CST are not well defined in neonatal rabbits, limiting our ability to study CST-specific contributions to motor deficits.

The goal of this study is to identify the location and trajectory of the CST in neonatal rabbits. Pregnant rabbits undergo surgery to induce HI injury in developing kits. At postnatal day 1, kits are perfused, and the brain and spinal cord are dissected intact. Lipophilic dyes (DiO, DiD) are injected into the medullary pyramids, where CST axons converge before decussation. These dyes integrate into axonal membranes and travel bidirectionally over time, allowing CST projections to be traced to both the primary motor cortex and the spinal cord.

Mapping the CST is essential for identifying the primary motor cortex in neonatal rabbits. This enables future studies to manipulate CST activity and examine its role in spinal reflex circuits. Our findings show that extended incubation improves tracer diffusion, highlighting both the feasibility and limitations of postmortem CST mapping in this model. Overall, this study establishes a foundation for investigating CST organization and dysfunction in CP.



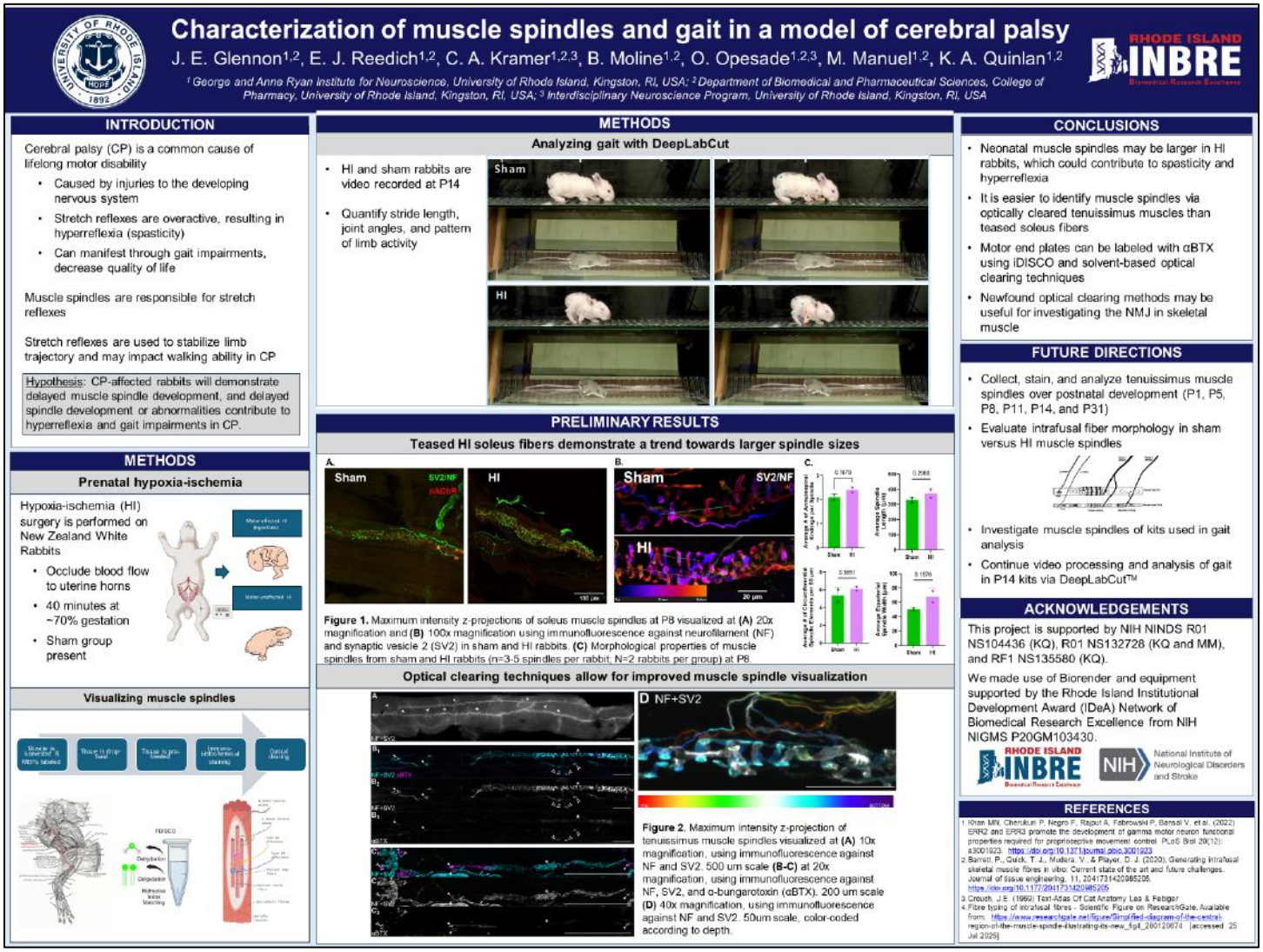
A Translational Framework for Bacteriophage Therapeutics in Pancreatic Cancer

Sydney Suffoletto, Asha Bahroos, Sara Cho, Skyla Kohanski, Meghna Potluri, Revaa Goyal, Anna Carlino, Lindsey Alemany, Connor Charbonneau, Joseph Iannuccilli, Callan Bleick, Kaitlin M. Dailey

Pancreatic cancer has one of the poorest prognoses of any solid malignancy. This disease is driven by a desmoplastic, hypoxic tumor microenvironment that promotes metabolic reprogramming, inhibits therapeutic activity, and ultimately leads to treatment resistance. Emerging evidence suggests that tumor-adjacent and gut microbial communities shape pancreatic tumor biology through metabolism-linked mechanisms including immune modulation, nutrient competition, and drug biotransformation. Gammaproteobacteria recently demonstrated the clinical relevance of the tumor microbiome with enzymatic inactivation of gemcitabine by intratumoral via cytidine deaminase, converting active drug to an inactive metabolite and contributing to chemoresistance.

Bacteriophages have the potential to be leveraged as a metabolically informed precision therapeutic with selective depleting bacteria implicated in tumor-promoting inflammation and/or drug-modifying enzymatic activity while minimizing broader microbiome disruption. Beyond bacterial lysis, engineered phage platforms would support targeted delivery and biomarker development to stratify patients whose tumor–microbiome profiles suggest metabolically mediated resistance. Translation of pancreatic cancer therapeutics faces distinct barriers such as contamination-prone tumor samples, narrow phage host range and delivery constraints imposed by dense stroma. Manufacturing and regulatory requirements for biologics-grade phage products further limit rapid iteration and must be accounted for even at early stages of experimentation.

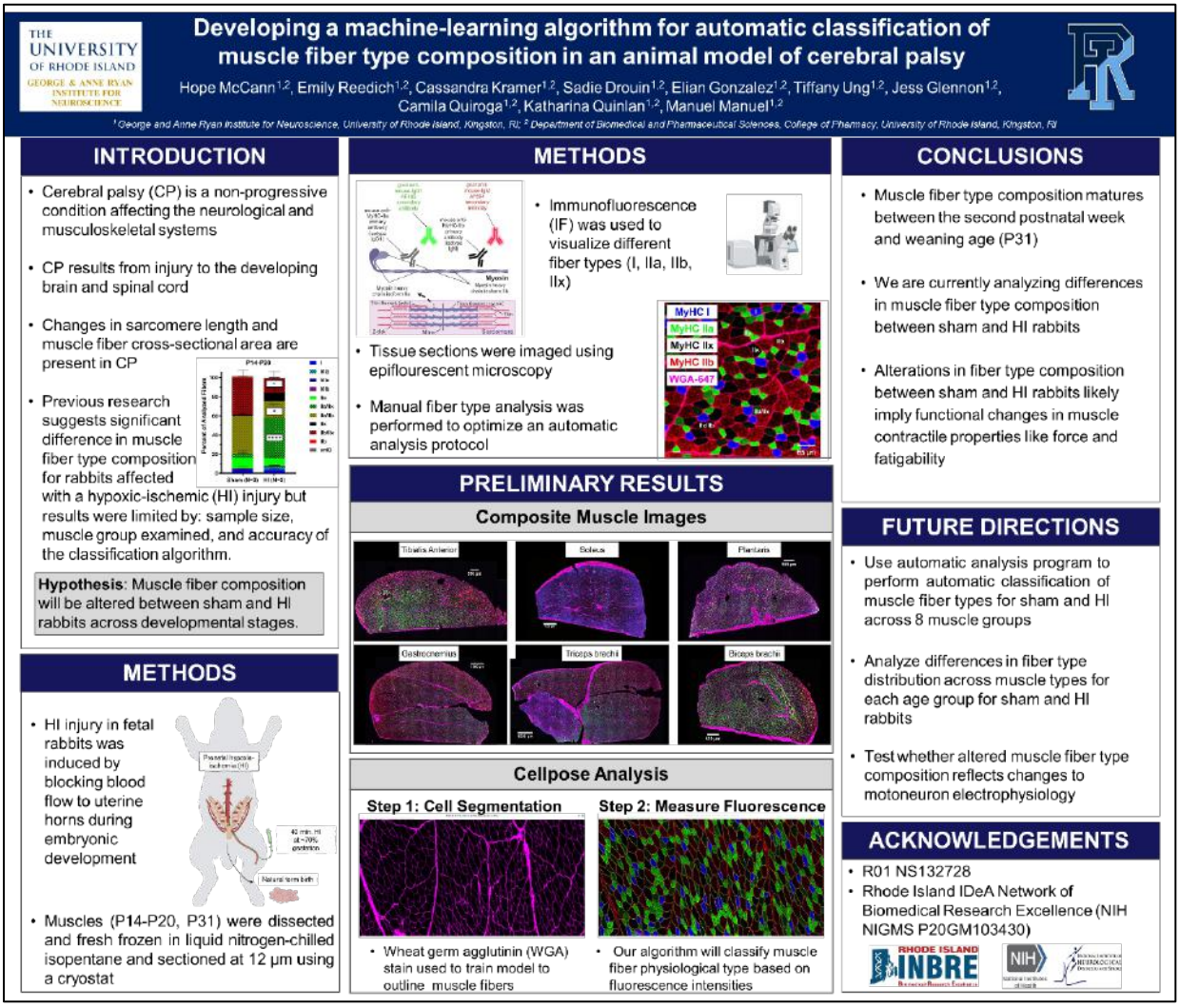
Here, we synthesize the potential and constraints of bacteriophage-based therapeutics as a translational roadmap. The framework begins with detection strategies and orthogonal validation, moves through biomarker identification with rapid phage matching and cocktail design, addresses delivery optimization under pancreatic tumor stromal constraints, and culminates in plausible clinical applications ultimately eliciting positive patient response. This approach aims to convert mechanistic plausibility into clinical trial-ready strategies for bacteriophage-mediated therapeutics in pancreatic cancers.



Characterization of Muscle Spindles and Gait in a Model of Cerebral Palsy

J. E. Glennon, E. J. Reedich, C. A. Kramer, B. Moline, O. Opesade, M. Manuel, K. A. Quinlan

Cerebral palsy (CP) is a collection of motor disorders that is the most common cause of lifelong motor disability worldwide, affecting approximately 1 in 500 live births. It is caused by injuries to the developing nervous system during late gestation or early childhood, and typically involves spasticity (marked by hyperreflexia) and difficulties with gait (e.g. crouch gait). Stretch reflexes are attributed to sensory organs called muscle spindles, which detect stretch in skeletal muscles and activate Ia sensory afferents. Hyperreflexia in CP could involve irregularities in muscle spindle physiology, but this remains unexplored. In turn, hyperreflexia and irregular muscle spindle morphology may be correlated with gait abnormalities seen in CP. To explore this, we are investigating muscle spindle structure in developing rabbits that have experienced prenatal hypoxia-ischemia (HI) injury (via surgical procedure at 70-80% gestation) and in sham-operated control rabbits that have been prenatally exposed to anesthetics but not HI. We have developed a tissue clearing and immunofluorescence pipeline for three dimensional visualization of muscle spindles in the tenuissimus, which has high spindle density and plays an important role in proprioceptive sensory feedback in the hindlimb. We hypothesize that muscle spindles from HI rabbits will demonstrate delayed development when compared to that of sham kits; it is possible that delayed development or structural abnormalities within muscle spindles could contribute to hyperreflexia and gait abnormalities in CP. Gait will be assessed in rabbit kits at two weeks of age using video recording and then analyzed in DeepLabCutTM to assess stride length, joint angle, and other limb activity seen within sham and HI rabbits. Findings from this project will contribute to further understanding of neuromuscular impairment in CP and development of potential therapeutic strategies to normalize muscle spindle physiology in this disorder.



Developing a machine-learning algorithm for automatic classification of muscle fiber type composition in an animal model of cerebral palsy

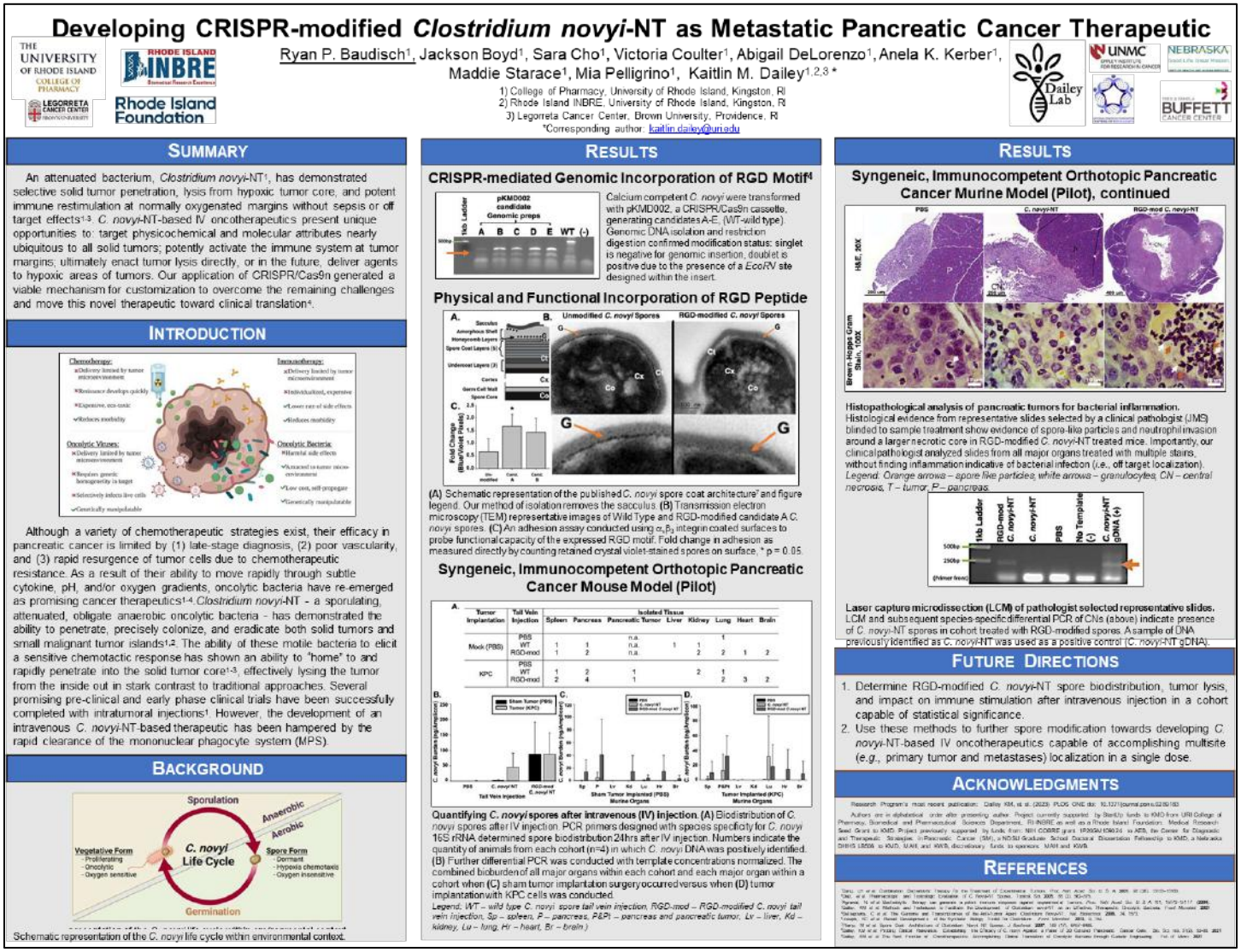
Hope McCann, Emily Reedich, Cassandra Kramer, Sadie Drouin, Elian Gonzalez, Tiffany Ung, Jess Glennon, Camila Quiroga, Katharina Quinlan, Manuel Manuel

Cerebral palsy (CP) is a nonprogressive condition that affects the neurological and musculoskeletal systems due to injury to the developing brain and spinal cord, resulting in symptoms of hypertonia, spasticity, and increased neuromuscular activity. In addition to neural deficits, skeletal muscle pathologies are present in CP, including changes to sarcomere length and muscle fiber cross-sectional area. Skeletal muscle is composed of heterogeneous fiber physiological types defined by myosin heavy chain (MHC) isoform expression, and it remains unclear whether CP is associated with systematic shifts in fiber type composition.

MHC type I fibers are slow-twitch fibers that are fatigue resistant and produce small forces. Type IIa fibers are fast-twitch, oxidative-glycolytic fibers which are less fatigue resistant than type I fibers and produce intermediate forces. Type IIx and IIb fibers are fast-twitch glycolytic fibers that are highly fatigable but have the greatest force-generative capacity. Whether the relative proportions of these fiber types are altered in CP has not been clearly established.

To address this question, we are using a rabbit model of CP, in which a prenatal hypoxic-ischemic (HI) injury is performed in the pregnant dam, enabling analysis of neuromuscular alterations in newborn kits. We performed immunofluorescent staining to label muscle fiber types across various muscles from hypertonic HI, non-hypertonic HI, and sham rabbits at two developmental stages. We are developing an automatic analysis pipeline to classify the fiber type of large numbers of muscle fibers, and measure the percentage of each fiber type.

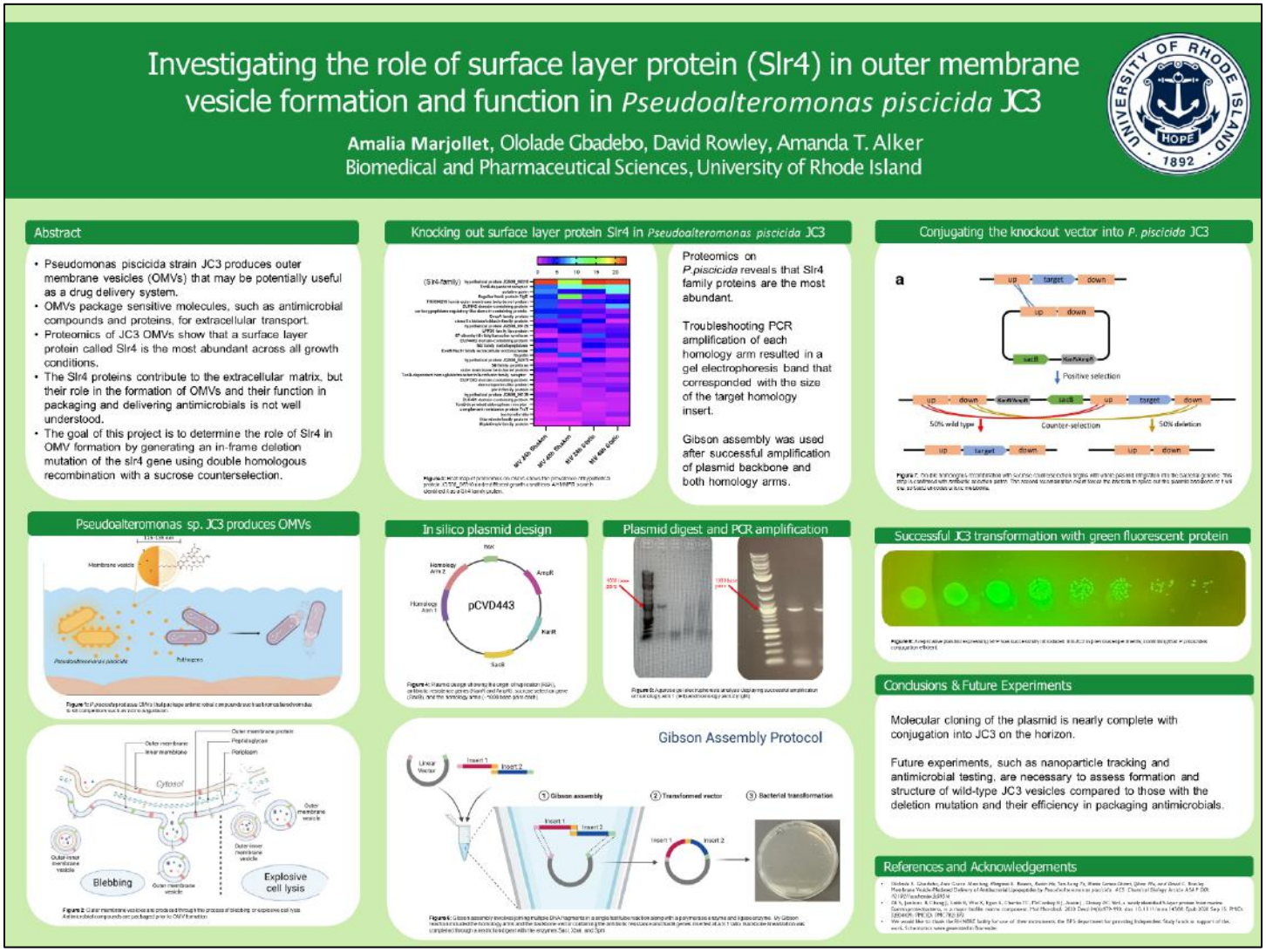
This work will provide a quantitative assessment of how prenatal HI injury influences muscle fiber composition, establishing a foundation for future studies aimed at understanding disease mechanisms and evaluating therapeutic strategies.



Developing CRISPR-modified Clostridium novyi-NT as Metastatic Pancreatic Cancer Therapeutic

Ryan P. Baudisch, Jackson Boyd, Sara Cho, Victoria Coulter, Abigail DeLorenzo, Anela K. Kerber, Maddie Starace, Mia Pelligrino, Kaitlin M. Dailey

Clostridium novyi has demonstrated selective efficacy against solid tumors largely due to the microenvironment contained within dense tumor cores. The core of a solid tumor is typically hypoxic, acidic, and necrotic—impeding the penetration of current therapeutics. C. novyi is attracted to the tumor microenvironment and once there, can both lyse and proliferate while simultaneously re-activating the suppressed immune system. C. novyi systemic toxicity is easily mitigated by knocking out the phage DNA plasmid encoded alpha toxin resulting in C. novyi-NT; but, after intravenous injection spores are quickly cleared by phagocytosis before accomplishing significant tumor localization. C. novyi-NT could be designed to accomplish intravenous delivery with the potential to target all solid tumors and their metastases in a single dose. This study characterizes CRISPR/Cas9 modified C. novyi-NT to insert the gene for RGD, a tumor targeting peptide, expressed within the promoter region of a spore coat protein. Expression of the RGD peptide on the outer spore coat of C. novyi-NT indicates an increased capacity for tumor localization of C. novyi upon intravenous introduction based on the natural binding of RGD with the αvβ3 integrin commonly overexpressed on the epithelial tissue surrounding a tumor, and lead to immune stimulation.

