NEOMED

Office of Research and Sponsored Programs' Student Research Fellowship Program

2026 Project Catalog

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PROGRAM GOALS, PARTICIPATION POLICY AND PROGRAM REQUIREMENTS

GOALS

The fellowship projects provide summer experiences for NEOMED's medical and pharmacy students, in a variety of disciplines. The Summer Research Fellowship Program is a mentored research program, designed to provide intensive training in research procedures and principles on projects in basic and clinical disciplines; to enhance students' research horizons; and develop scientific presentation and writing skills. These projects are funded by the Office of Research and Sponsored Programs (ORSP).

PARTICIPATION

Phase 1, M1, M2, P1, P2, and graduate students *in good standing* may participate in the ORSP's Summer Research Fellowship Program.

M3, M4, P3 and P4 students who have completed their clerkships and have no conflict with