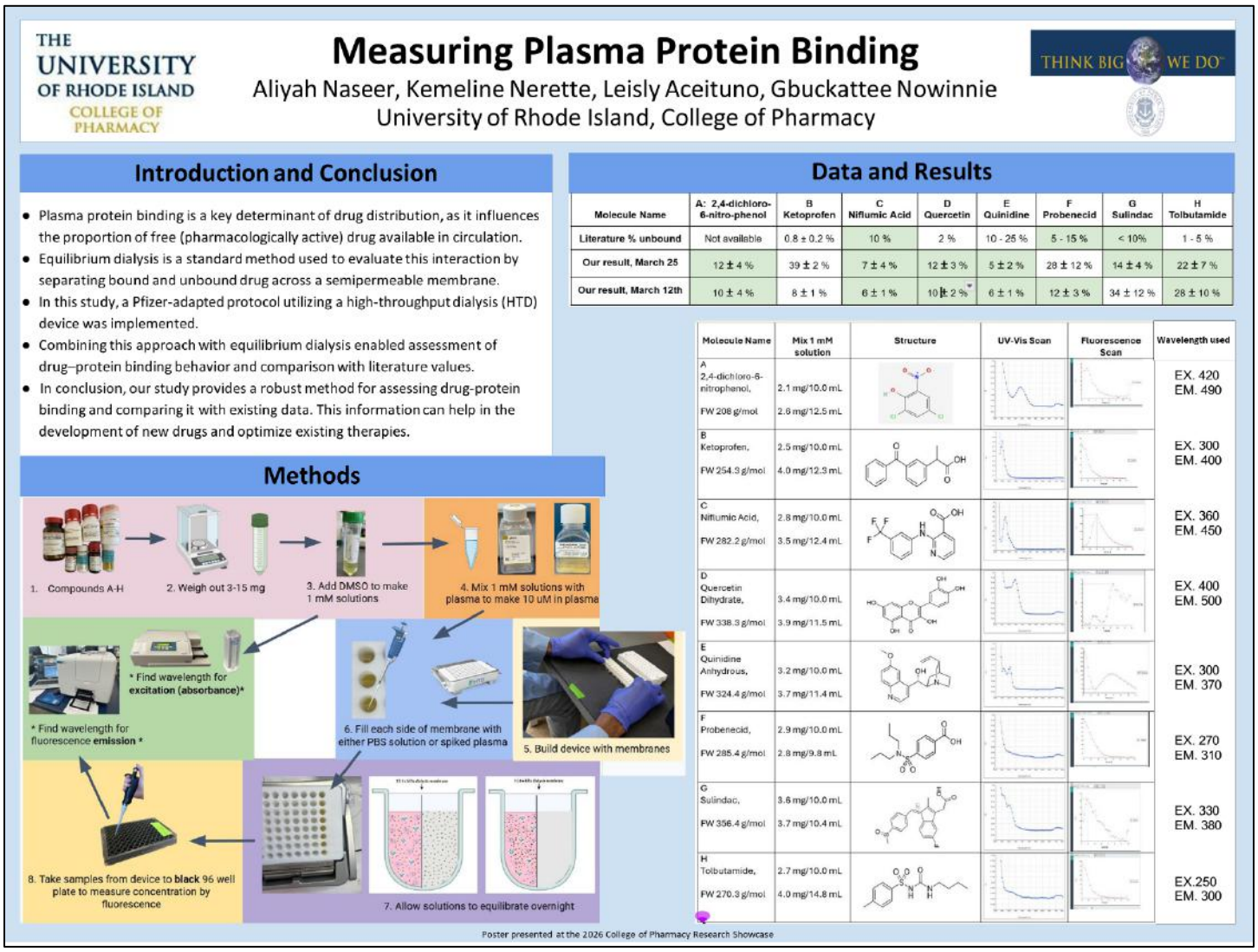


Investigating the role of surface layer protein (Slr4) in outer membrane vesicle formation and function in Pseudoalteromonas piscicida JC3

Amalia Marjollet, Ololade Gbadebo, David Rowley, Amanda T. Alker

Pseudoalteromonas piscicida strain JC3, a marine bacterium isolated from whiteleg shrimp, is known to produce outer membrane vesicles (OMVs) that may be potentially useful as a drug delivery system. Prokaryotic cells use OMVs to package sensitive molecules such as nucleic acids, enzymes, lipophilic compounds, and other specialized metabolites. In particular, JC3 has been found to produce a class of compounds called bromoalterochromides, which possess antibacterial properties against human pathogens. OMVs produced by JC3 serve as packaging and delivery systems of toxic cargo, like bromoalterochromides, against bacterial pathogens and competitors.1 Proteomics of JC3 OMVs found that an s-layer protein named Slr4 was by far the most abundant. These Slr4 proteins form lattices that compose the outermost layer of prokaryotic cells and contribute to the extracellular matrix of Pseudoalteromonas biofilms. However, the role of Slr4 in the formation of OMVs and their function in packaging antimicrobials such as bromoalterochromides remains largely unclear. 2

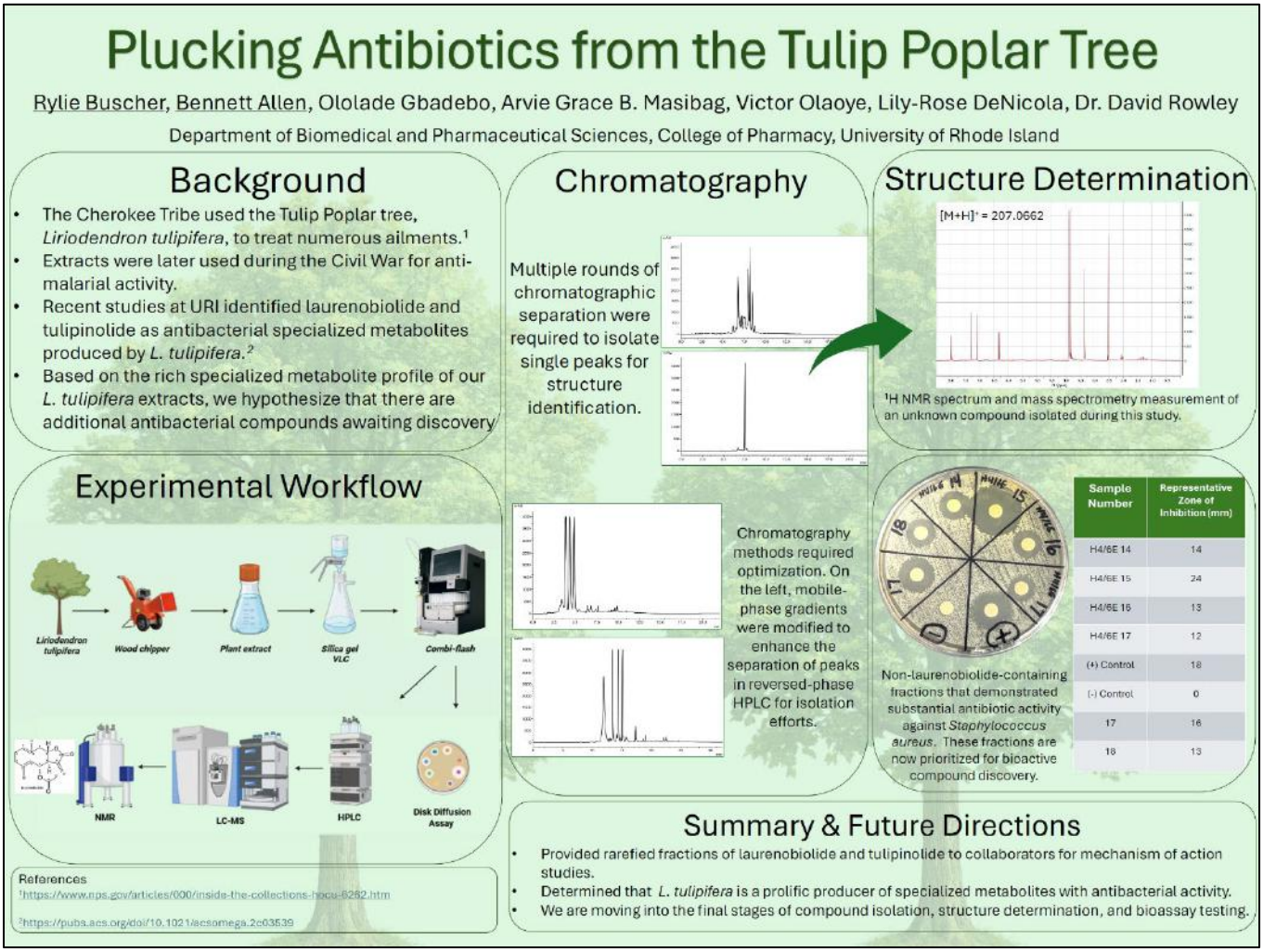
This project will determine the role of Slr4 in antibacterial vesicles formation of JC3 by generating an in-frame deletion mutation of the Slr4 gene using double homologous recombination with a sucrose counterselection. Molecular cloning of the plasmid is nearly complete with conjugation on the horizon. Future experiments, such as nanoparticle tracking and antimicrobial testing, are necessary to assess formation and structure of wild-type JC3 vesicles compared to those with the deletion mutation and their efficiency in packaging bromoalterochromides.



Measuring Plasma Protein Binding

Aliyah Naseer, Kemeline Nerette, Leisly Aceituno, Gbuckattee Nowinnie

- Plasma protein binding is a key determinant of drug distribution, as it influences the proportion of free (pharmacologically active) drug available in circulation.
- Equilibrium dialysis is a standard method used to evaluate this interaction by separating bound and unbound drug across a semipermeable membrane.
- In this study, a Pfizer-adapted protocol utilizing a high-throughput dialysis (HTD) device was implemented.
- Combining this approach with equilibrium dialysis enabled assessment of drug–protein binding behavior and comparison with literature values.
- In conclusion, our study provides a robust method for assessing drug-protein binding and comparing it with existing data. This information can help in the development of new drugs and optimize existing therapies.

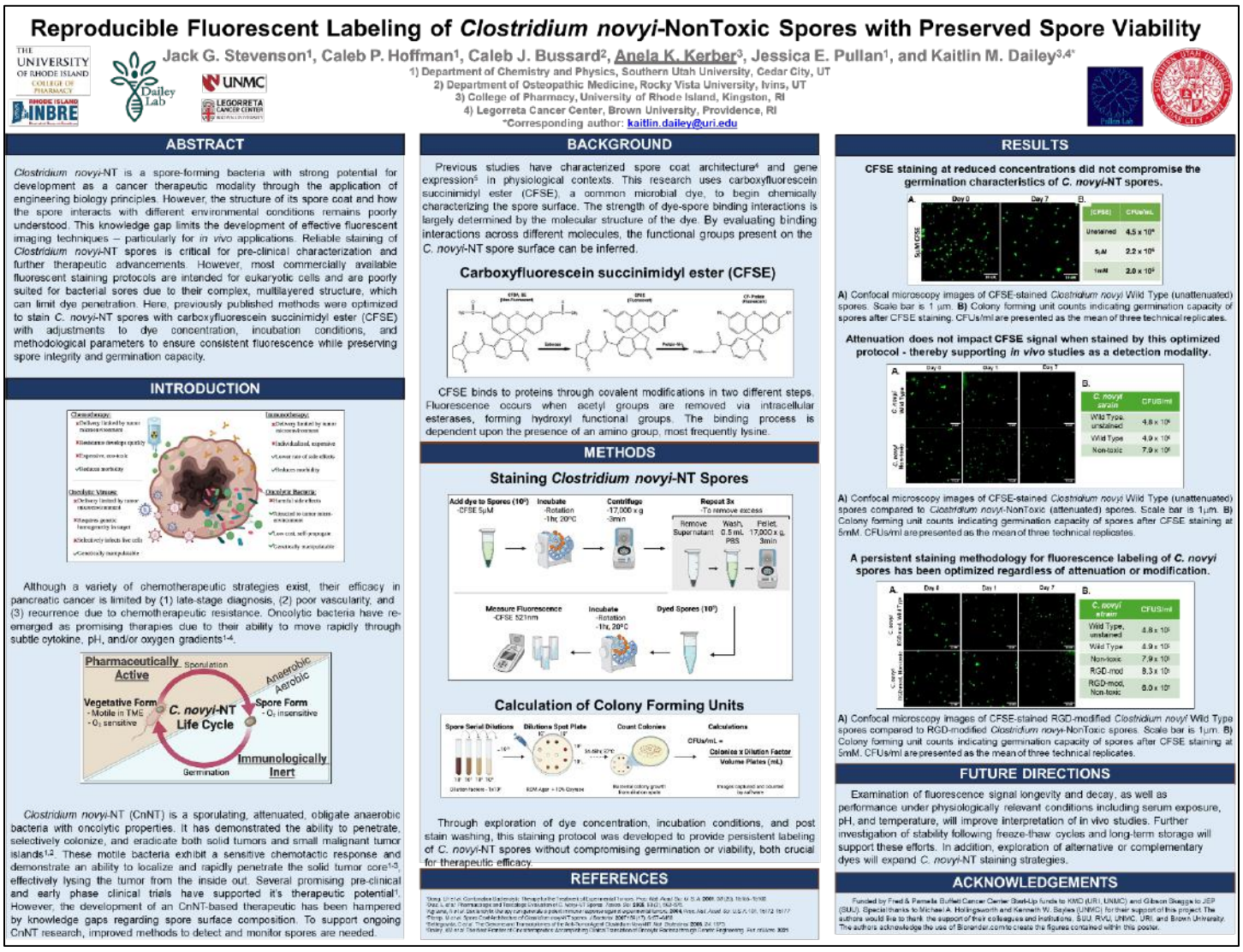


Plucking Antibiotics from the Tulip Poplar Tree

Rylie Buscher, Bennett Allenm, Ololade Gbadebo, Arvie Grace B. Masibag, Victor Olaoye, Lily-Rose DeNicola, David Rowley

The tulip poplar tree (Liriodendron tulipifera) has a long history of medicinal use, including traditional applications by the Cherokee and later reports of antimalarial use during the U.S. Civil War. Recent studies at the University of Rhode Island identified laurenobiolide and tulipinolide as antibacterial specialized metabolites produced by L. tulipifera. Based on the rich specialized metabolite profile of L. tulipifera extracts, we hypothesized that additional antibacterial compounds remain to be discovered beyond these known constituents.

To investigate this, we fractionated L. tulipifera extracts and performed iterative chromatographic separations, optimizing reversed phase HPLC gradients to improve peak resolution for isolation. Bioactivity screening revealed non laurenobiolide–containing fractions with substantial antibiotic activity against Staphylococcus aureus, prioritizing these fractions for bioactive compound discovery. Rarefied fractions of laurenobiolide and tulipinolide were also provided to collaborators to support mechanism of action studies. Overall, these findings support L. tulipifera as a prolific source of antibacterial specialized metabolites, and ongoing work is focused on completing compound isolation, structure determination, and confirmatory bioassay testing of newly prioritized active fractions.



Reproducible Fluorescent Labeling of Clostridium novyi-NonToxic Spores with Preserved Spore Viability

Jack G. Stevenson, Caleb P. Hoffman, Caleb J. Bussard, Anela K. Kerber, Jessica E. Pullan, Kaitlin M. Dailey

Clostridium novyi-NT is a spore-forming bacteria with strong potential for development as a cancer therapeutic modality through the application of engineering biology principles. However, the structure of its spore coat and how the spore interacts with different environmental conditions remains poorly understood. This knowledge gap limits the development of effective fluorescent imaging techniques – particularly for in vivo applications. Reliable staining of Clostridium novyi-NT spores is critical for pre-clinical characterization and further therapeutic advancements. However, most commercially available fluorescent staining protocols are intended for eukaryotic cells and are poorly suited for bacterial sores due to their complex, multilayered structure, which can limit dye penetration. Here, previously published methods were optimized to stain C. novyi-NT spores with carboxyfluorescein succinimidyl ester (CFSE) with adjustments to dye concentration, incubation conditions, and methodological parameters to ensure consistent fluorescence while preserving spore integrity and germination capacity. Preservation of these capacities directly impacts therapeutic efficacy and are therefore anti-cancer activities. Through development of a low cost, accessible, and reproducible methodology, this approach enables consistent detection and visualization of C. novyi-NT spores and provides a framework adaptable to alternative fluorophores and related spore-forming systems. Ultimately, this undergraduate research project developing alternative C. novyi-NT detection modalities will expand downstream experimental applications and facilitate clinical translation, including therapeutic strategies for metastatic pancreatic cancer and other solid tumors.

Using Concept Mapping to Identify and Prioritize Strategies for Improving CDK4/6 Inhibitor Persistence in Breast Cancer

Salma Taghzout, Michelle L. Caetano, Guannan Gong, Maryam Lustberg, Robert Legare, Mariah Ramos, Jessica Liu, Britny R. Brown

Cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) have significantly improved outcomes in hormone receptor-positive (HR+), HER2-negative breast cancer; however, real-world adherence and persistence remain suboptimal. Stakeholder-informed interventions are needed to address modifiable barriers and support long-term therapy. This study aimed to identify and prioritize patient- and provider-informed strategies to improve CDK4/6i persistence based on feasibility and expected impact.

A two-phase concept mapping approach was employed. In Phase 1, a Qualtrics survey was distributed to CDK4/6i-treated patients (n=63) and multidisciplinary clinicians (n=94) to assess treatment experiences and collect open-ended recommendations. Responses (29 patients, 17 clinicians; 29.3% response rate) were thematically coded and synthesized into candidate strategies. Three primary themes emerged: provider communication and support, symptom and adverse-effect management, and social support needs. Patients emphasized timely communication, clear expectations, and proactive management of toxicities (e.g., fatigue, neutropenia, diarrhea), while clinicians identified adverse effects, financial and access barriers, and disease progression as key contributors to non-persistence.

In Phase 2, participants rated proposed strategies on feasibility and expected impact (18 patients, 17 clinicians; 23.5% response rate). Strategies were organized into six domains: education and informational support, patient monitoring and follow-up, adherence tools and resources, multidisciplinary care and collaboration, financial and access support, and treatment optimization. High-priority strategies included enhanced medication and side-effect education, expanded patient resources, dedicated pre-treatment counseling, routine follow-up check-ins, use of adherence tools, increased pharmacist integration, and dose titration when appropriate.

Limitations include single-institution sampling, potential selection bias from opt-in electronic recruitment, and restriction to English-speaking participants. This concept mapping approach generated stakeholder-driven insights, promoting patient-centered, equitable care. Findings informed the development of a patient-reported outcomes module within the electronic medical record.

Postdoc / Resident

Graduate Students

1st Postdoc / Resident

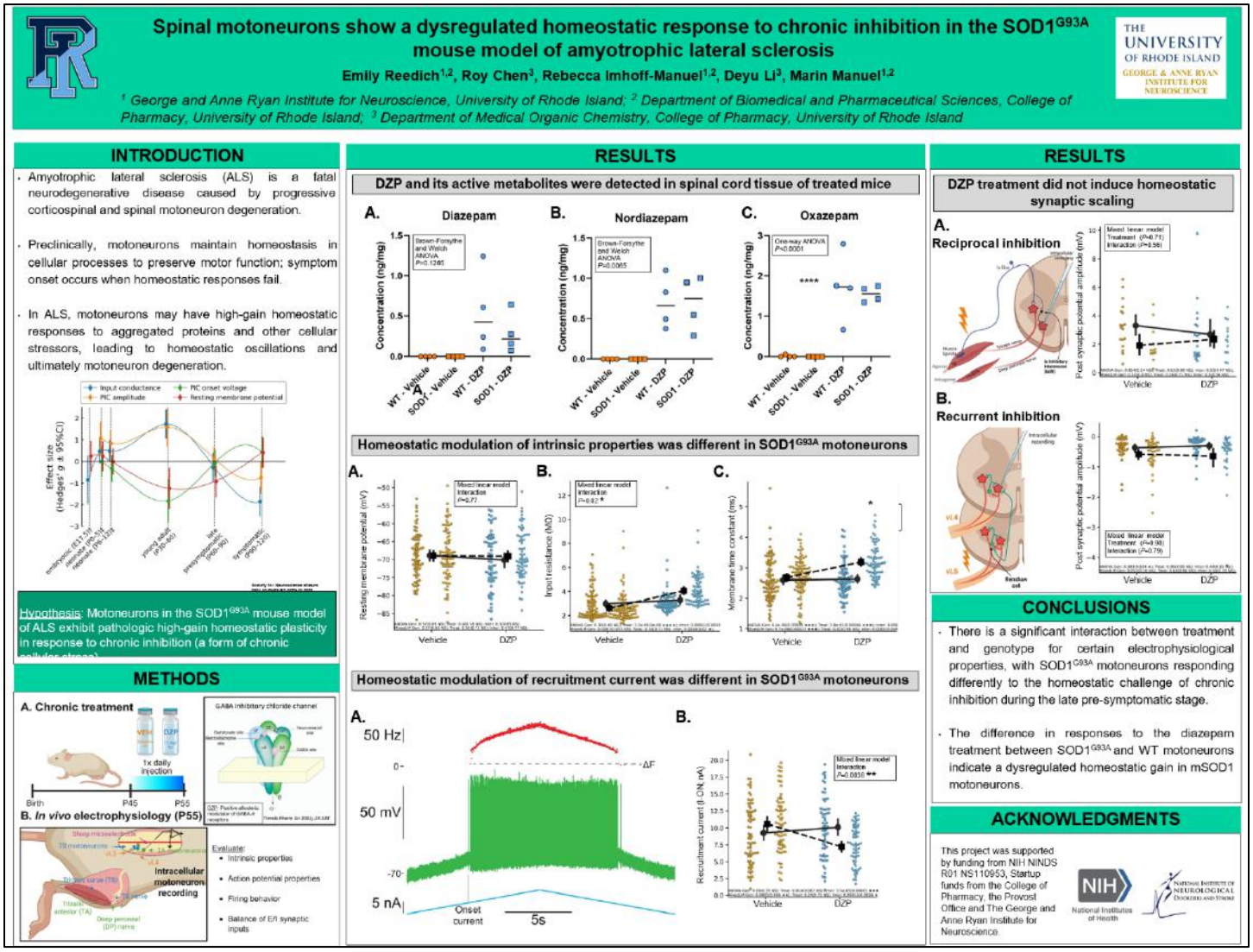
Emily Reedich accepting on behalf of the winning poster

2nd Postdoc / Resident

Xiaoyue Zhu accepting on behalf of the second placed poster

3rd Postdoc / Resident

Tasneem Al Huniti accepting on behalf of the third placed poster

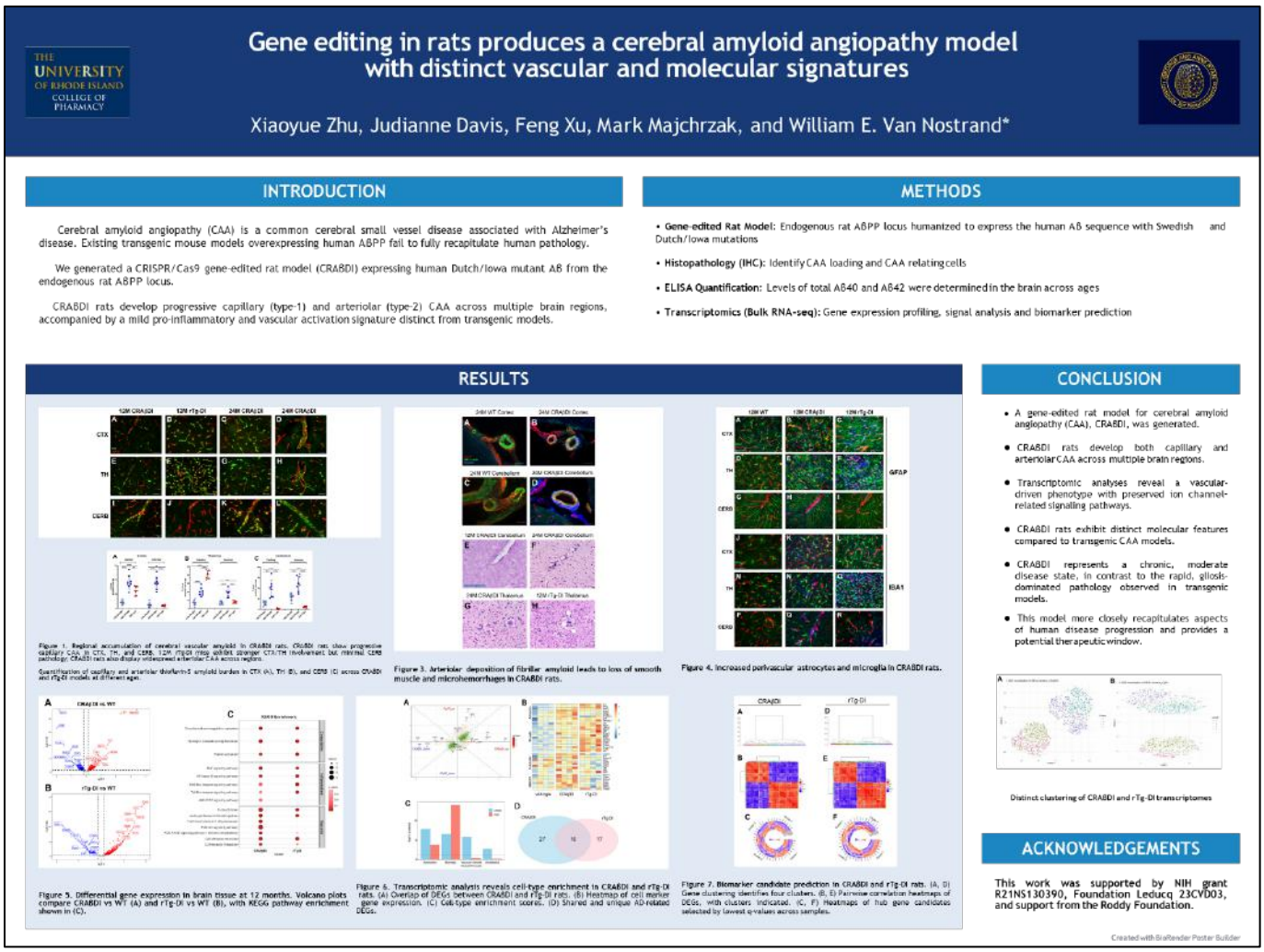


1st Postdoc / Resident

First Place - Spinal motoneurons show a dysregulated homeostatic response to chronic inhibition in the SOD1G93A mouse model of amyotrophic lateral sclerosis

Emily Reedich, Roy Chen, Rebecca Imhoff-Manuel, Deyu Li, Marin Manuel

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease that involves rapid paralysis due to progressive corticospinal and spinal motoneuron degeneration. During the preclinical stage, motoneurons maintain homeostasis in cellular processes to effectively preserve motor function; symptom onset occurs when homeostatic responses fail. In ALS, motoneurons may have dysregulated, high-gain homeostatic responses to aggregated proteins and other cellular stressors, leading to homeostatic oscillations and ultimately motoneuron degeneration. Here, we tested the hypothesis that motoneurons in the SOD1G93A mouse model of ALS exhibit pathologic high-gain homeostatic plasticity in response to chronic inhibition (a form of chronic cellular stress). We treated wild type and SOD1G93A mice in the late pre-symptomatic phase with vehicle (sesame oil) or diazepam (15 mg/kg/day; for 10 days), a benzodiazepine that exerts its effects through enhancing inhibitory neurotransmission mediated by gamma-aminobutyric acid (GABA) receptors. On the last day of treatment, we made in vivo intracellular motoneuron recordings in anesthetized mice and measured motoneuron passive properties, active properties, and assessed synaptic scaling. We found that chronic diazepam treatment induced homeostatic plasticity in wild type and mutant SOD1 motoneurons. For the intrinsic properties of input resistance and membrane time constant, as well as recruitment current on a triangular current ramp (the firing property I-ON), there was a significant interaction between treatment and genotype, with mutant SOD1 motoneurons responding differently to the homeostatic challenge of chronic diazepam treatment. The difference in homeostatic responses to chronic inhibition by diazepam suggests a dysregulated homeostatic gain in mutant SOD1 motoneurons.



2nd
Postdoc / Resident

Second Place - Gene editing in rats produces a cerebral amyloid angiopathy model with distinct vascular and molecular signatures

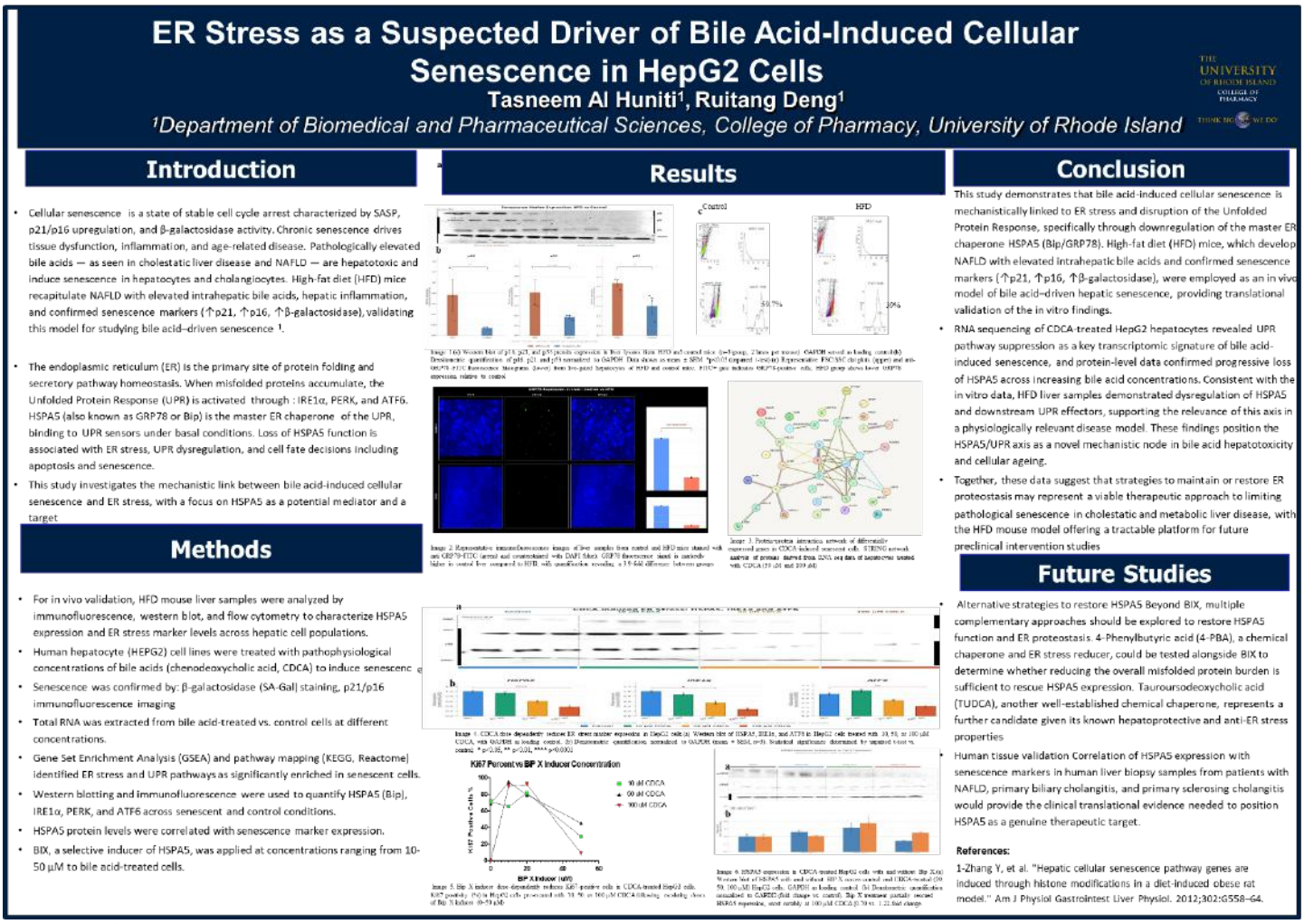
Xiaoyue Zhu, Judianna Davis, Feng Xu, Mark Majchrzak, William E. Van Nostrand

INTRODUCTION: Cerebral amyloid angiopathy (CAA) is a prevalent cerebral small vessel disease linked to Alzheimer's disease and related disorders, with existing transgenic mouse models overexpressing human amyloid β-protein precursor (AβPP) showing limitations in recapitulating human pathology.

METHODS: A gene-edited rat model was generated (CRAβDI) expressing human Dutch/Iowa CAA mutant Aβ via endogenous rat AβPP using CRISPR/Cas9-mediated genome engineering. Pathological and transcriptomic analyses were conducted to assess the resulting CAA phenotype.

RESULTS: CRAβDI rats develop progressive capillary CAA type-1 and significant arteriolar CAA type-2 across multiple brain regions. Transcriptomic analyses reveal a mild pro-inflammatory phenotype with prominent vascular activation, distinguishing it from transgenic models.

DISCUSSION: Gene-edited CRAβDI rats provide a new preclinical model of CAA that exhibits distinct pathological and molecular features compared to transgenic CAA models facilitating improved understanding of disease mechanisms and evaluation of therapeutic strategies.

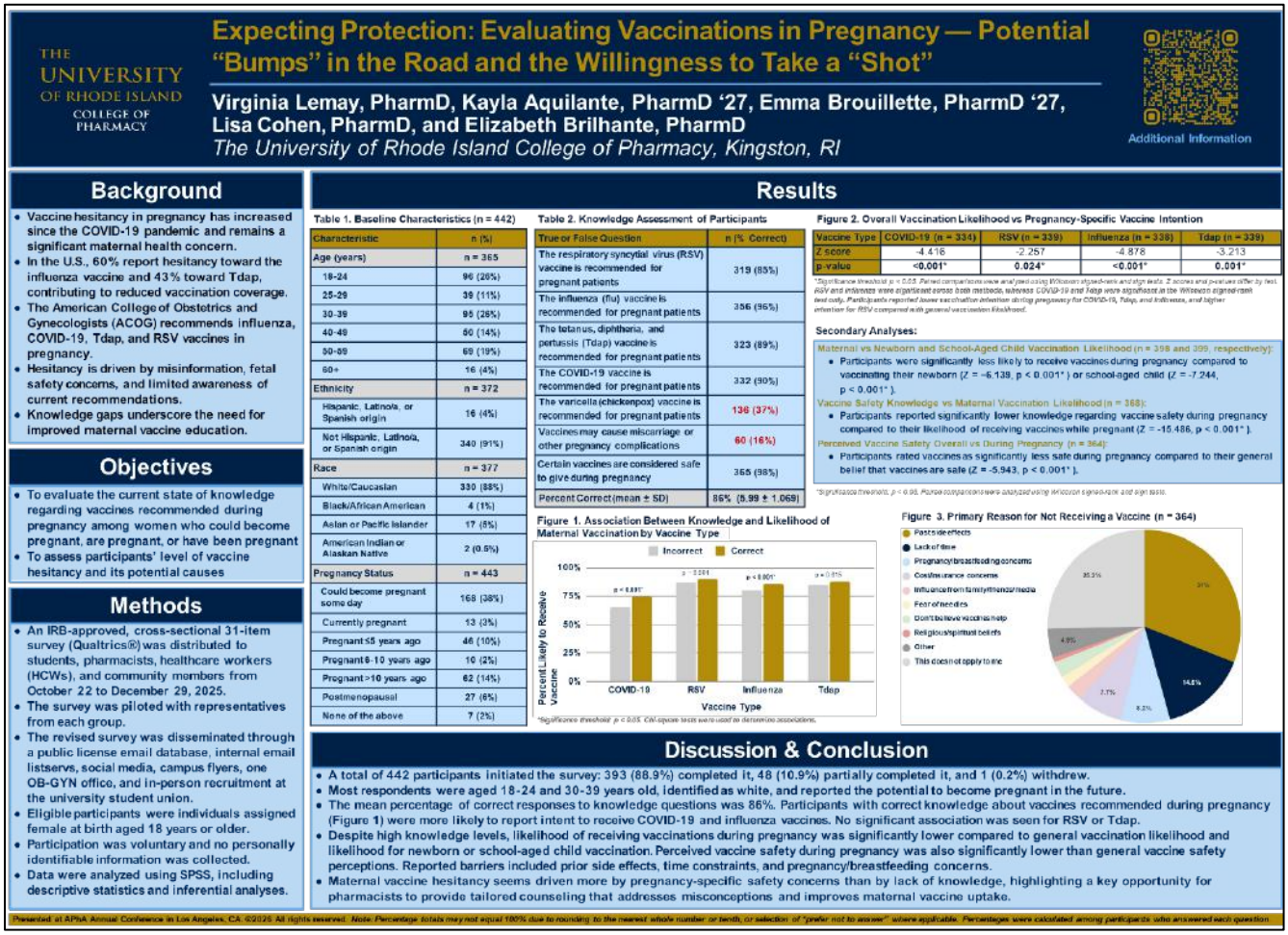


3rd
Postdoc / Resident

Third Place - ER Stress as a Suspected Driver of Bile Acid-Induced Cellular Senescence in HepG2 Cells

Tasneem Al Huniti, Ruitang Deng

Cellular senescence is increasingly recognized as a key driver of metabolic liver disease, yet the mechanisms linking bile acid accumulation to hepatocyte senescence remain poorly understood. Using high-fat diet (HFD)-fed mice as an in vivo model — which exhibit elevated circulating bile acid levels — we investigated whether bile acid accumulation drives hepatocyte senescence and explored the underlying pathways. In vitro, HepG2 cells treated with chenodeoxycholic acid (CDCA; 10, 50, and 100 µM) demonstrated dose-dependent induction of cellular senescence, confirmed by established senescence markers. RNA sequencing and western blot analysis revealed significant downregulation of HSPA5 (GRP78/Bip), a master regulator of ER stress, alongside reduced expression of the ER stress sensors IRE1α and ATF6, suggesting impaired unfolded protein response (UPR) signalling in bile acid-induced senescent cells. To investigate whether restoring HSPA5 function could reverse the senescent phenotype, cells were treated with BIP X inducer across multiple CDCA concentrations. BIP X treatment partially rescued HSPA5 protein levels and reduced Ki67-positive cell loss in a dose-dependent manner, indicating attenuation of the senescence programme. Collectively, these findings suggest that bile acid-driven suppression of the UPR, particularly through HSPA5 downregulation, contributes to hepatocyte senescence and that pharmacological restoration of BiP activity may represent a novel therapeutic strategy in metabolic liver disease.



Expecting Protection: Evaluating Vaccinations in Pregnancy — Potential "Bumps" in the Road and the Willingness to Take a "Shot"

Virginia Lemay, Kayla Aquilante, Emma Brouillette, Lisa Cohen, Elizabeth Brilhante

NOTE: Not included in judging, presented only

Background: Vaccine hesitancy in pregnancy has increased since the COVID-19 pandemic, driven by misinformation, fetal safety concerns, and limited awareness of current recommendations, highlighting the need for improved maternal vaccine education.

Objectives: This study evaluated the current state of knowledge regarding vaccines recommended during pregnancy among women who could become pregnant, are pregnant, or have been pregnant, and assessed vaccine hesitancy and factors contributing to it.

Methods: An IRB-approved, cross-sectional 31-item survey was administered via Qualtrics® to students, pharmacists, other healthcare workers (HCWs), and community members between October 22 and December 29, 2025. The piloted survey was distributed through a public license email database, internal listservs, social media platforms, campus flyers, a single OB-GYN office, and in-person recruitment at the university's student union. Eligible participants were assigned female at birth and aged ≥18 years. Participation was voluntary and anonymous. Data were analyzed using SPSS, including descriptive statistics and inferential analyses.

Results: Among 442 participants who initiated the survey, the mean correct response rate on knowledge questions was 86%. Accurate knowledge about pregnancy-recommended vaccines was associated with higher intent to receive COVID-19 and influenza vaccines. However, there was no significant association seen for RSV or Tdap vaccines. Despite high knowledge, participants reported lower likelihood of vaccination during pregnancy compared with general vaccination or vaccination of newborns/school-aged children. Perceived vaccine safety during pregnancy was also significantly lower than general vaccine safety perceptions. Common barriers included prior side effects, time constraints, and pregnancy/breastfeeding concerns.

Conclusion: Maternal vaccine hesitancy seems driven more by pregnancy-specific safety concerns than by knowledge gaps, underscoring an opportunity for pharmacists to provide targeted counseling to address misconceptions and improve maternal vaccine uptake. Future research should be performed to explore effective strategies to enhance maternal vaccination during pregnancy.

PHP 508

Note summaries are AI generated for these posters

PHP 508

1st PHP508

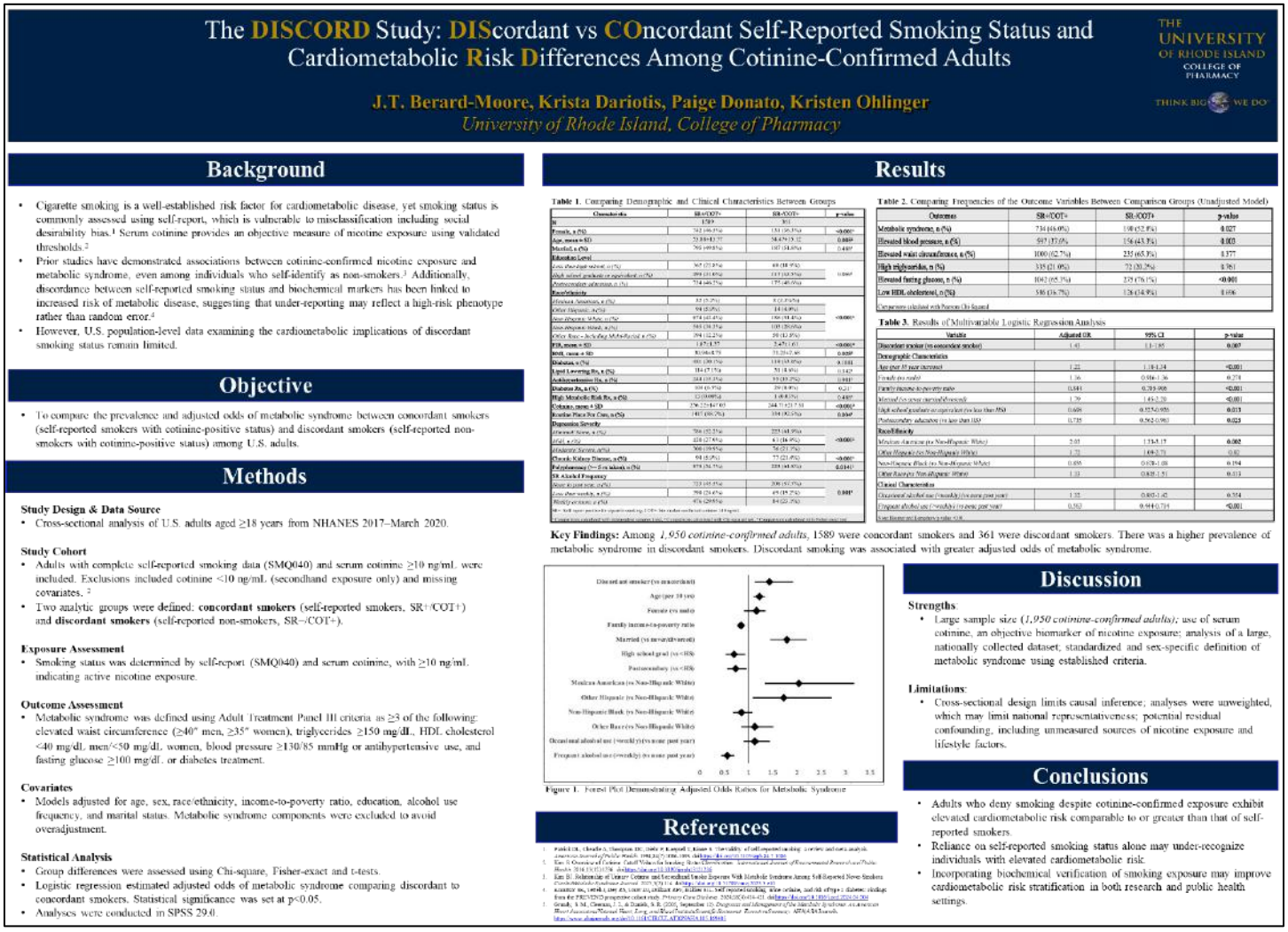
J.T. Berard-Moore, Krista Dariotis, Paige Donato, Kristen Ohlinger

2nd PHP508

Grace Bevins, Andreana Moutopoulos, Sophannara Bun, Dillan Day

3rd PHP508

Kayla Aquilante, Sara Yahya, Nicole Sagias, Andrew Jones



1st PHP508

First Place - The DISCORD Study: DIScordant vs Concordant Self-Reported Smoking Status and Cardiometabolic Risk Differences Among Cotinine-Confirmed Adults

J.T. Berard-Moore, Krista Dariotis, Paige Donato, Kristen Ohlinger

Group 18

Summarizes adults whose smoking status is measured two ways: what they report and what their blood test (serum cotinine) shows. The background explains that self-reported smoking can be inaccurate, and cotinine is an objective marker of nicotine exposure. The objective is to compare metabolic syndrome risk between two cotinine-confirmed groups: people who report smoking (concordant smokers) and people who report not smoking even though cotinine indicates active exposure (discordant smokers). In the discussion and conclusions, the authors report that discordant smokers had a higher prevalence of metabolic syndrome and higher adjusted odds of metabolic syndrome compared with concordant smokers. They conclude that relying on self-report alone can miss people with elevated cardiometabolic risk, and that adding biochemical verification may improve risk identification in research and public health settings.

Comparison of the incidence of gastroesophageal reflux disease in patients taking non-dihydropyridine calcium channel blockers versus dihydropyridine calcium channel blockers.

Grace Bevins, Sophannara Bun, Dillan Day, Andreana Moutopoulos
University of Rhode Island, College of Pharmacy

Background

Gastroesophageal reflux disease (GERD) affects approximately 1 billion people worldwide.[1] Calcium channel blockers (CCBs) are prescribed for cardiovascular diseases, and are known to decrease lower esophageal sphincter tone, contributing to GERD. Dihydropyridine (DHP) and non-dihydropyridine (non-DHP) CCBs differ in their smooth muscle effects, which could differ their effect on GERD. There is currently no data that directly compares the association between GERD with DHP CCBs and non-DHP CCBs.

Objectives

The main objective of this study was to compare the incidence of GERD in patients taking non-DHP CCBs versus those taking DHP CCBs.

Methods

- Data Source: National Health and Nutrition Examination Survey (NHANES) from January 2017 to March 2020.
- Study Design: Cross-sectional survey design of participants receiving any CCB.
- Cohort Selection: Participants taking a DHP or a non-DHP CCB were included. Participants taking both DHP and non-DHP CCBs were excluded.
- Exposure Definition: The exposure of interest was DHP or non-DHP CCB use.
- Outcome Assessment: The outcome of interest was GERD, defined using the ICD-10 code for GERD.
- Covariates: Age, gender, smoking history, alcohol use, and BMI
- Statistical Analysis: For continuous data, P-values were obtained using a Student T-test. For categorical data, P-values were obtained using a Pearson Chi-Square test. A multivariable logistic regression was performed to compare the exposures of interest after adjusting for covariates. All analyses were conducted using SPSS version 29.0 and a significance level of $p < 0.05$ was used.

Results

Table 1. Comparing Demographic and Clinical Characteristics Between DHP and Non-DHP CCB Groups

Characteristics	DHP CCB N=904	Non-DHP CCB N=117	P value
Age, Years, Mean ± SD	65.3 ± 11.9	68.3 ± 11.2	0.010[1]
Gender			
Female, N (%)	454 (50.2)	63 (53.8)	0.461[2]
Male, N (%)	450 (49.8)	81 (46.2)	
Smoked ≥ 100 Cigarettes in Life			
Yes, N (%)	441 (48.8)	61 (52.1)	0.495[2]
No, N (%)	463 (51.2)	56 (47.9)	
Alcohol Use			
≥ Weekly, N (%)	418 (46.3)	53 (45.3)	0.807[2]
< Weekly, N (%)	276 (30.5)	37 (31.6)	
Missing, N (%)	210 (23.2)	27 (23.1)	
BMI*,			
BMI ≥ 30 (Obese), N (%)	415 (45.9)	59 (50.4)	0.116[2]
BMI < 30, N (%)	395 (43.7)	40 (34.2)	
Missing, N (%)	94 (10.4)	18 (15.4)	

Note:
[1]: Student T test; [2]: Chi-square test
*BMI: Body mass index

Table 2. Comparison of GERD Between DHP CCB and Non-DHP CCB Users

Outcome	DHP CCB N=904	Non-DHP CCB N=117	P value
GERD Yes, N (%)	133 (14.7%)	27 (23.1%)	0.019[1]
GERD No, N (%)	771 (85.3%)	90 (76.9%)	

Note:
1: Chi-square test

Table 3. Results of Multivariable Logistic Regression Analysis

Characteristics	Adjusted Odds Ratio	95%CI	P Value
non-DHP CCB vs DHP CCB	1.8	(1.1-3.1)	0.02
Age, every 10 years older	1.2	(1.0-1.4)	0.04
Male vs Female	0.8	(0.5-1.1)	0.18
Smoked ≥ 100 cigarettes in lifetime vs. Smoked < 100 cigarettes	0.9	(0.6-1.4)	0.73
Alcohol use ≥ weekly vs alcohol use < weekly	1.2	(0.8-1.8)	0.39
BMI* ≥ 30 (Obese) vs. BMI < 30	1.2	(0.8-1.8)	0.28

Note:
*BMI: Body mass index

Discussion/Conclusion

- The results of this study suggest that patients taking non-DHP CCBs are approximately 80% more likely to have GERD compared to patients taking DHP CCBs (aOR = 1.8, 95% CI 1.1-3.1)
- Strengths: Use of NHANES data provided a large, nationally representative sample in a cost-effective manner.
- Limitations: The cross-sectional design limits causal inference. Self reported covariates, smoking history and alcohol use, may not accurately reflect behaviors. Unmeasured or unadjusted confounders, such as dose, length of therapy, other medication use, comorbidities, family history, and diet may influence GERD risk.
- Prior studies reported mixed results on the association between DHP and non-DHP CCBs, and GERD,[2,3] but there were no direct comparisons.
- Further studies are needed to determine the true association and guide future drug selection and monitoring parameters.

References

1. Xie F, Yang B, Yan Z, et al. Global temporal trends and projections of gastroesophageal reflux disease prevalence: Age-period-cohort analysis 2021. PLoS One. 2025;20(): e0334396.
2. Hughes J, Lockhart J, Joyce A. Do calcium antagonists contribute to gastro-oesophageal reflux disease and concomitant noncardiac chest pain? Br J Clin Pharmacol. 2007;64:83-9. doi: 10.1111/j.1365-2125.2007.02851.x. Epub
3. Wu JH, Chang CS, Chen GH, Poon SK, Ko CW. Felodipine does not increase the reflux episodes in patients with gastroesophageal reflux disease. Hepatogastroenterology. 2000;47:1328-31.

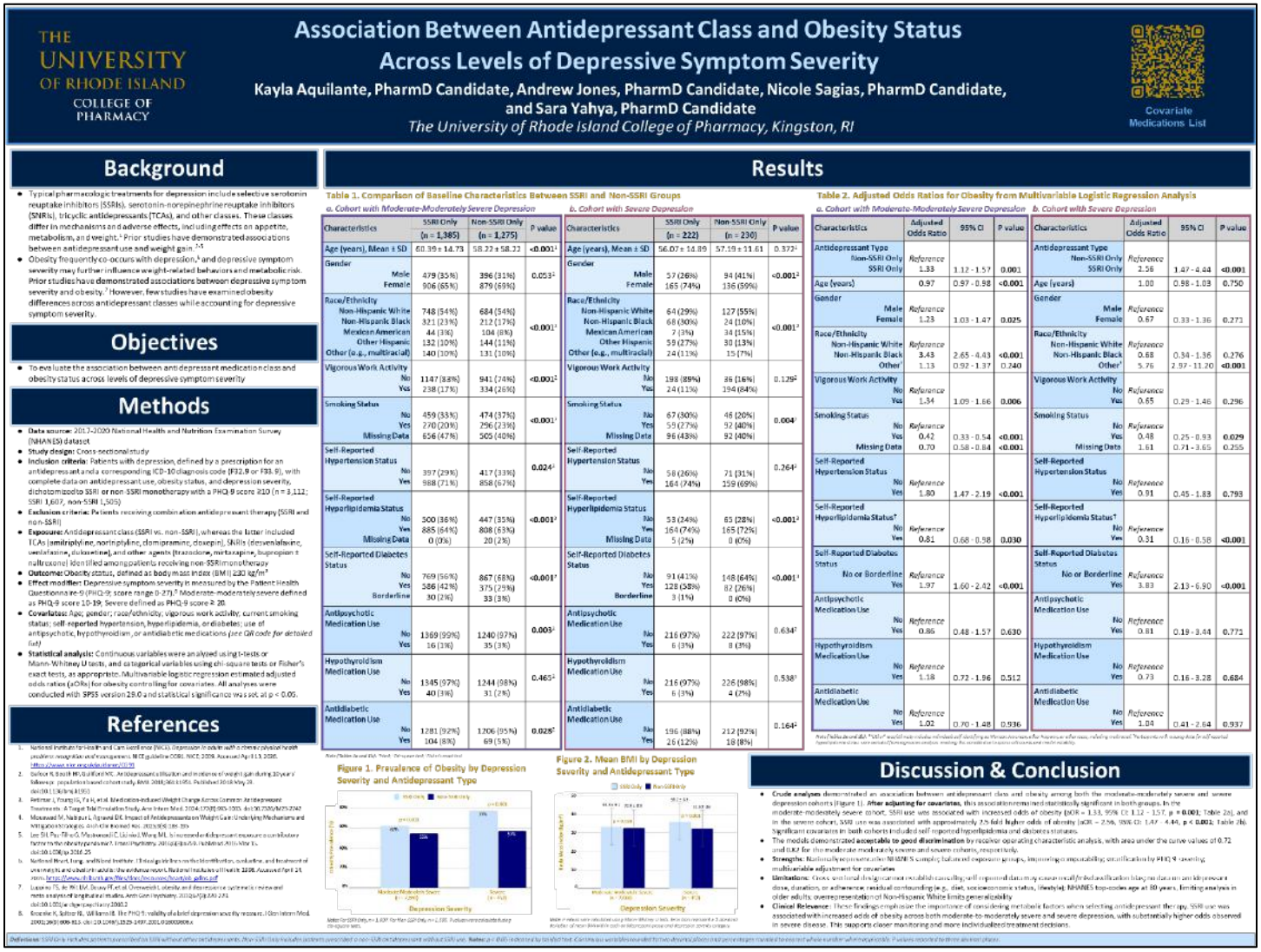
2nd
PHP508

Second Place - Comparison of the incidence of gastroesophageal reflux disease in patients taking non-dihydropyridine calcium channel blockers versus dihydropyridine calcium channel blockers

Grace Bevins, Sophannara Bun, Dillan Day, Andreana Moutopoulos

Group 10

Profiles whether the type of calcium channel blocker (CCB) a person takes is linked to gastroesophageal reflux disease (GERD). The background explains that GERD is very common, and that CCBs can lower the tone of the lower esophageal sphincter, which may contribute to reflux. It also notes that dihydropyridine (DHP) and non-dihydropyridine (non-DHP) CCBs affect smooth muscle differently, and that there has not been direct comparison data on GERD between these two CCB types. The objective is to compare how often GERD occurs in people taking non-DHP CCBs versus DHP CCBs. In the discussion and conclusion, the authors report that non-DHP CCB use was associated with higher likelihood of GERD compared with DHP CCB use after adjustment for several patient factors. They note strengths such as using a large, nationally representative dataset, and limitations such as the cross-sectional design and possible missing factors like dose, duration, diet, and other medications. They conclude that more research is needed to confirm the relationship and help guide medication selection and monitoring.



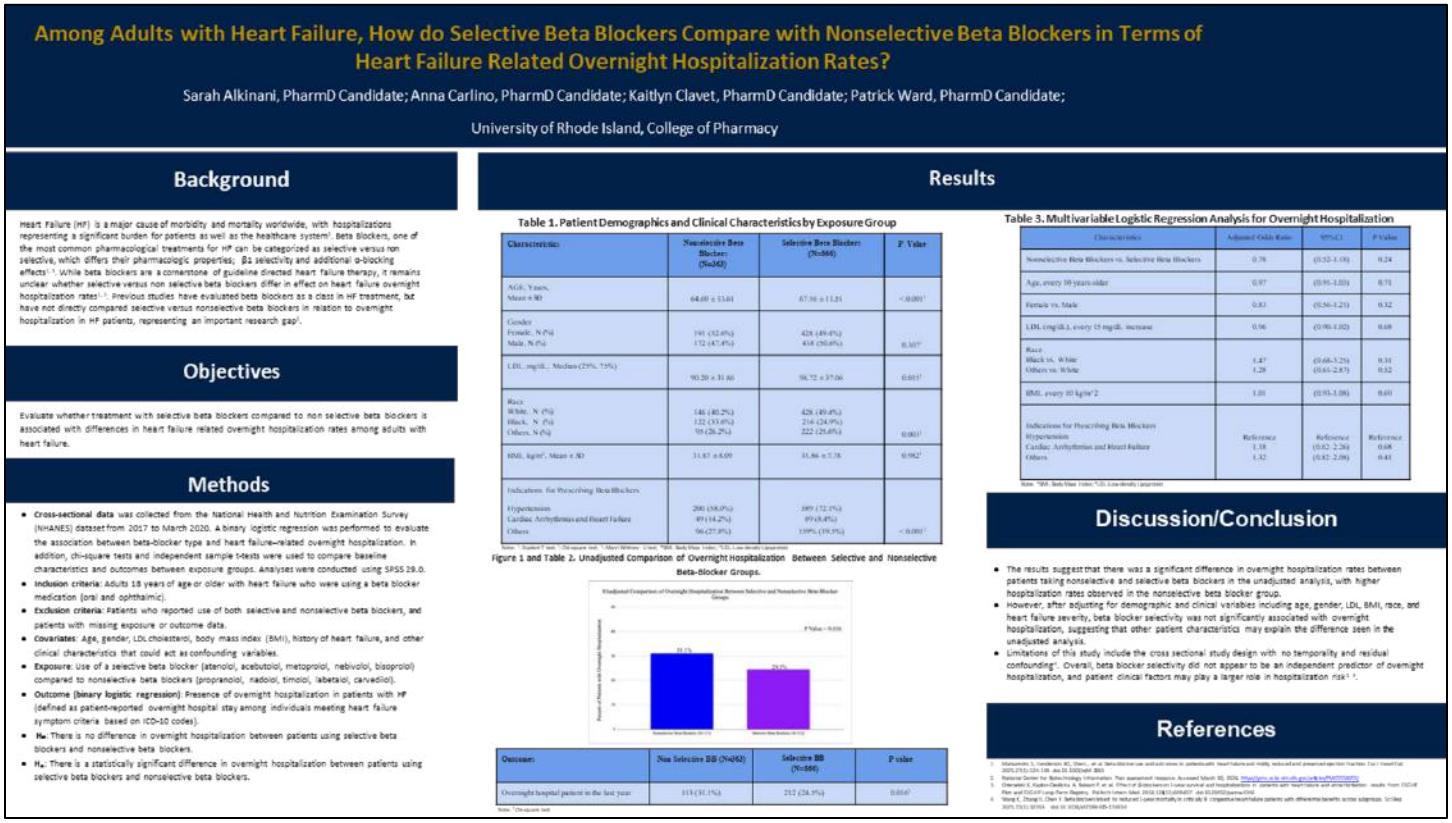
3rd PHP508

Third Place - Association Between Antidepressant Class and Obesity Status Across Levels of Depressive Symptom Severity

Kayla Aquilante, Andrew Jones, Nicole Sagias, Sara Yahya

Group 6

Looks at whether the type of antidepressant a person takes is linked to obesity, and whether that relationship changes depending on how severe their depressive symptoms are. The background explains that different antidepressant classes can affect appetite, metabolism, and weight, and that obesity and depression often occur together. The objective is to compare obesity status between people taking SSRIs versus non-SSRIs while accounting for depression severity measured by PHQ-9. In the discussion and conclusion, the authors report that SSRI use was associated with higher odds of obesity in both the moderate-to-moderately severe and severe depression groups, with a much stronger association in the severe group. They conclude that antidepressant choice should consider metabolic risk and that closer monitoring and more individualized treatment may be especially important for patients with more severe depression.



Among Adults with Heart Failure, How do Selective Beta Blockers Compare with Nonselective Beta Blockers in Terms of Heart Failure Related Overnight Hospitalization Rates?

Sarah Alkinani, Anna Carlino, Kaitlyn Clavet, Patrick Ward

Group 1

Examines whether adults with heart failure who take selective beta blockers have different rates of heart-failure–related overnight hospital stays compared with those taking nonselective beta blockers. The background notes beta blockers are a key treatment for heart failure, but it is unclear if selectivity changes hospitalization risk. In the discussion/conclusion, the authors report that nonselective beta blockers appeared linked to higher hospitalization in the unadjusted comparison, but after accounting for patient differences, beta-blocker selectivity was not an independent predictor; they conclude other clinical factors likely play a larger role.

THE UNIVERSITY OF RHODE ISLAND COLLEGE OF PHARMACY

Association Between Serum Cotinine Levels and Systemic Inflammation Among Self-Reported Non-Smoking Adults

Ava Scarpaci, PharmD Candidate; Griffin Geist, PharmD Candidate; Hailey Joo, PharmD Candidate; Ramez Rizk, PharmD/MS Candidate
University of Rhode Island College of Pharmacy, Kingston, RI

Background

Cotinine, the primary metabolite of nicotine, is the gold standard biomarker of recent nicotine exposure from active or secondhand smoke.[1] Smoking status is often measured by self-report, but self-report may underestimate true exposure.[2] Prior studies have mainly focused on validating self-reported smoking or on inflammation in smokers and secondhand smoke exposure more broadly. Less is known about whether self-reported non-smoking adults with detectable cotinine also have higher high-sensitivity C-reactive protein (hs-CRP), a biomarker of systemic inflammation linked to future cardiovascular risk.[3] This subgroup may represent a hidden at-risk population that is missed when smoking status is based on self-report alone.

Objectives

To examine whether elevated serum cotinine levels among self-reported non-smoking adults are associated with elevated hs-CRP compared with those with undetectable cotinine.

Methods

Design and Data Source: Cross-sectional study using data from the National Health and Nutrition Examination Survey (NHANES), a nationally representative survey of the U.S. civilian, noninstitutionalized population (2017 to March 2020).[4]

Inclusion Criteria: Adults aged ≥18 years who self-reported not smoking and had available serum cotinine and hs-CRP data

Exclusion: Participants reporting current smoking or with missing data on serum cotinine levels or hs-CRP.

Exposure: Serum cotinine categorized as undetectable (<0.05 ng/mL) and detectable cotinine (>0.05 ng/mL), which was classified as low/moderate (0.05-0.215 ng/mL), and high (>0.215 ng/mL), with undetectable cotinine as reference group.

Outcome: Elevated high-sensitivity C-reactive protein (hs-CRP), defined as >3 mg/L, a clinically established threshold indicating higher systemic inflammation and cardiovascular risk.[3]

Covariates: Age, sex, race/ethnicity, body mass index, diabetes mellitus, high cholesterol, and hypertension were included as adjustment variables in regression models. Education level and ratio of family income to poverty were also included to examine differences in socioeconomic characteristics.

Statistical analysis: Baseline characteristics were compared using independent-samples t-tests for continuous variables and chi-square tests for categorical variables (Table 1). Elevated hs-CRP across cotinine exposure groups was compared using chi-square tests, and the Cochran-Armitage trend test assessed linear trend across ordered exposure levels (Table 2, Figure 1). Multivariable logistic regression estimated adjusted odds ratios with 95% confidence intervals while controlling for confounders (Table 3). All analyses were conducted using SPSS version 29.0. P-value < 0.05 was considered statistically significant.

Results

Table 1: Baseline Demographic and Clinical Characteristics: Undetectable vs Low/Moderate vs High Cotinine*

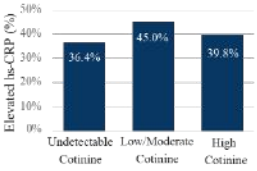
Variable	Undetectable	Low/Moderate	High	p-value
Age, mean ± SD	61.69 ± 15.42	57.73 ± 15.87	50.60 ± 17.83	<0.001[a]
Sex, n (%)				0.021[b]
Male	684 (60.1%)	147 (55.9%)	337 (65.5%)	
Female	454 (39.9%)	116 (44.1%)	177 (34.4%)	
Race, n (%)				<0.001[b]
Mexican American	157 (13.8%)	23 (8.7%)	43 (8.4%)	
Other Hispanic	128 (11.2%)	24 (9.1%)	25 (4.9%)	
Non-hispanic White	568 (49.9%)	102 (38.8%)	228 (44.4%)	
Non-hispanic Black	155 (13.6%)	81(30.8%)	146 (28.4%)	
Other race	130 (11.4%)	33 (12.5%)	72 (14.0%)	
BMI, mean ± SD	30.63 ± 7.00	32.87 ± 8.02	30.58 ± 7.38	<0.001[a]
Hypertension n (%)	592 (52.0%)	133 (50.6%)	211 (41.1%)	<0.001[b]
Diabetes n (%)	260 (22.8%)	64 (24.3%)	90 (17.5%)	0.011[b]
High Cholesterol n (%)	591 (51.9%)	117 (44.5%)	178 (34.6%)	<0.001[b]
Education level, n (%)				<0.001[b]
Less than 12th grade or without diploma	217 (19.1%)	58 (22.1%)	104 (20.2%)	
High school graduate/GED or equivalent	247 (21.7%)	70 (26.6%)	158 (30.7%)	
Some college or AA degree	375 (33.0%)	99 (37.6%)	187 (36.4%)	
College graduate or above	296 (26.0%)	34 (12.9%)	58 (11.3%)	
Ratio of family income to poverty, mean ± SD	2.97 ⊥ 1.57	2.22 ⊥ 1.48	2.37 ⊥ 1.53	<0.001[a]

*Undetectable, low-moderate, and high cotinine were defined as <0.05 ng/mL, 0.05–0.215 ng/mL, and >0.215 ng/mL serum cotinine, respectively.
[a] P-values from one-way ANOVA for continuous variables. [b] P-values from chi-square test for categorical variables.

Results: Participants with higher cotinine exposure were younger (p<0.001). BMI differed significantly across groups (p<0.001), with the highest values observed in the low–moderate exposure group. Cotinine exposure also differed significantly by sex, race/ethnicity, education level, hypertension, diabetes, high cholesterol, and family income to poverty ratio.

Table 2/Figure 1: Unadjusted Comparison of Elevated hs-CRP by Cotinine Exposure Levels

Cotinine Exposure	Elevated hs- CRP*	Non-Elevated hs-CRP*	Total	p-value
Undetectable Cotinine (<0.05 ng/mL)	410 (36.4%)	716 (63.6%)	1126	0.011[1]
Low/moderate Cotinine levels (0.05-0.215 ng/mL)	116 (45.0%)	142 (55.0%)	258	0.17[2]
High Cotinine Levels (>0.215 ng/mL)	203 (39.8%)	307 (60.2%)	510	0.19[3]
Overall Comparison			1894	0.03[4]



*Elevated and non-elevated hs-CRP is defined as >3 mg/L and ≤3 mg/L, respectively
1. Pairwise chi-square test: undetectable vs low/moderate cotinine
2. Pairwise chi-square test: low/moderate vs high cotinine
3. Pairwise chi-square test: undetectable vs high cotinine
4. Overall chi-square test across all cotinine groups: $X^2(2) = 6.99$, $p = 0.03$

Results: The prevalence of elevated hs-CRP differed across cotinine groups: undetectable (36.4%, n=410), low/moderate (45.0%, n=116), and high (39.8%, n=203). The overall chi-square test was significant ($X^2(2) = 6.99$, $p = 0.03$). Pairwise comparisons showed that only the difference between the undetectable and low/moderate cotinine groups was statistically significant ($p = 0.011$). The Cochran-Armitage trend test was not significant ($Z = 1.62$, $p = 0.11$), indicating no significant linear trend across ordered cotinine exposure levels.

Table 3: Results of Multivariable Logistic Regression Analyses for Elevated hs-CRP

Cotinine Exposure	Adjusted* odds ratio (95% CI)	p-value
Undetectable Cotinine (<0.05 ng/mL)	Reference	--
Detectable Cotinine (>0.05 ng/mL)	1.261 (1.006-1.581)	0.044
Undetectable Cotinine (<0.05 ng/mL)	Reference	--
Low/moderate Cotinine levels (0.05-0.215 ng/mL)	1.159 (0.845 - 1.589)	0.360
High Cotinine Levels (>0.215 ng/mL)	1.325 (1.022 - 1.719)	0.034

*Adjusted for age, sex, race/ethnicity, body mass index, diabetes mellitus, high cholesterol, and hypertension

Results: Detectable cotinine was associated with higher adjusted odds of elevated hs-CRP compared with no detectable cotinine (aOR=1.261). High cotinine was associated with higher adjusted odds of elevated hs-CRP compared with no detectable cotinine (aOR=1.325), whereas low/moderate cotinine was not significantly associated with elevated hs-CRP compared with no detectable cotinine (aOR=1.159). Both logistic regression models demonstrated acceptable fit based on the Hosmer-Lemeshow goodness-of-fit test, with χ^2=2.535, df=8, p=0.960 and χ^2=5.582, df=8, p=0.694, respectively.

Discussion

- In the unadjusted comparisons, the pattern was not strictly linear, since the only significant pairwise difference was between the undetectable and low/moderate groups and the Cochran-Armitage trend test was not significant. However, after adjustment for key covariates, detectable cotinine was associated with higher odds of elevated hs-CRP, and the strongest adjusted association was observed in the high-cotinine group.
- These findings are supported by related, though not directly comparable, studies showing that secondhand smoke exposure has been associated with higher inflammatory markers in other populations, including never-smokers, nonsmoking youth, and occupational cohorts. There are also prior reports of higher CRP among never-smokers exposed to secondhand smoke, as well as elevated inflammatory biomarkers in cotinine-exposed workers and youth.
- The association is biologically plausible because tobacco-smoke exposure, including secondhand exposure, has been linked to inflammation, oxidative stress, and endothelial dysfunction.[5] Cotinine should be interpreted primarily as an objective exposure biomarker that identifies recent nicotine exposure rather than the sole causal mediator.
- Strengths include use of different levels of serum cotinine rather than a binary comparison alone, use of a clinically significant measure of inflammation (hs-CRP), a large nationally representative NHANES sample, and multivariable adjustment for major demographic and clinical covariates.
- Limitations include the cross-sectional design, possible residual confounding (exposure duration, environment, stress), no separate classification of former smokers, possible influence of recent acute inflammatory illness on hs-CRP, and reliance on a single cotinine measurement that reflects recent rather than long-term exposure.

Conclusion

Among self-reported non-smoking adults, detectable cotinine was associated with elevated hs-CRP, with the strongest association observed in the high cotinine group. These findings suggest a potential concentration-response relationship that should be further investigated and indicate that objective nicotine exposure assessment may identify hidden inflammatory risk not captured by self-report alone.

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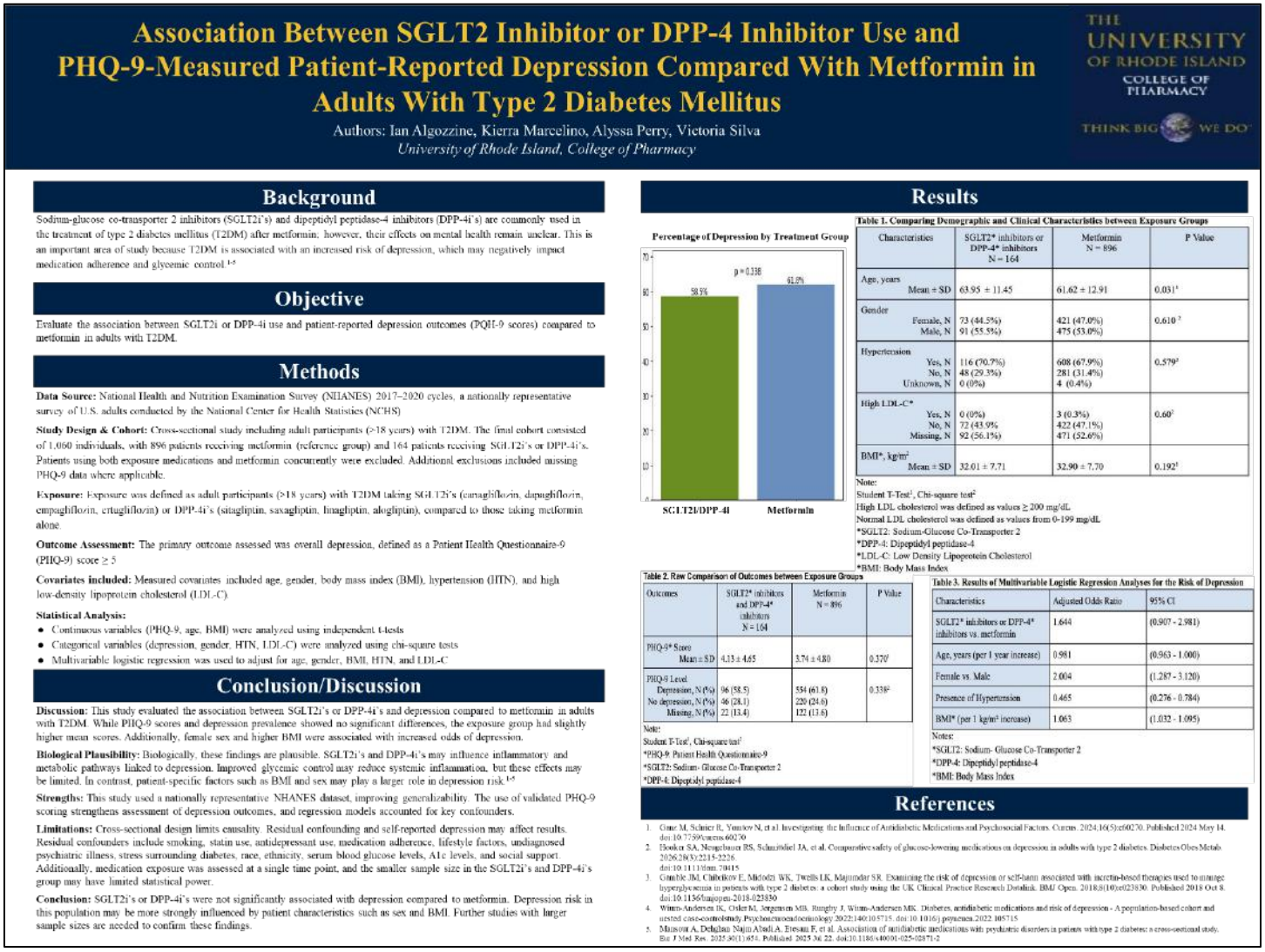
Association Between Serum Cotinine Levels and Systemic Inflammation Among Self-Reported Non-Smoking Adults

Ava Scarpaci, Griffin Geist, Hailey Joo, Ramez Rizk

Group 2

Explores adults who say they do not smoke, but may still be exposed to nicotine (for example through secondhand smoke). The background explains that cotinine is a reliable blood marker of recent nicotine exposure, and that relying on self-reported non-smoking can miss people with real exposure. The objective is to see whether non-smokers with detectable cotinine also have higher levels of hs-CRP, a marker of body-wide inflammation linked to future cardiovascular risk. In the discussion and conclusion, the authors report that detectable cotinine was associated with higher odds of elevated hs-CRP, with the strongest association in the higher-cotinine group. They conclude that objective cotinine testing may help identify a “hidden” group of self-reported non-smokers with higher inflammation risk that would not be recognized using self-report alone.

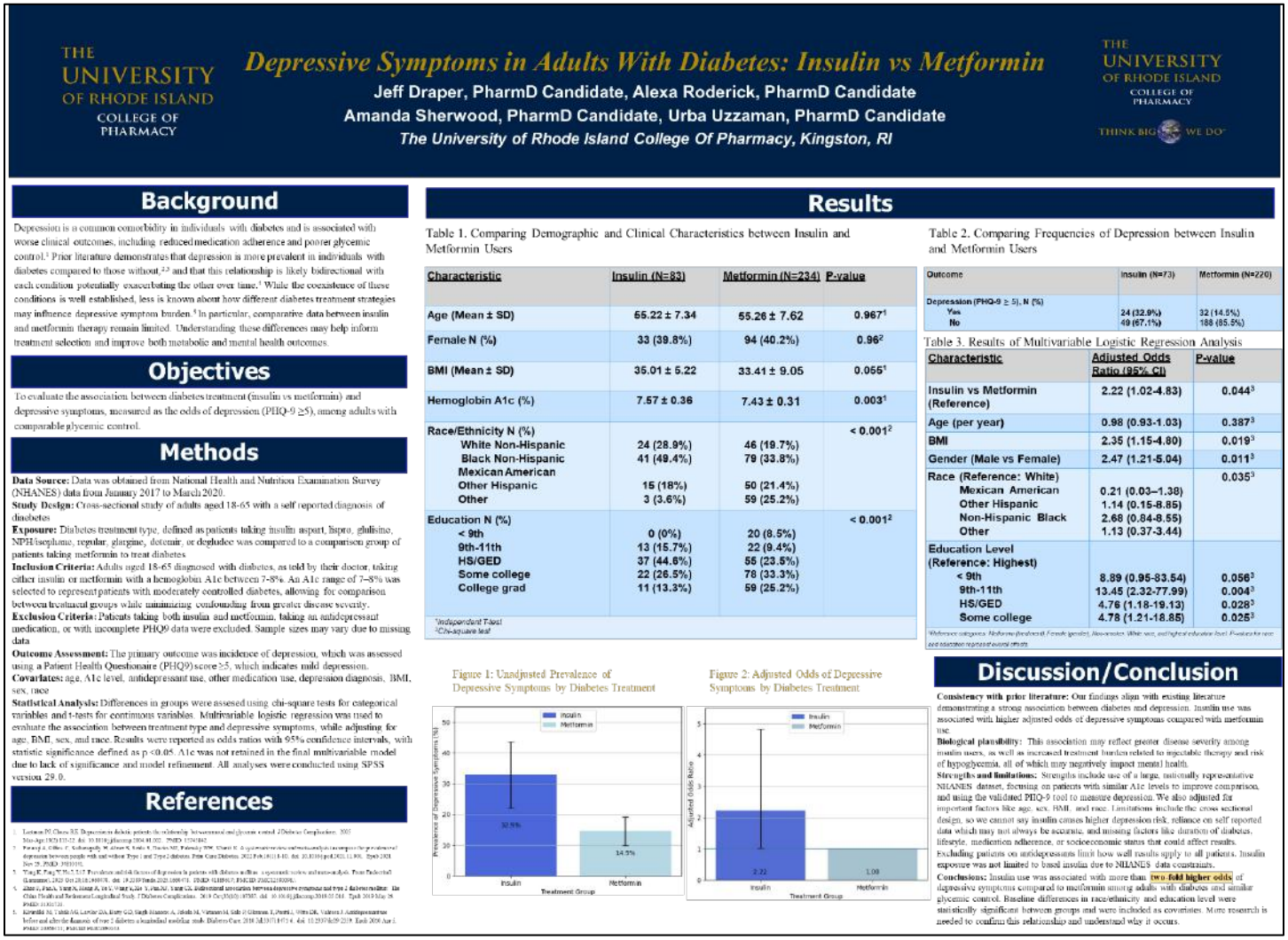


Association Between SGLT2 Inhibitor or DPP-4 Inhibitor Use and PHQ-9-Measured Patient-Reported Depression Compared With Metformin in Adults With Type 2 Diabetes Mellitus

Ian Algozzine, Kierra Marcelino, Alyssa Perry, Victoria Silva

Group 3

Analyzes adults with type 2 diabetes and examines whether taking an SGLT2 inhibitor or a DPP-4 inhibitor is linked to different patient-reported depression outcomes compared with taking metformin. The background explains that these diabetes medicines are commonly used after metformin, but their mental health effects are not clear, and depression is an important concern in type 2 diabetes because it can affect medication use and blood sugar control. In the discussion, the authors report that PHQ-9 scores and the overall rate of depression did not differ significantly between the treatment groups, although the SGLT2/DPP-4 group had slightly higher average scores. They also note that factors like being female and having a higher BMI were associated with higher odds of depression. The conclusion is that SGLT2 inhibitors or DPP-4 inhibitors were not significantly associated with depression compared with metformin, and that patient characteristics may matter more; they recommend larger studies to confirm the findings.

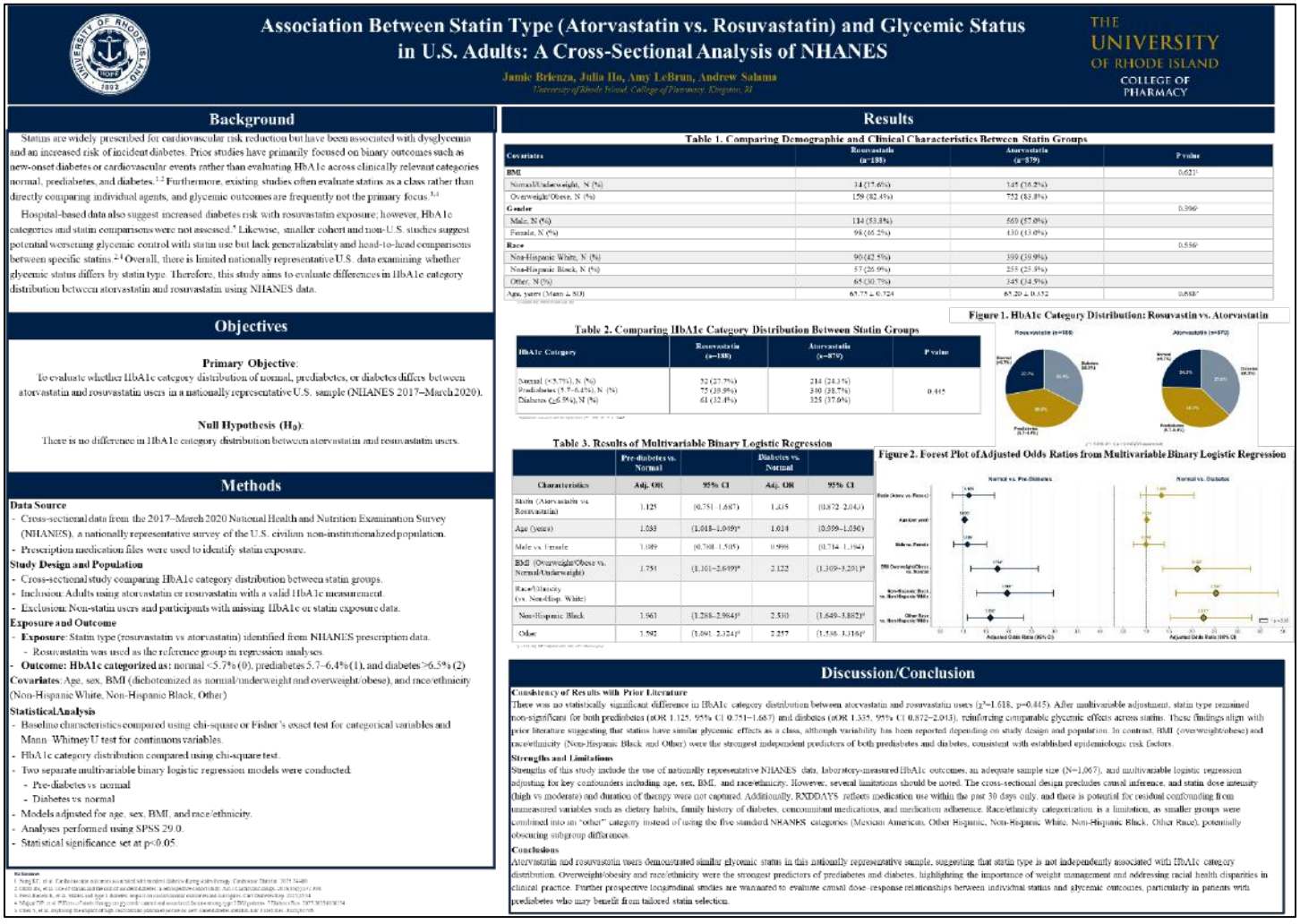


Depressive Symptoms in Adults With Diabetes: Insulin vs Metformin

Jeff Draper, Alexa Roderick, Amanda Sherwood, Urba Uzzaman

Group 4

Investigates depression symptoms in adults with diabetes and compares people treated with insulin versus metformin. The background explains that depression is common in diabetes and can worsen outcomes, but it is less clear whether different diabetes treatments relate to differences in depression symptoms. The objective is to test whether treatment type (insulin vs metformin) is associated with depressive symptoms measured using the PHQ-9. In the discussion and conclusion, the authors report that insulin use was associated with higher odds of depressive symptoms compared with metformin among adults with similar blood sugar control. They suggest this may be related to greater illness severity and the added burden of injectable therapy and hypoglycemia risk. They note that the study cannot prove cause and effect and may miss other factors that influence depression, but conclude that insulin users may have higher risk and that more research is needed to confirm and explain the relationship.

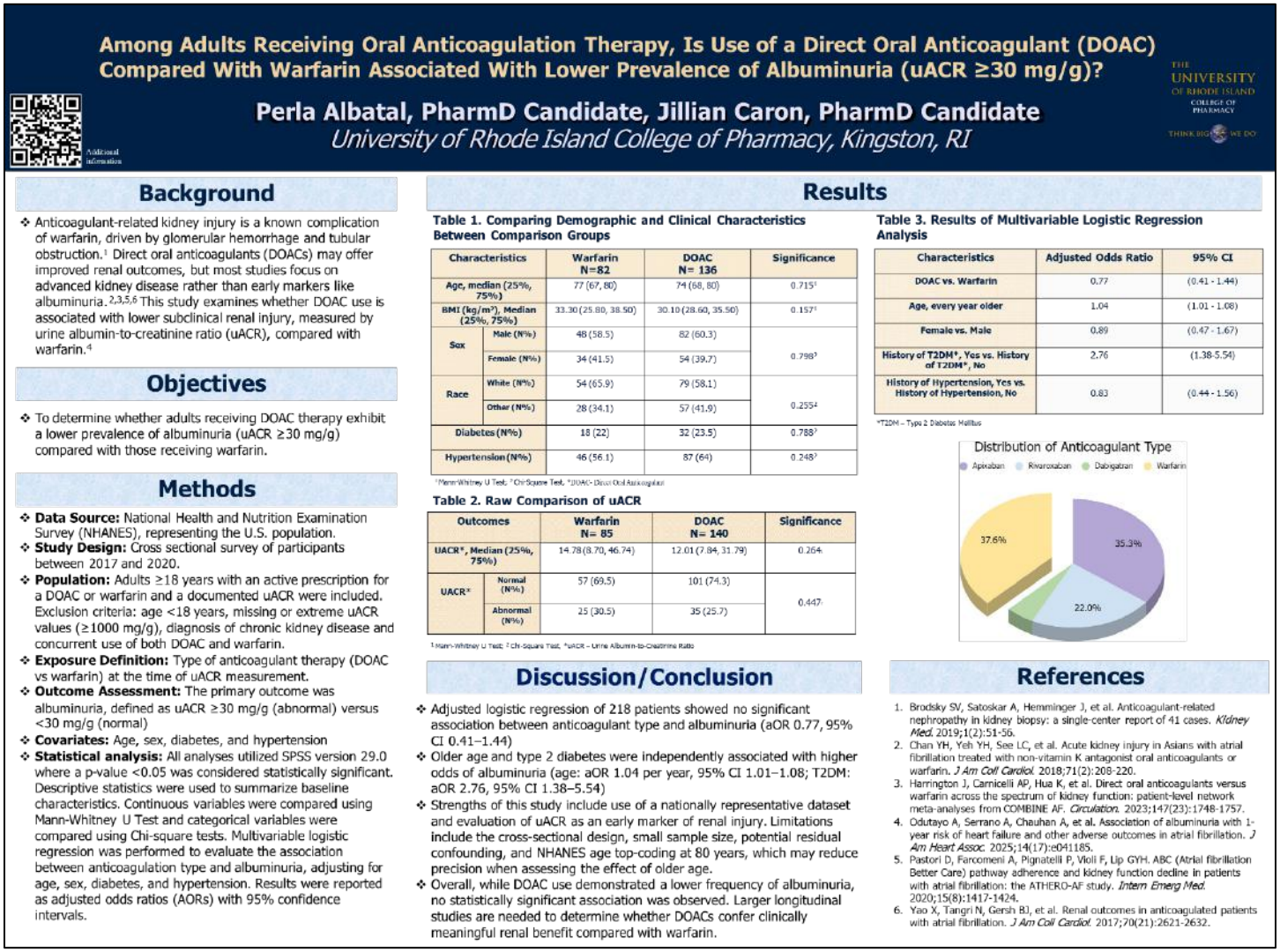


Association Between Statin Type (Atorvastatin vs. Rosuvastatin) and Glycemic Status in U.S. Adults: A Cross-Sectional Analysis of NHANES

Jamie Brienza, Julia Ho, Amy LeBrun, Andrew Salama

Group 5

Reviews whether two common statins—atorvastatin and rosuvastatin—are linked to different blood sugar status in U.S. adults. The background explains that statins have been associated with higher diabetes risk, but many studies focus on "new diabetes" as a yes/no outcome and often do not compare specific statins or look at HbA1c categories. The objective is to see if the distribution of HbA1c categories (normal, prediabetes, diabetes) differs between atorvastatin and rosuvastatin users using NHANES data. In the discussion and conclusion, the authors report no meaningful difference in HbA1c category distribution between the two statins, and statin type was not an independent predictor after adjustment. They note that factors such as overweight/obesity and race/ethnicity were stronger predictors of being in the prediabetes or diabetes categories. They conclude that atorvastatin and rosuvastatin users showed similar glycemic status in this sample, and suggest future studies to better understand whether dose and longer-term use could matter.

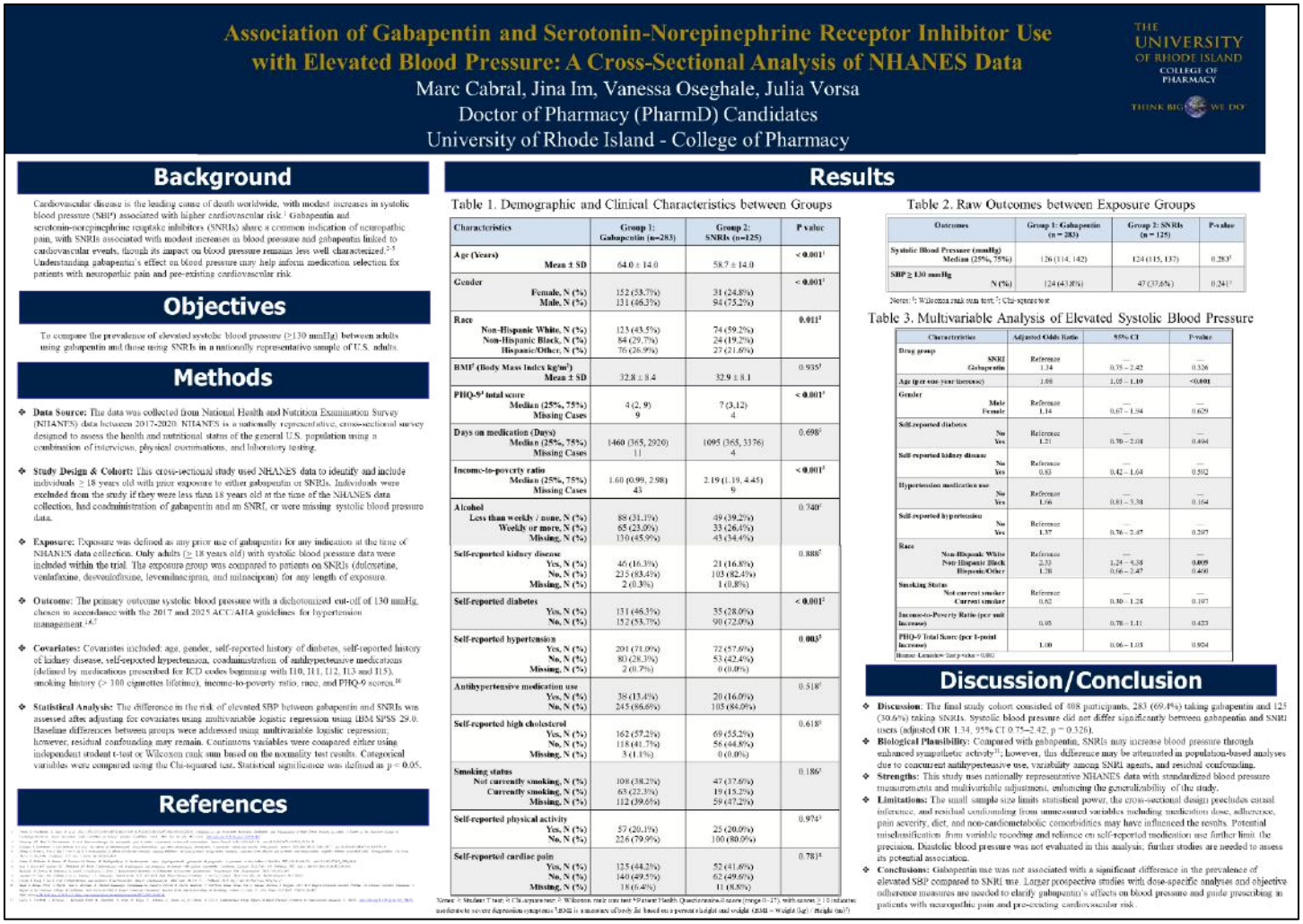


Among Adults Receiving Oral Anticoagulation Therapy, Is Use of a Direct Oral Anticoagulant (DOAC) Compared With Warfarin Associated With Lower Prevalence of Albuminuria (uACR ≥30 mg/g)?

Perla Albatal, Jillian Caron

Group 7

Tests whether adults taking a direct oral anticoagulant (DOAC) have a lower rate of early kidney injury compared with adults taking warfarin. The background explains that warfarin can cause kidney injury, and that prior research on DOACs often focuses on people with more advanced kidney disease rather than early warning signs like albumin in the urine. The objective is to compare albuminuria (based on the urine albumin-to-creatinine ratio) between DOAC and warfarin users. In the discussion and conclusion, the authors report that although albuminuria was less common in the DOAC group, the adjusted analysis did not find a statistically significant difference between DOACs and warfarin. They also note that older age and type 2 diabetes were linked to higher odds of albuminuria. They conclude that larger, longer-term studies are needed to determine whether DOACs provide meaningful kidney benefit compared with warfarin.

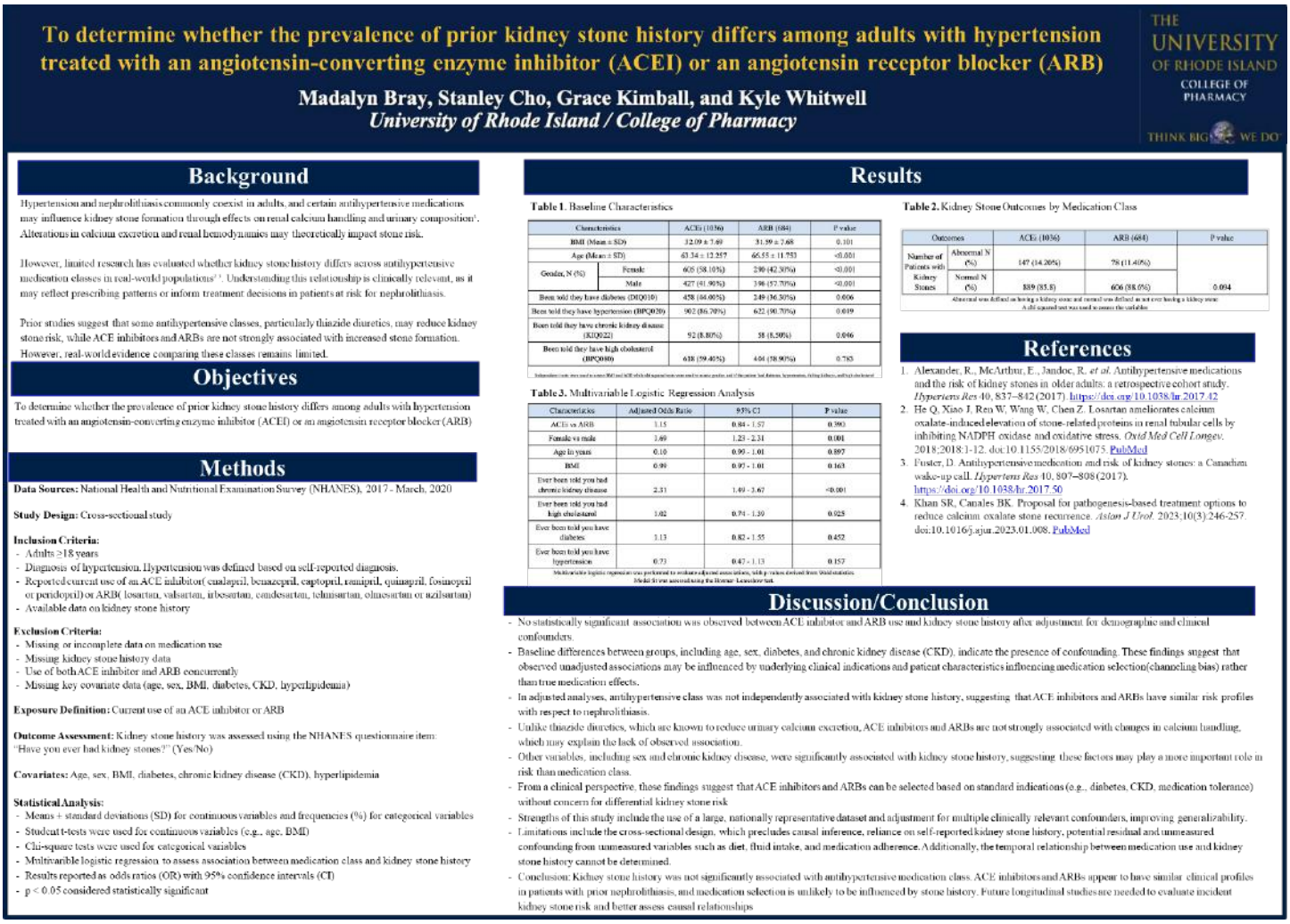


Association of Gabapentin and Serotonin-Norepinephrine Receptor Inhibitor Use with Elevated Blood Pressure: A Cross-Sectional Analysis of NHANES Data

Marc Cabral, Jina Im, Vanessa Oseghale, Julia Vorsa

Group 8

Summarizes blood pressure in adults using gabapentin versus adults using SNRIs, using NHANES data. The background explains that even modest increases in systolic blood pressure can raise cardiovascular risk, that gabapentin and SNRIs are both used for neuropathic pain, and that SNRIs are known to raise blood pressure slightly while gabapentin's effect on blood pressure is less clear. The objective is to compare how common elevated systolic blood pressure (at or above 130 mmHg) is in gabapentin users versus SNRI users. In the discussion and conclusion, the authors report that systolic blood pressure did not differ significantly between the two groups after adjustment. They note possible reasons this difference might be hard to detect in a population sample (such as other medications and differences among SNRI drugs) and point out limits such as cross-sectional design and possible confounding. They conclude that gabapentin was not associated with a meaningful difference in elevated systolic blood pressure compared with SNRIs, and that larger future studies are needed to clarify gabapentin's effect on blood pressure.

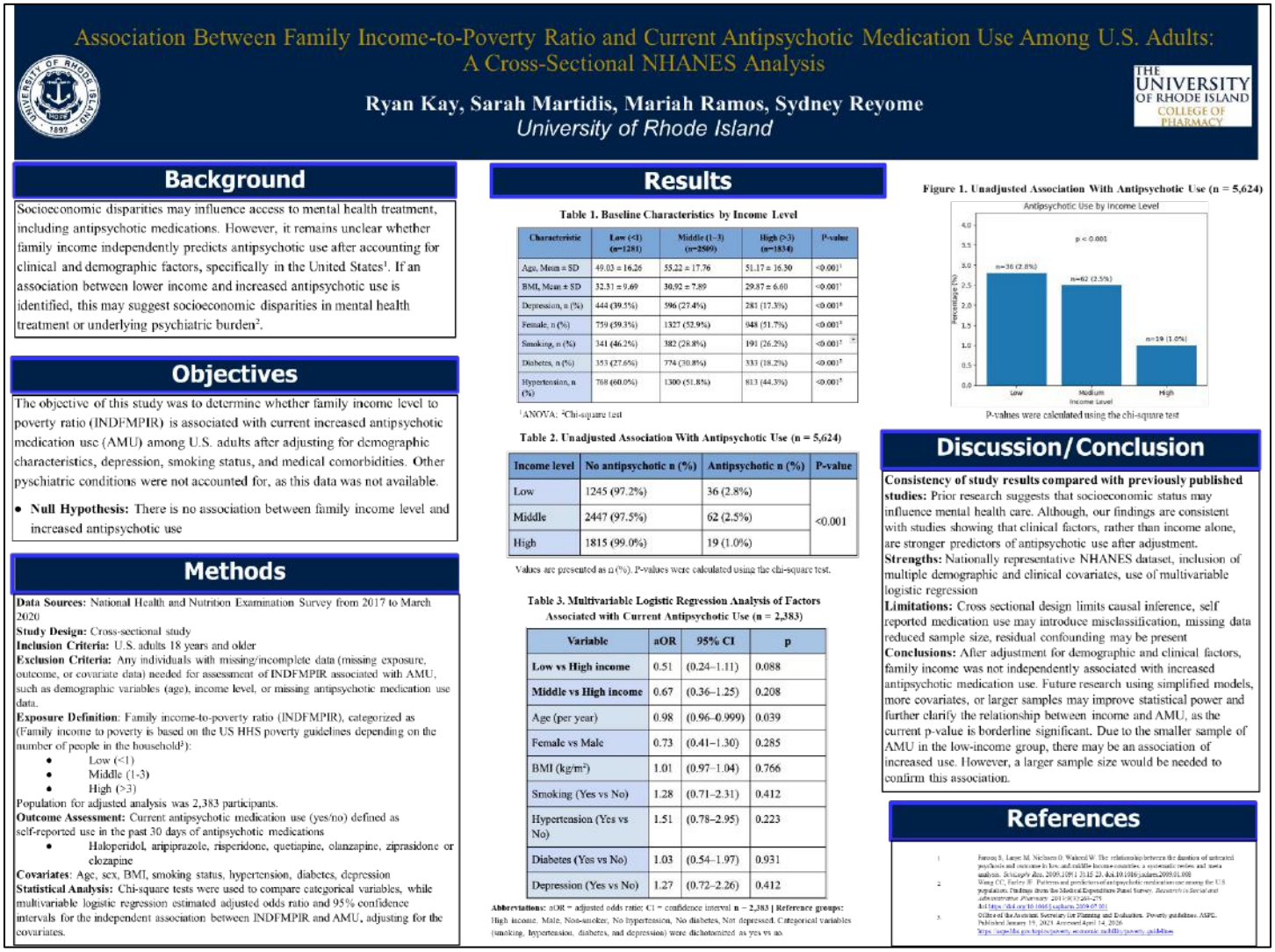


To determine whether the prevalence of prior kidney stone history differs among adults with hypertension treated with an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB)

Madalyn Bray, Stanley Cho, Grace Kimball, Kyle Whitwell

Group 9

Studies adults with hypertension and examines whether having a history of kidney stones differs between people taking ACE inhibitors and people taking ARBs. The background explains that hypertension and kidney stones often occur together, and some blood pressure medicines may affect stone risk, but there is limited real-world research comparing ACE inhibitors and ARBs for kidney stone history. In the discussion and conclusion, the authors report that after accounting for patient differences, there was no significant association between ACE inhibitor versus ARB use and kidney stone history. They conclude that ACE inhibitors and ARBs appear to have similar kidney stone risk profiles, so medication choice can be based on usual clinical reasons rather than concern about different stone risk, and they recommend future longitudinal studies to better assess cause-and-effect.

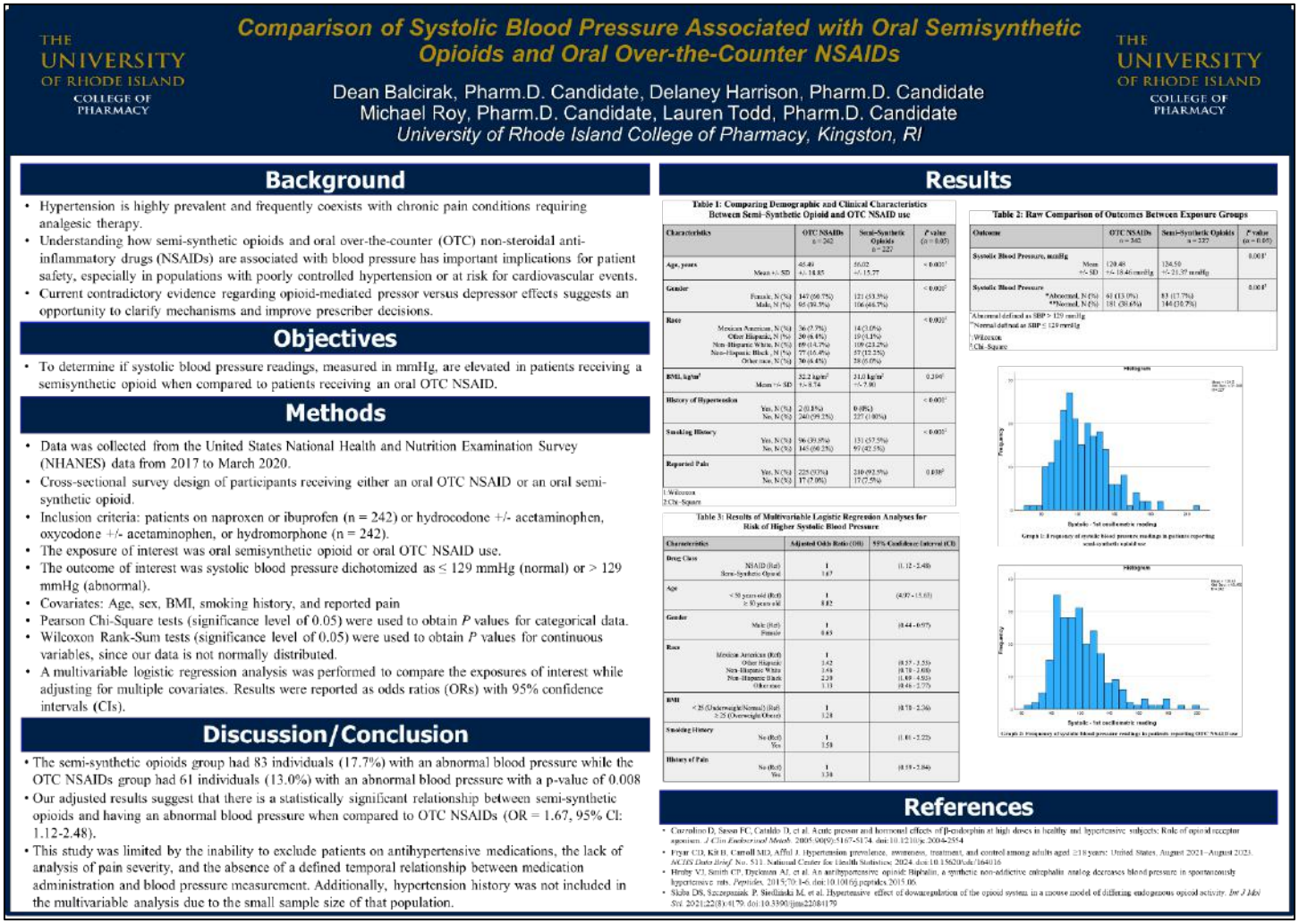


Association Between Family Income-to-Poverty Ratio and Current Antipsychotic Medication Use Among U.S. Adults: A Cross-Sectional NHANES Analysis

Ryan Kay, Sarah Martidis, Mariah Ramos, Sydney Reyome

Group 11

Examines whether family income level (measured as the income-to-poverty ratio) is related to current antipsychotic medication use among U.S. adults. The background notes that socioeconomic differences may affect access to mental health treatment, but it is unclear whether income predicts antipsychotic use once other factors are considered. The objective is to test whether income-to-poverty ratio is associated with current antipsychotic use after adjusting for demographic and clinical factors such as depression, smoking, and medical conditions. In the discussion and conclusion, the authors report that after adjustment, family income was not independently associated with current antipsychotic medication use, and that clinical factors appeared to be stronger predictors. They note limitations such as the cross-sectional design and self-reported medication use, and they suggest that a larger sample or additional factors could help clarify whether there is a relationship.

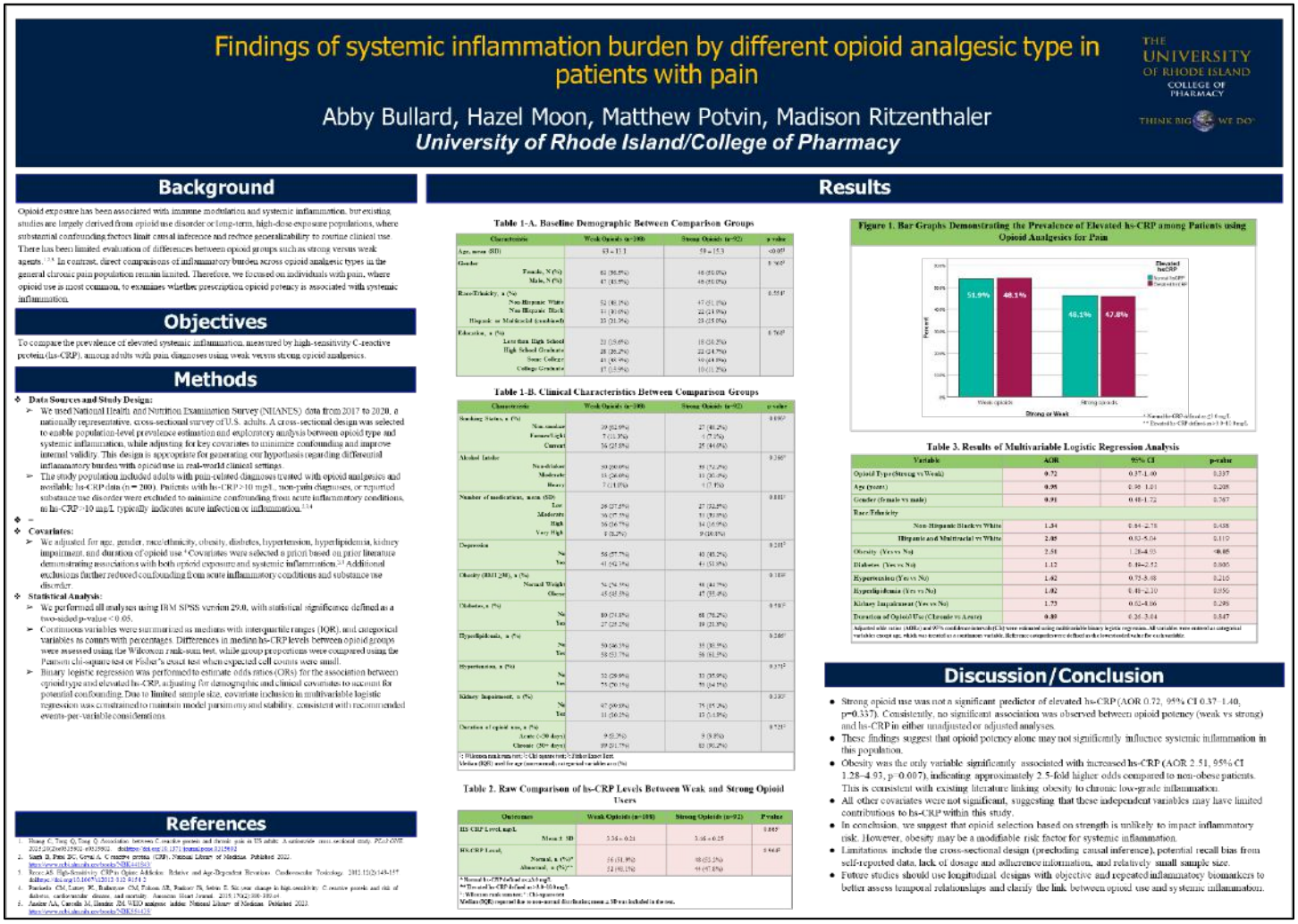


Comparison of Systolic Blood Pressure Associated with Oral Semisynthetic Opioids and Oral Over-the-Counter NSAIDs

Dean Balcirak, Delaney Harrison, Michael Roy, Lauren Todd

Group 12

Explores people who need pain medicines and examines whether systolic blood pressure differs between those taking oral semisynthetic opioids and those taking oral over-the-counter NSAIDs. The background notes that high blood pressure is common and often occurs alongside chronic pain, so understanding how these medications relate to blood pressure is important for safety. The objective is to determine whether systolic blood pressure is higher in patients receiving a semisynthetic opioid compared with patients receiving an oral OTC NSAID. In the discussion and conclusion, the authors report that the semisynthetic opioid group had a higher proportion of abnormal systolic blood pressure than the OTC NSAID group, and that this association remained significant after adjusting for factors like age, sex, BMI, smoking history, and reported pain. They note limitations such as not being able to exclude people taking blood pressure medications, not analyzing pain severity, and the cross-sectional design, which makes it hard to know timing and cause-and-effect.

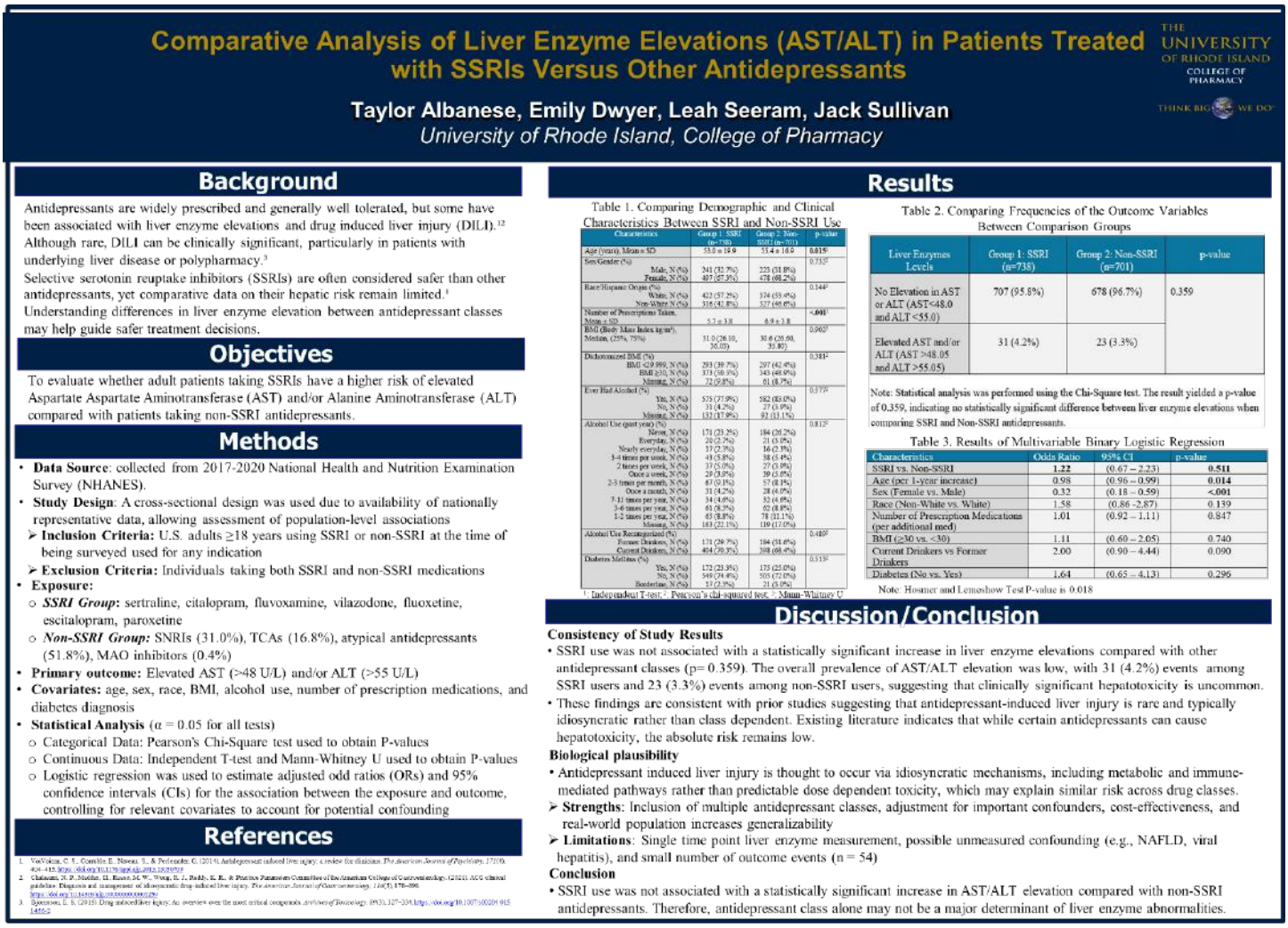


Findings of systemic inflammation burden by different opioid analgesic type in patients with pain

Abby Bullard, Hazel Moon, Matthew Potvin, Madison Ritzenthaler

Group 13

Analyzes adults with pain who are taking prescription opioids and asks whether opioid strength (weak versus strong opioids) is linked to higher levels of systemic inflammation. The background notes that opioids have been connected with immune effects and inflammation, but much of the past research comes from opioid use disorder or long-term high-dose exposure, and there has been limited direct comparison of different opioid types in typical pain patients. The objective is to compare how often high-sensitivity C-reactive protein (hs-CRP), a marker of inflammation, is elevated among people using weak versus strong opioid analgesics. In the discussion and conclusion, the authors report that opioid potency was not significantly associated with elevated hs-CRP in either unadjusted or adjusted analyses. They note that obesity was the main factor associated with higher hs-CRP, suggesting it may be a more important and modifiable driver of inflammation in this population. They conclude that choosing an opioid based on strength alone is unlikely to change inflammation risk, and recommend larger, longitudinal studies with repeated biomarker measurements.

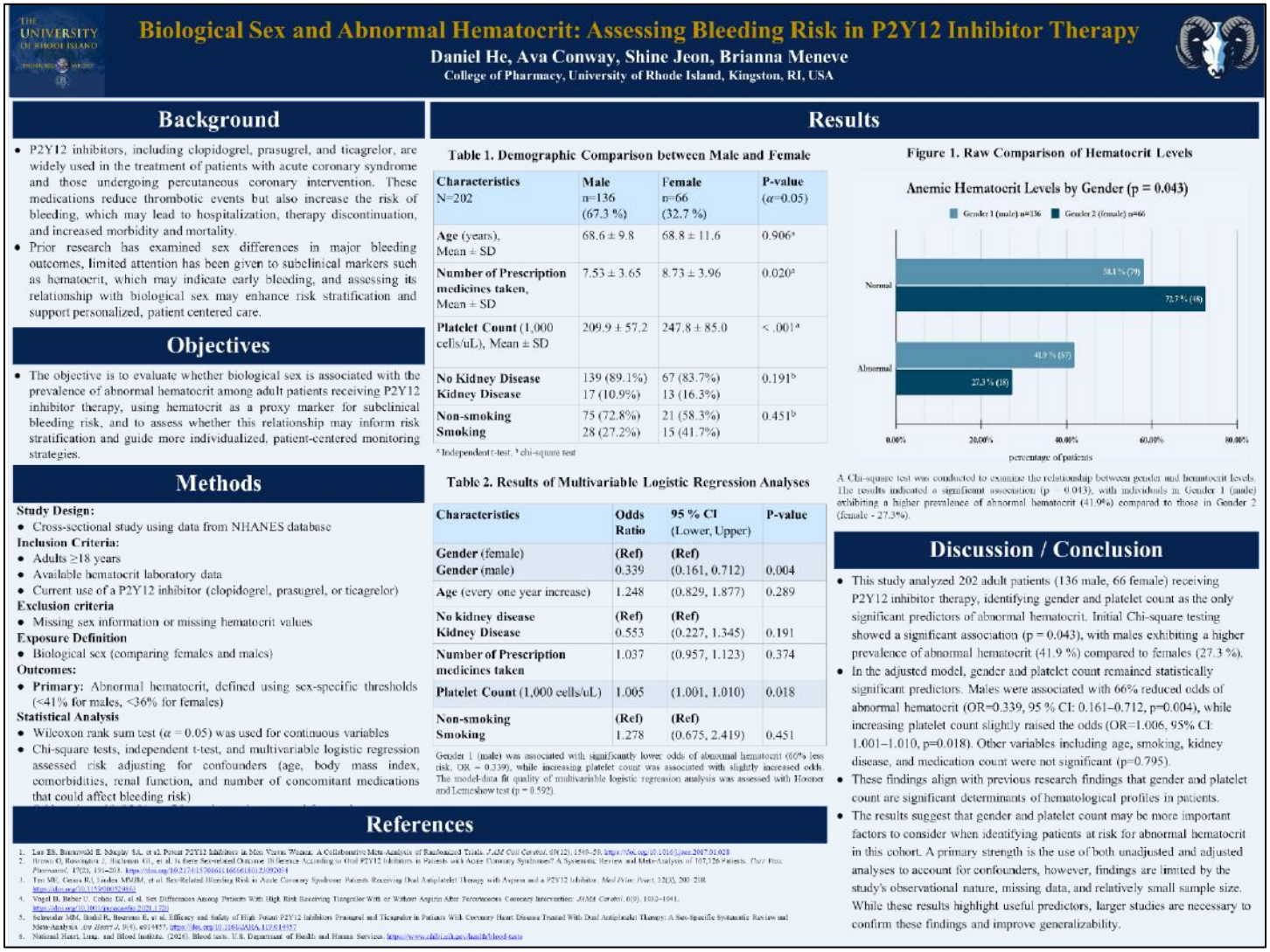


Comparative Analysis of Liver Enzyme Elevations (AST/ALT) in Patients Treated with SSRIs Versus Other Antidepressants

Taylor Albanese, Emily Dwyer, Leah Seeram, Jack Sullivan

Group 14

Investigates whether people taking SSRIs have a higher risk of elevated liver enzymes compared with people taking other types of antidepressants. The background explains that antidepressants are generally safe but can sometimes be linked to liver enzyme elevations and drug-induced liver injury, which can be important in people with liver disease or those taking many medications. The objective is to compare the risk of elevated AST and/or ALT in adults using SSRIs versus non-SSRI antidepressants using NHANES data. In the discussion and conclusion, the authors report that SSRI use was not associated with a statistically significant increase in liver enzyme elevations compared with other antidepressant classes, and that overall enzyme elevations were uncommon. They conclude that antidepressant class alone may not be a major driver of liver enzyme abnormalities, and note limitations such as having only one measurement time point and the possibility of unmeasured liver-related factors.

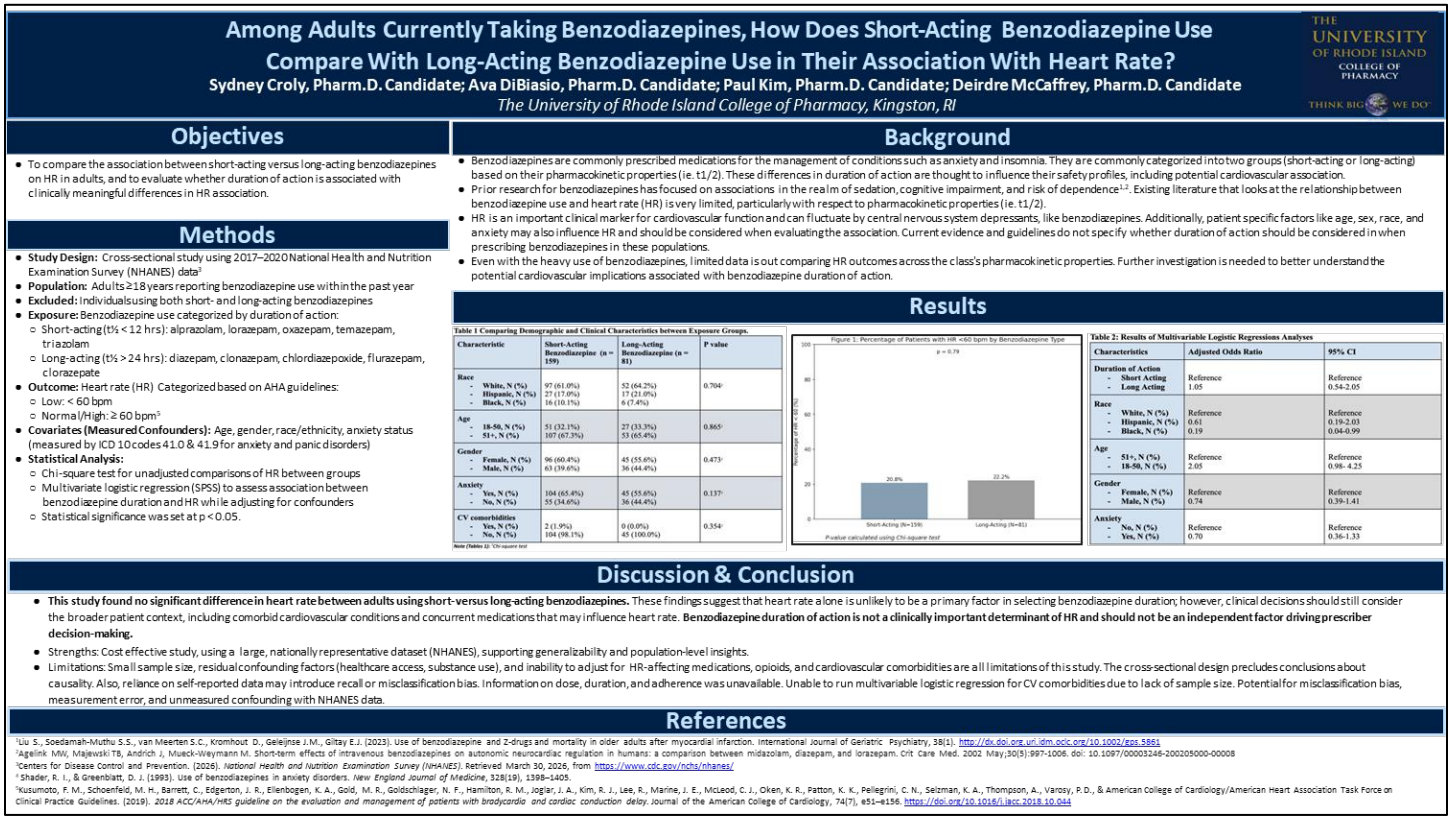


Biological Sex and Abnormal Hematocrit: Assessing Bleeding Risk in P2Y12 Inhibitor Therapy

Daniel He, Ava Conway, Shine Jeon, Brianna Meneve

Group 15

Reviews adults taking P2Y12 inhibitors and asks whether biological sex is associated with abnormal hematocrit, used as an early marker of possible bleeding risk. The background explains that these medications reduce clotting events but can increase bleeding risk, and that sex differences in major bleeding have been studied while earlier lab markers like hematocrit have been explored less. The objective is to evaluate whether abnormal hematocrit differs by sex in people using P2Y12 inhibitors and whether this could help with monitoring and risk assessment. In the discussion and conclusion, the authors report that sex and platelet count were the main factors related to abnormal hematocrit in their analysis. They note limitations such as the observational, cross-sectional design, missing data, and a relatively small sample size, and conclude that larger studies are needed to confirm these findings and improve how patients are stratified and monitored.

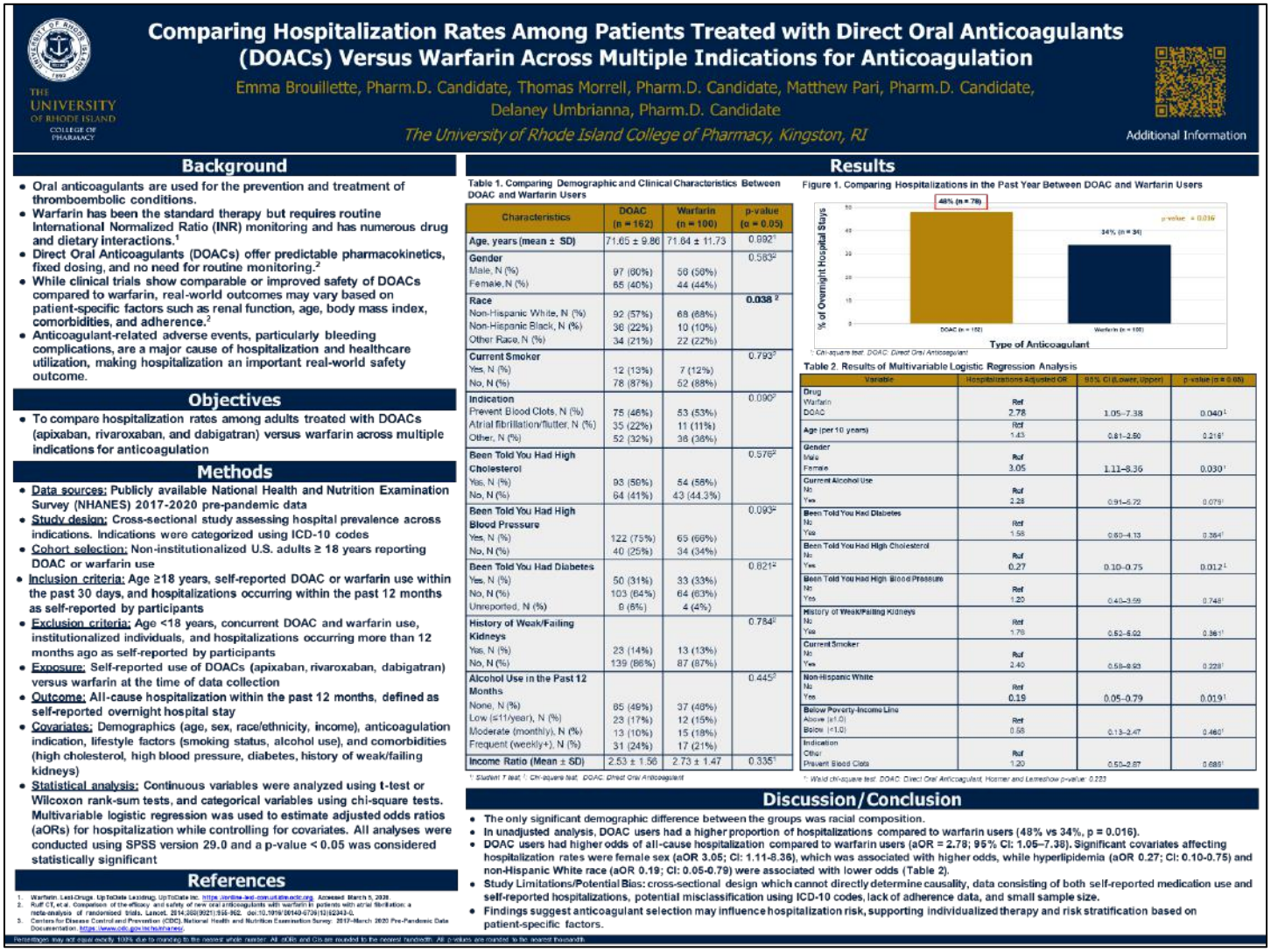


Among Adults Currently Taking Benzodiazepines, How Does Short-Acting Benzodiazepine Use Compare With Long-Acting Benzodiazepine Use in Their Association With Heart Rate?

Sydney Croly, Ava DiBiasio, Paul Kim, Deirdre McCaffrey

Group 16

Compares adults taking benzodiazepines and asks whether short-acting versus long-acting benzodiazepines are linked to different heart rate outcomes. The background explains that benzodiazepines are often grouped by how long they last in the body, and that these differences might affect safety, including possible cardiovascular effects, but there is limited evidence comparing heart rate by duration of action. The objective is to compare heart rate between short-acting and long-acting benzodiazepine users in adults. In the discussion and conclusion, the authors report that they did not find a meaningful difference in heart rate between the two groups. They conclude that duration of action alone is unlikely to be an important reason to choose one benzodiazepine type over another based on heart rate, although other patient factors and medications should still be considered.

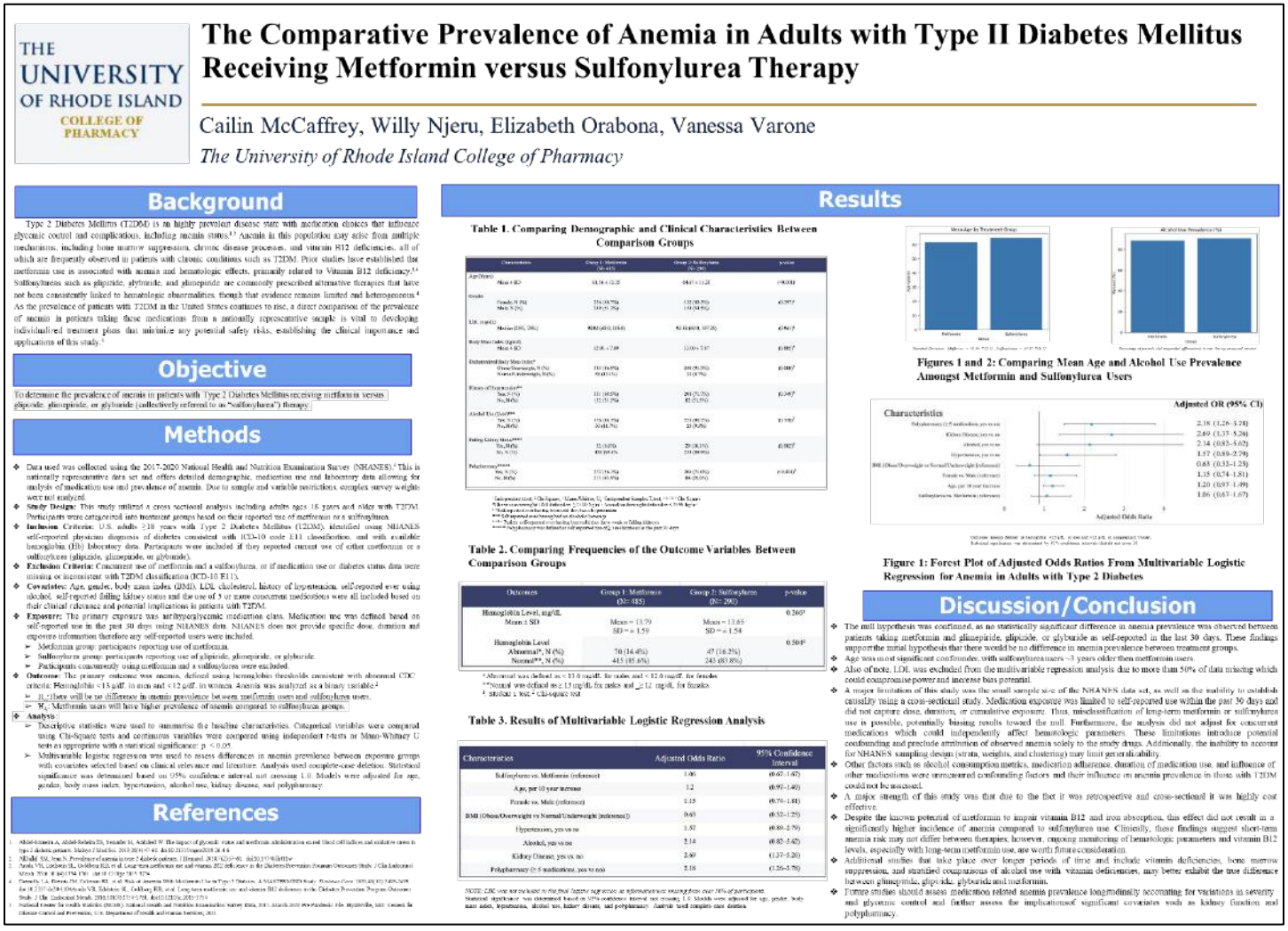


Comparing Hospitalization Rates Among Patients Treated with Direct Oral Anticoagulants (DOACs) Versus Warfarin Across Multiple Indications for Anticoagulation

Emma Brouillette, Thomas Morrell, Matthew Pari, Delaney Umbrianna

Group 17

Considers hospitalization rates in adults using direct oral anticoagulants (DOACs) versus warfarin. The background explains that warfarin requires INR monitoring and has many interactions, while DOACs have more predictable dosing and typically do not require routine monitoring, but real-world outcomes can vary based on patient factors. The objective is to compare all-cause overnight hospitalization within the past year between adults using DOACs and those using warfarin, across multiple anticoagulation indications. In the discussion and conclusion, the authors report that DOAC users had a higher proportion of hospitalizations than warfarin users and higher odds of hospitalization after adjustment. They note limitations such as the cross-sectional design, self-reported medication use and hospitalizations, possible misclassification, lack of adherence data, and small sample size, and conclude that anticoagulant selection may relate to hospitalization risk and should be individualized using patient-specific factors and risk stratification.

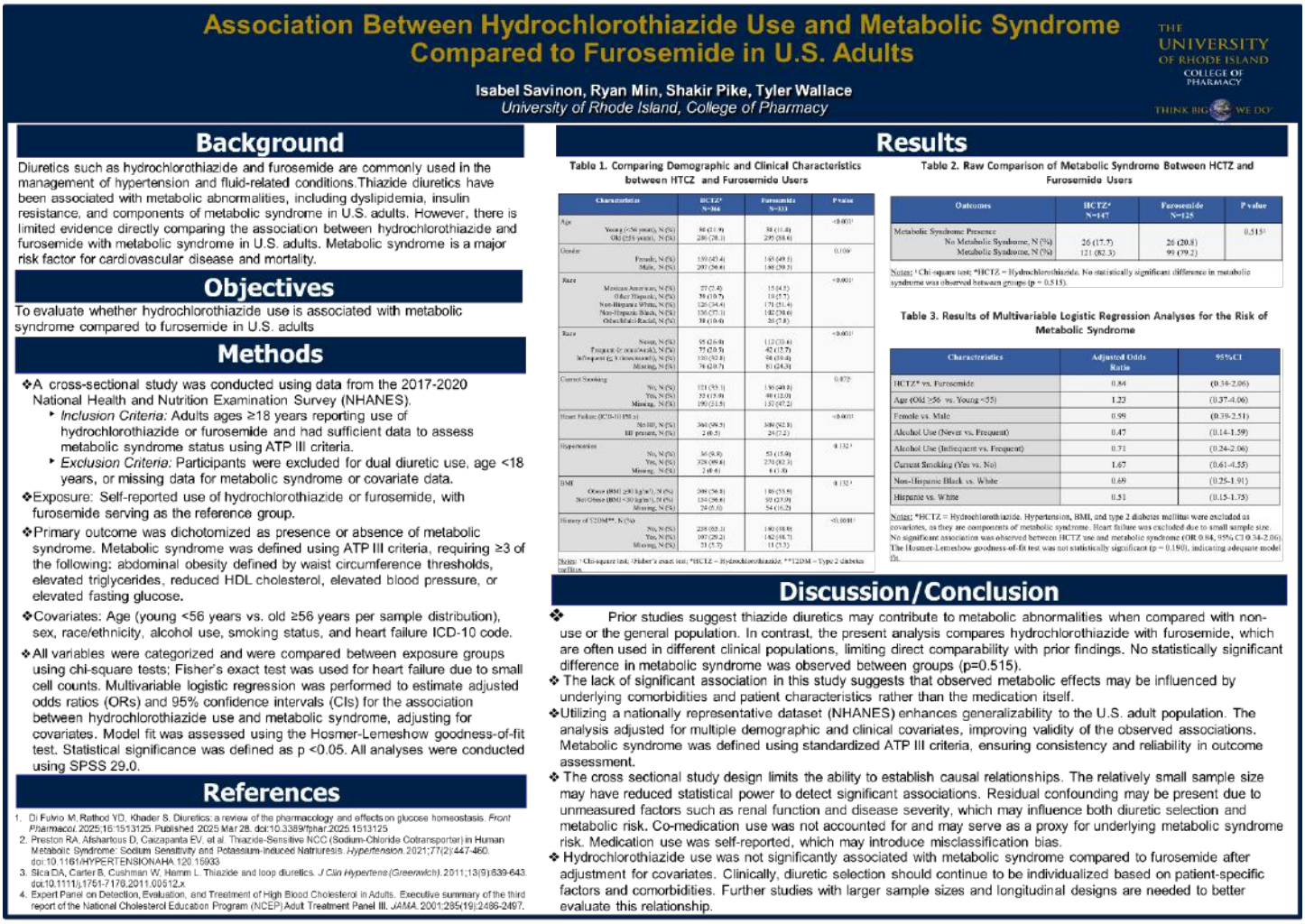


The Comparative Prevalence of Anemia in Adults with Type II Diabetes Mellitus Receiving Metformin versus Sulfonylurea Therapy

Cailin McCaffrey, Willy Njeru, Elizabeth Orabona, Vanessa Varone

Group 19

Compares adults with type 2 diabetes who are taking metformin versus those taking sulfonylureas (glipizide, glimepiride, or glyburide) to see whether anemia is more common in one group. The background explains that anemia can occur in people with type 2 diabetes for several reasons, and that metformin has been linked to anemia mainly through vitamin B12 deficiency, while evidence for sulfonylureas is more limited. The objective is to determine and compare the prevalence of anemia between these treatment groups using NHANES data. In the discussion and conclusion, the authors report that they did not find a statistically significant difference in anemia prevalence between metformin users and sulfonylurea users. They note important limitations such as small sample size, cross-sectional design, and self-reported short-window medication exposure, which could hide longer-term effects. They conclude that short-term anemia risk may not differ between therapies, but suggest continued monitoring—especially with long-term metformin use—and recommend longer-term studies that include vitamin deficiency measures.



Association Between Hydrochlorothiazide Use and Metabolic Syndrome Compared to Furosemide in U.S. Adults

Isabel Savinon, Ryan Min, Shakir Pike, Tyler Wallace
University of Rhode Island, College of Pharmacy

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Background

Diuretics such as hydrochlorothiazide and furosemide are commonly used in the management of hypertension and fluid-related conditions.Thiazide diuretics have been associated with metabolic abnormalities, including dyslipidemia, insulin resistance, and components of metabolic syndrome in U.S. adults. However, there is limited evidence directly comparing the association between hydrochlorothiazide and furosemide with metabolic syndrome in U.S. adults. Metabolic syndrome is a major risk factor for cardiovascular disease and mortality.

Objectives

To evaluate whether hydrochlorothiazide use is associated with metabolic syndrome compared to furosemide in U.S. adults

Methods

- A cross-sectional study was conducted using data from the 2017-2020 National Health and Nutrition Examination Survey (NHANES).
  - *Inclusion Criteria:* Adults ages ≥18 years reporting use of hydrochlorothiazide or furosemide and had sufficient data to assess metabolic syndrome status using ATP III criteria.
  - *Exclusion Criteria:* Participants were excluded for dual diuretic use, age <18 years, or missing data for metabolic syndrome or covariate data.
- Exposure: Self-reported use of hydrochlorothiazide or furosemide, with furosemide serving as the reference group.
- Primary outcome was dichotomized as presence or absence of metabolic syndrome. Metabolic syndrome was defined using ATP III criteria, requiring ≥3 of the following: abdominal obesity defined by waist circumference thresholds, elevated triglycerides, reduced HDL cholesterol, elevated blood pressure, or elevated fasting glucose.
- Covariates: Age (young <56 years vs. old ≥56 years per sample distribution), sex, race/ethnicity, alcohol use, smoking status, and heart failure ICD-10 code.
- All variables were categorized and were compared between exposure groups using chi-square tests; Fisher's exact test was used for heart failure due to small cell counts. Multivariable logistic regression was performed to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the association between hydrochlorothiazide use and metabolic syndrome, adjusting for covariates. Model fit was assessed using the Hosmer-Lemeshow goodness-of-fit test. Statistical significance was defined as $p < 0.05$. All analyses were conducted using SPSS 29.0.

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Results

Table 1. Comparing Demographic and Clinical Characteristics between HTCZ and Furosemide Users

Characteristics	HCTZ* N=304	Furosemide N=333	P-value
Age			<0.001[1]
Young (<56 years), N (%)	86 (21.9)	38 (11.4)	
Old (≥56 years), N (%)	286 (78.1)	295 (88.6)	
Gender			0.109[1]
Female, N (%)	159 (43.4)	165 (49.5)	
Male, N (%)	207 (56.6)	168 (50.5)	
Race			<0.001[1]
Mexican American, N (%)	27 (7.4)	15 (4.5)	
Other Hispanic, N (%)	39 (10.7)	19 (5.7)	
Non-Hispanic White, N (%)	120 (34.4)	171 (51.4)	
Non-Hispanic Black, N (%)	136 (37.1)	102 (30.6)	
Other/Multi-Racial, N (%)	30 (8.0)	26 (7.8)	
Race			<0.001[1]
Never, N (%)	95 (26.0)	112 (33.6)	
Frequent (≥ once/week), N (%)	77 (20.5)	42 (12.7)	
Infrequent (< 1/month), N (%)	180 (52.8)	98 (29.4)	
Missing, N (%)	76 (20.7)	81 (24.3)	
Current Smoking			0.072[1]
No, N (%)	121 (55.1)	136 (69.8)	
Yes, N (%)	53 (19.9)	40 (12.0)	
Missing, N (%)	190 (21.5)	157 (47.2)	
Heart Failure (ICD-10 I50.x)			<0.001[2]
No HF, N (%)	360 (99.5)	306 (92.1)	
HF present, N (%)	2 (0.5)	24 (7.2)	
Hypertension			0.132[1]
No, N (%)	56 (9.8)	53 (15.9)	
Yes, N (%)	328 (90.4)	270 (82.1)	
Missing, N (%)	2 (0.6)	6 (1.8)	
BMI			0.132[1]
Obese (BMI ≥30 kg/m²), N (%)	208 (56.8)	186 (53.9)	
Not Obese (BMI <30 kg/m²), N (%)	134 (36.6)	93 (27.0)	
Missing, N (%)	24 (6.6)	54 (16.2)	
History of T2DM**, N (%)			<0.001[1]
No, N (%)	238 (65.3)	190 (58.6)	
Yes, N (%)	107 (29.2)	162 (48.7)	
Missing, N (%)	21 (5.7)	11 (3.3)	

Notes: [1] Chi-square test; [2]Fisher's exact test; *HCTZ = Hydrochlorothiazide; **T2DM = Type 2 diabetes mellitus.

Table 2. Raw Comparison of Metabolic Syndrome Between HCTZ and Furosemide Users

Outcomes	HCTZ* N=147	Furosemide N=125	P value
Metabolic Syndrome Presence			0.515[1]
No Metabolic Syndrome, N (%)	26 (17.7)	26 (20.8)	
Metabolic Syndrome, N (%)	121 (82.3)	99 (79.2)	

Notes: [1] Chi-square test; *HCTZ = Hydrochlorothiazide. No statistically significant difference in metabolic syndrome was observed between groups ($p = 0.515$).

Table 3. Results of Multivariable Logistic Regression Analyses for the Risk of Metabolic Syndrome

Characteristics	Adjusted Odds Ratio	95%CI
HCTZ* vs. Furosemide	0.84	(0.34-2.06)
Age (Old ≥56 vs. Young <55)	1.23	(0.37-4.06)
Female vs. Male	0.99	(0.39-2.51)
Alcohol Use (Never vs. Frequent)	0.47	(0.14-1.59)
Alcohol Use (Infrequent vs. Frequent)	0.71	(0.24-2.06)
Current Smoking (Yes vs. No)	1.67	(0.61-4.55)
Non-Hispanic Black vs. White	0.69	(0.25-1.91)
Hispanic vs. White	0.51	(0.15-1.75)

Notes: *HCTZ = Hydrochlorothiazide. Hypertension, BMI, and type 2 diabetes mellitus were excluded as covariates, as they are components of metabolic syndrome. Heart failure was excluded due to small sample size. No significant association was observed between HCTZ use and metabolic syndrome (OR 0.84, 95% CI 0.34-2.06). The Hosmer-Lemeshow goodness-of-fit test was not statistically significant ($p = 0.190$), indicating adequate model fit.

Discussion/Conclusion

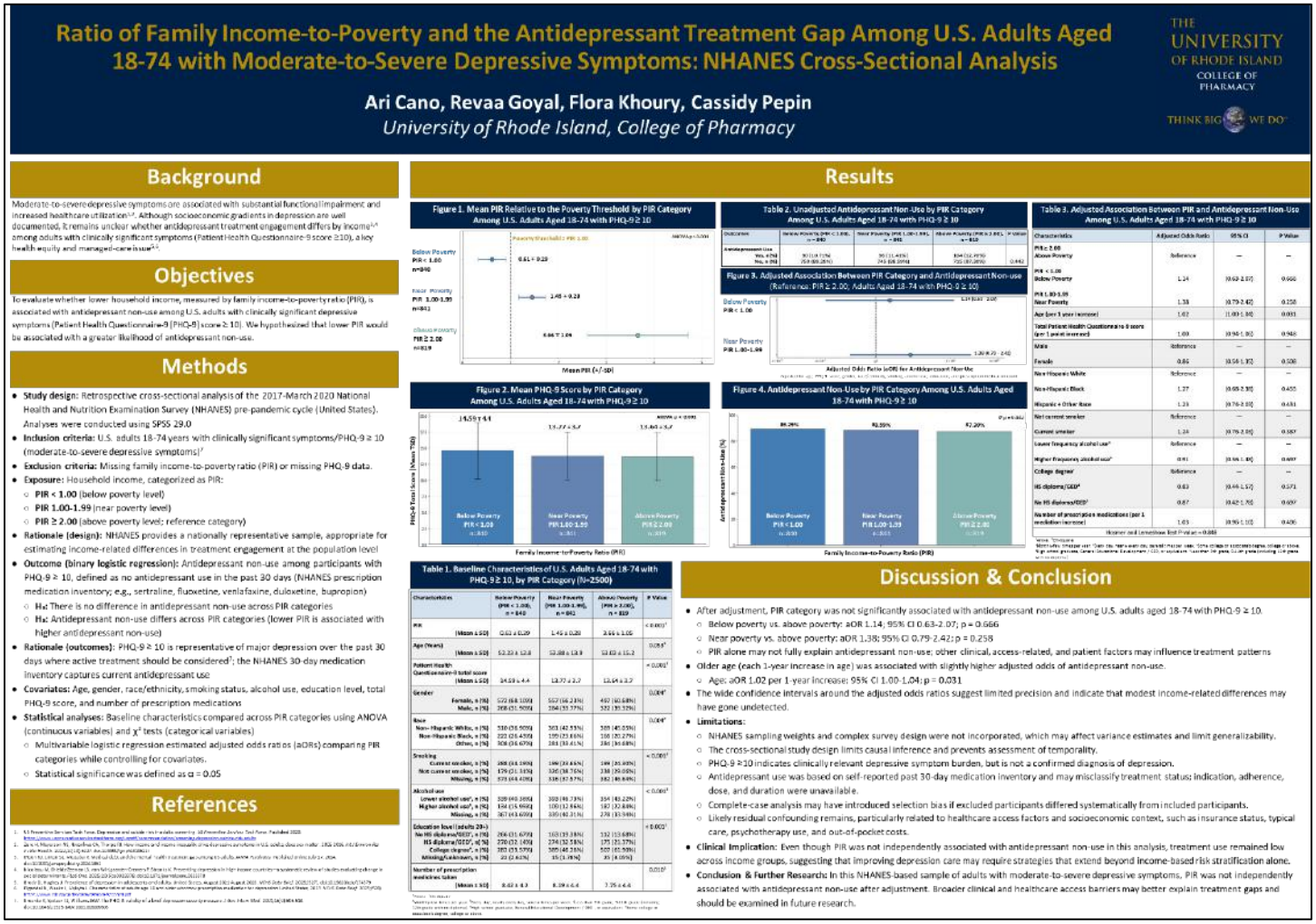
- Prior studies suggest thiazide diuretics may contribute to metabolic abnormalities when compared with non-use or the general population. In contrast, the present analysis compares hydrochlorothiazide with furosemide, which are often used in different clinical populations, limiting direct comparability with prior findings. No statistically significant difference in metabolic syndrome was observed between groups (p=0.515).
- The lack of significant association in this study suggests that observed metabolic effects may be influenced by underlying comorbidities and patient characteristics rather than the medication itself.
- Utilizing a nationally representative dataset (NHANES) enhances generalizability to the U.S. adult population. The analysis adjusted for multiple demographic and clinical covariates, improving validity of the observed associations. Metabolic syndrome was defined using standardized ATP III criteria, ensuring consistency and reliability in outcome assessment.
- The cross sectional study design limits the ability to establish causal relationships. The relatively small sample size may have reduced statistical power to detect significant associations. Residual confounding may be present due to unmeasured factors such as renal function and disease severity, which may influence both diuretic selection and metabolic risk. Co-medication use was not accounted for and may serve as a proxy for underlying metabolic syndrome risk. Medication use was self-reported, which may introduce misclassification bias.
- Hydrochlorothiazide use was not significantly associated with metabolic syndrome compared to furosemide after adjustment for covariates. Clinically, diuretic selection should continue to be individualized based on patient-specific factors and comorbidities. Further studies with larger sample sizes and longitudinal designs are needed to better evaluate this relationship.

Association Between Hydrochlorothiazide Use and Metabolic Syndrome Compared to Furosemide in U.S. Adults

Isabel Savinon, Ryan Min, Shakir Pike, Tyler Wallace

Group 20

Profiles two diuretics—hydrochlorothiazide and furosemide—and asks whether hydrochlorothiazide use is linked to metabolic syndrome in U.S. adults. The background explains that thiazide diuretics have been associated with metabolic problems, but there is limited evidence directly comparing hydrochlorothiazide with furosemide for metabolic syndrome risk. The objective is to evaluate whether hydrochlorothiazide use is associated with metabolic syndrome compared with furosemide. In the discussion and conclusion, the authors report that no statistically significant difference in metabolic syndrome was observed between the groups, and they suggest that underlying patient characteristics and comorbidities may influence observed metabolic effects more than the medication choice alone. They note limitations such as the cross-sectional design, relatively small sample size, and possible unmeasured confounding, and conclude that hydrochlorothiazide was not significantly associated with metabolic syndrome compared with furosemide after adjustment; they recommend larger, longitudinal studies.

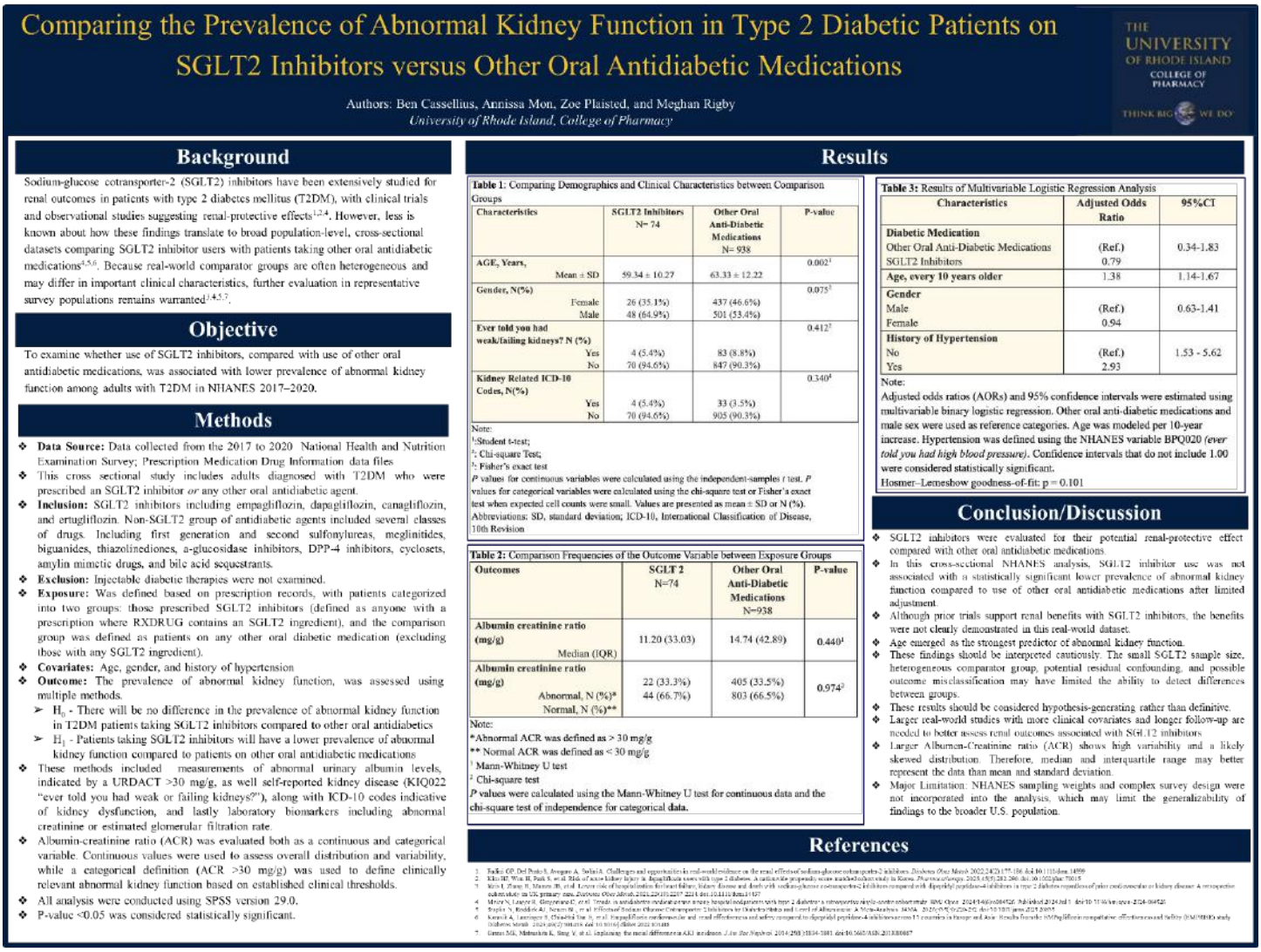


Ratio of Family Income-to-Poverty and the Antidepressant Treatment Gap Among U.S. Adults Aged 18-74 with Moderate-to-Severe Depressive Symptoms: NHANES Cross-Sectional Analysis

Ari Cano, Revaa Goyal, Flora Khoury, Cassidy Pepin

Group 21

Examines whether household income is linked to a “treatment gap” in depression care among U.S. adults with moderate-to-severe depressive symptoms. The background explains that people with higher depression symptom burden often have significant impairment, and while lower income is linked to depression risk, it is less clear whether antidepressant treatment engagement differs by income among adults with PHQ-9 scores of 10 or higher. The objective is to test whether lower family income-to-poverty ratio (PIR) is associated with not taking antidepressants among adults aged 18–74 with PHQ-9 ≥ 10. In the discussion and conclusion, the authors report that after adjustment, PIR category was not significantly associated with antidepressant non-use, and that treatment non-use was high across all income groups. They note limitations such as not incorporating survey weights, cross-sectional design, and limited medication details, and conclude that barriers beyond income alone may better explain antidepressant treatment gaps and should be explored in future research.

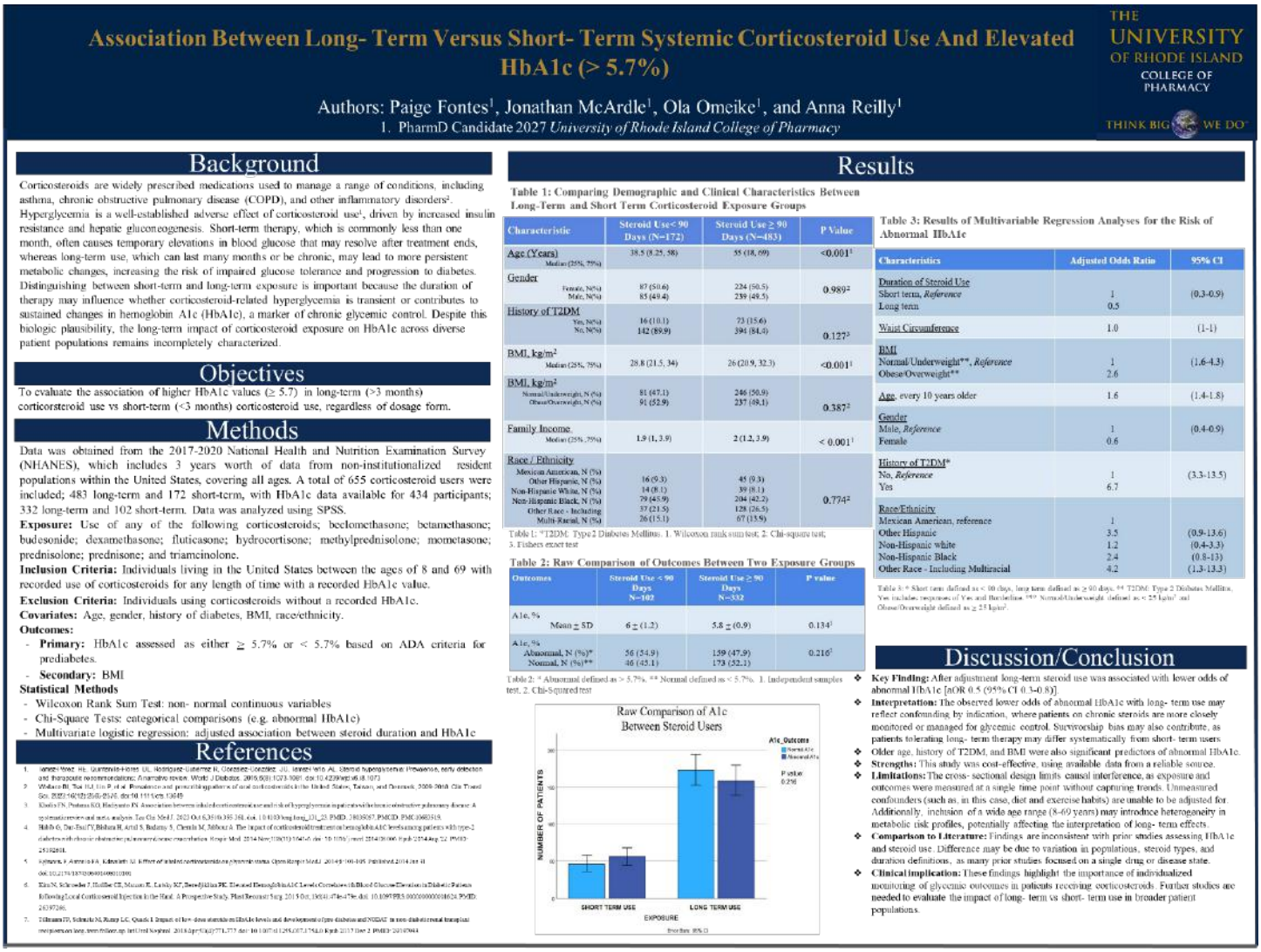


Comparing the Prevalence of Abnormal Kidney Function in Type 2 Diabetic Patients on SGLT2 Inhibitors versus Other Oral Antidiabetic Medications

Ben Cassellius, Annissa Mon, Zoe Plaisted, Meghan Rigby

Group 22

Explores adults with type 2 diabetes and asks whether people taking SGLT2 inhibitors have a lower prevalence of abnormal kidney function compared with people taking other oral diabetes medications. The background notes that clinical trials often show kidney-protective effects with SGLT2 inhibitors, but it is less clear how well this translates to broad population survey data where comparison groups can be very mixed. The objective is to test whether SGLT2 inhibitor use is associated with lower abnormal kidney function in NHANES 2017–2020. In the discussion and conclusion, the authors report that SGLT2 inhibitor use was not linked to a statistically significant lower prevalence of abnormal kidney function compared with other oral antidiabetics after limited adjustment. They note that age was the strongest predictor of abnormal kidney function, and emphasize limitations such as a small SGLT2 sample size, a heterogeneous comparison group, possible residual confounding and outcome misclassification, and not using NHANES survey weights. They conclude the results are best viewed as hypothesis-generating and that larger real-world studies with more covariates and longer follow-up are needed.

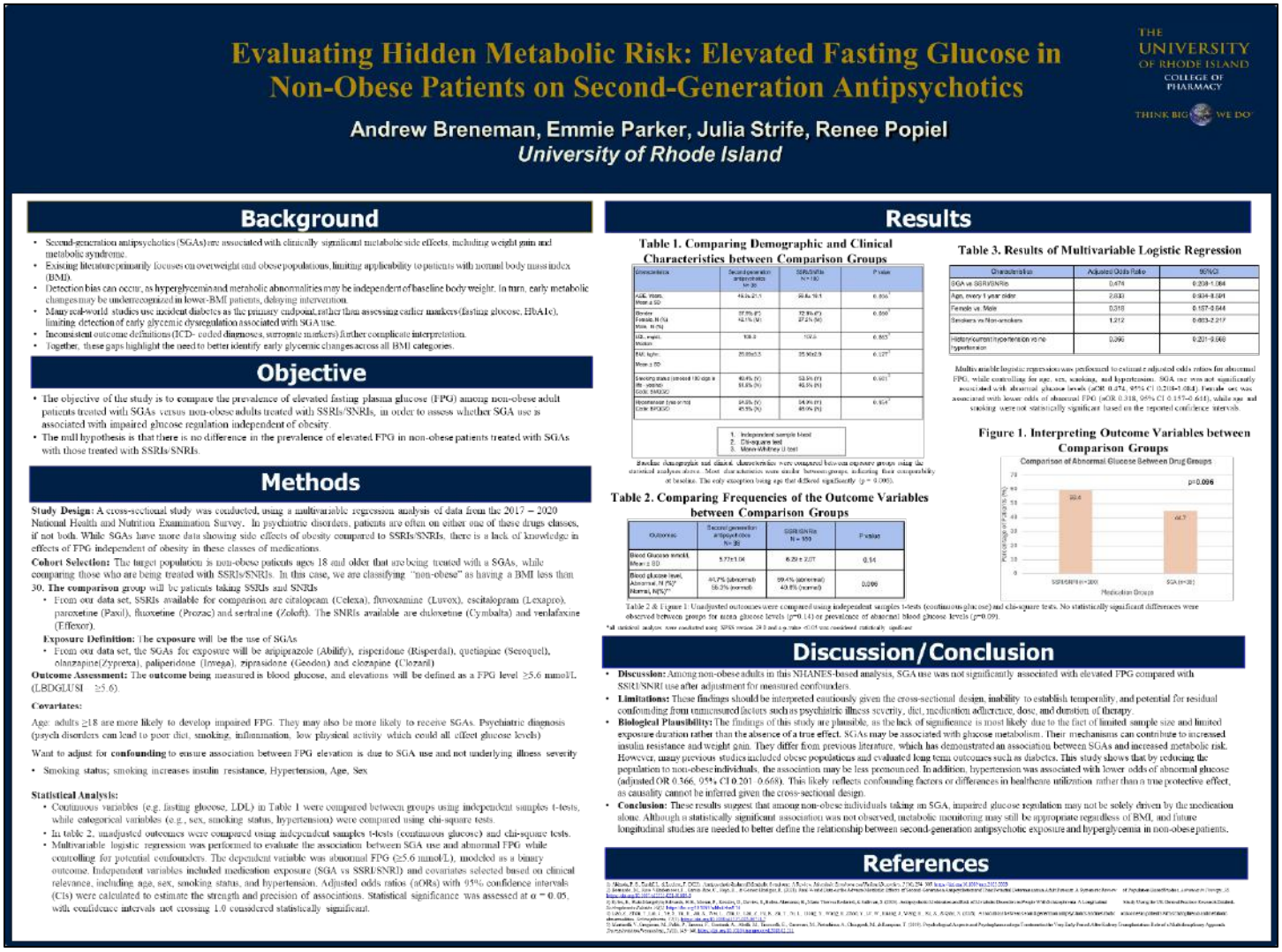


Association Between Long-Term Versus Short-Term Systemic Corticosteroid Use And Elevated HbA1c (> 5.7%)

Paige Fontes, Jonathan McArdle, Ola Omeike, Anna Reilly

Group 23

Analyzes whether people who use systemic corticosteroids for a longer time are more likely to have an elevated HbA1c (above 5.7%), compared with people who use corticosteroids for a shorter time. The background explains that steroids can raise blood sugar, and that longer exposure could lead to more lasting effects on blood sugar control. The objective is to compare elevated HbA1c in long-term steroid users (more than 3 months) versus short-term users (less than 3 months). In the discussion and conclusion, the authors report that after adjustment, long-term steroid use was associated with lower odds of elevated HbA1c. They suggest this unexpected finding may be due to factors like closer monitoring and treatment of blood sugar in long-term users, or differences between people who remain on long-term therapy versus short-term users. They conclude that individualized monitoring of blood sugar remains important for patients on corticosteroids, and that more research is needed to better understand long-term versus short-term effects.



Evaluating Hidden Metabolic Risk: Elevated Fasting Glucose in Non-Obese Patients on Second-Generation Antipsychotics

Andrew Breneman, Emmie Parker, Julia Strife, Renee Popiel

Group 24

Investigates whether non-obese adults taking second-generation antipsychotics (SGAs) have a higher prevalence of elevated fasting plasma glucose compared with non-obese adults taking SSRIs or SNRIs. The background explains that SGAs are known to cause metabolic side effects, but most research focuses on overweight or obese patients and often uses diabetes as the endpoint instead of earlier warning signs like fasting glucose. The objective is to see if elevated fasting glucose occurs more often in non-obese SGA users, which could indicate metabolic risk that might be missed when monitoring is based mainly on body weight. In the discussion and conclusion, the authors report that SGA use was not significantly associated with elevated fasting glucose compared with SSRI/SNRI use after adjusting for measured factors. They note the cross-sectional design, limited sample size, and possible unmeasured factors such as diet, psychiatric illness severity, medication dose and duration, and adherence. They conclude that metabolic monitoring may still be appropriate regardless of BMI, and larger longitudinal studies are needed.

Association of Angiotensin-Converting Enzyme Inhibitors vs. Angiotensin II Receptor Blockers Use With Albuminuria Among Adults with Hypertension

Sami Gangji, Nisha Kakwani, Elena Silva

The University of Rhode Island College of Pharmacy

THE UNIVERSITY OF RHODE ISLAND COLLEGE OF PHARMACY

THINK BIG WE DO

Background

- Albuminuria is an important marker of kidney damage and is associated with progression and cardiovascular risk.[1,2]
- Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARBs) are widely used in hypertension management, but their comparative association with albuminuria in a broader hypertensive population remains unclear.[3,4]
- Class-level comparisons have generally focused on effectiveness and safety outcomes rather than albuminuria as the primary endpoint, and many studies remain limited to selected high-risk populations.[3,4,5]
- Prior studies largely focused on blood pressure control, cardiovascular outcomes, chronic kidney disease progression, or composite renal endpoints rather than albuminuria as a primary outcome.[3,4,5]
- Together, these gaps support the need for a direct comparator analysis focused on albuminuria as the primary outcome in a broader hypertensive population.

Objectives

- To evaluate the association between ARB use versus ACEi use and albuminuria (urine albumin-creatinine ratio [uACR] ≥30 mg/g) among adults with hypertension.

Methods

- Data source: United States National Health and Nutrition Examination Survey (NHANES) from 2017 to March 2020.
- Study design: Cross-sectional analysis of adults with hypertension using prescription medication records and laboratory uACR data from NHANES.
- Study population: Adults aged ≥18 years with hypertension treated with either an ACEi or an ARB.
- Hypertension definition: Hypertension was identified using the medication-associated indication of primary "essential" hypertension in NHANES prescription records.
- Exposure group: ACEi users (benazepril, captopril, enalapril, enalaprilat, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril).
- Comparison group: ARB users (azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan).
- Primary outcome: Albuminuria, defined as urine albumin-creatinine ratio (uACR) ≥30 mg/g; no albuminuria was defined as uACR <30 mg/g. This aligns with the albuminuria definition and risk categories using 30 mg/g as a threshold.
- Covariates: Age, sex, body mass index (BMI), race, diabetes, kidney disease, smoking, and socioeconomic status.
- Statistical analysis: Pearson chi-square tests were used to compare categorical baseline characteristics and unadjusted albuminuria prevalence between groups. Multivariable logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between medication class and albuminuria after adjustment for prespecified covariates.
- Software/significance: Analyses were conducted using SPSS version 29.0 and a p-value <0.05 was considered statistically significant.

Results

Table 1: Demographic and Clinical Characteristics between ACE-I and ARB

Characteristics (N = 1450)	ACE-I (N = 866)	ARB (N = 584)	P-value[1]
Age, N (%)			
0-64 years	462 (53.3)	233 (39.9)	< 0.001
≥ 65 years	404 (46.7)	351 (60.1)	
Sex, N (%)			
Male	483 (55.8)	237 (40.6)	< 0.001
Female	383 (44.2)	347 (59.4)	
BMI (kg/m2), N (%)			
<25	110 (14.0)	87 (16.4)	0.231
25+	675 (86.0)	443 (83.6)	
Race, N (%)			
Non-Hispanic White	344 (39.7)	212 (36.3)	0.189
All Other	522 (60.3)	372 (63.7)	
Diabetes, N (%)			
HbA1c < 6.5	511 (65.7)	387 (75.1)	< 0.001
HbA1c ≥ 6.5	267 (34.3)	128 (24.9)	
Kidney Disease, N (%)			
Ever told had weak or failing kidneys:			
No	797 (92.0)	532 (91.9)	0.918
Yes	69 (8.0)	47 (8.1)	
Smoking, N (%)			
Smoked at least 100 cigarettes/lifetime:			
No	424 (49.0)	361 (61.9)	< 0.001
Yes	442 (51.0)	222 (38.1)	
Socioeconomic Status, N (%)			
Ratio of family income to poverty:			
≥ 1	607 (81.5)	409 (84.7)	0.147
< 1	138 (18.5)	74 (15.3)	

[1] *The p-values were derived from Pearson chi-square tests*

Table 2: Comparing Frequencies of the Outcome Variables between ACE-I and ARB

Outcome (N = 1317)	ACE-I (N = 785)	ARB (N = 532)	P-value
No Albuminuria, N (%) Normal: < 30 mg/g	598 (76.2)	386 (72.6)	0.138[1]
Albuminuria, N (%) Abnormal: ≥ 30 mg/g	187 (23.8)	146 (27.4%)	

[1] *The p-value was derived from a Pearson chi-square test*

Table 3: Results of Multivariable Logistic Regression Analysis of Factors Associated with Albuminuria

Variable		Adjusted OR	95% CI	P-value
Drug				
	ACE-I	(Ref)		
	ARB	1.25	0.916-1.702	0.159
Age				
	0-64 years	(Ref)		
	≥ 65 years	1.10	0.810-1.496	0.541
Sex				
	Male	(Ref)		
	Female	0.78	0.576-1.065	0.120
BMI (kg/m2)				
	< 25	(Ref)		
	25+	0.80	0.526-1.203	0.278
Race				
	Non-Hispanic White	(Ref)		
	All Other	1.08	0.783-1.484	0.646
Diabetes (HbA1c)				
	HbA1c < 6.5	(Ref)		
	HbA1c ≥ 6.5	2.50	1.835-3.407	< 0.001
Kidney Disease: *Ever told had weak or failing kidneys*				
	No	(Ref)		
	Yes	4.77	2.926-7.765	< 0.001
Smoking: *Smoked at least 100 cigarettes/lifetime*				
	No	(Ref)		
	Yes	1.41	1.032-1.915	0.031
Socioeconomic Status: *Ratio of family income to poverty*				
	≥ 1	(Ref)		
	< 1	1.67	1.148-2.429	0.007

The p-value from the Hosmer and Lemeshow test is 0.854.

Discussion/Conclusion

- The baseline differences between treatment groups suggest confounding by patient characteristics, supporting the importance of adjusted analysis when comparing ACEi and ARB users.
- In the unadjusted analysis, ARB users had a numerically higher prevalence of albuminuria than ACEi users; however, the absolute difference was small and not statistically significant, suggesting limited evidence of a between-group difference.
- In the adjusted analysis, controlling for demographic and clinical covariates did not materially change the interpretation, as ARB use remained not significantly associated with albuminuria compared with ACEi use.
- Overall, ARB use was not significantly associated with albuminuria relative to ACEi use in this cross-sectional analysis of adults with hypertension.
- Strengths: Use of a large national dataset increasing generalizability, standardized laboratory measurement to support consistent outcome assessment, adjustment for clinically relevant covariates, and use of publicly available data as a cost-effective and reliable source for analysis.
- Limitations: Cross-sectional design does not allow assessment of causation, residual confounding may remain because variables such as eGFR and treatment duration were not available, and limited sample size may have reduced statistical power and constrained additional covariate adjustment.
- These findings are generally consistent with prior comparative literature showing similar class-level renal effectiveness outcomes between ACEi and ARBs, while extending the comparison specifically to albuminuria in a broader hypertensive population.
- Longitudinal studies are needed to further evaluate whether ACEi and ARBs differ in albuminuria progression or other renal outcomes over time.
- Additional analyses would be strengthened by data on medication dose and adherence, treatment duration, blood pressure control, eGFR/CKD stage, albumin levels, and baseline severity of albuminuria, which were not fully available in NHANES.

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Association of Angiotensin-Converting Enzyme Inhibitors vs. Angiotensin II Receptor Blockers Use With Albuminuria Among Adults with Hypertension

Sami Gangji, Nisha Kakwani, Elena Silva

Group 25

Reviews adults with hypertension and examines whether people taking ARBs differ from people taking ACE inhibitors in how often they have albuminuria, which is a marker of kidney damage. The background explains that ACE inhibitors and ARBs are commonly used for hypertension, but direct comparisons focused on albuminuria in a broad hypertensive population are less common. The objective is to evaluate the association between ARB use versus ACE inhibitor use and albuminuria. In the discussion and conclusion, the authors report that although ARB users had a slightly higher albuminuria prevalence in the unadjusted comparison, the difference was small and not statistically significant, and the adjusted analysis did not change the interpretation. They conclude that ARB use was not significantly associated with albuminuria compared with ACE inhibitor use in this cross-sectional analysis, and that larger longitudinal studies are needed to assess changes in albuminuria and other kidney outcomes over time.


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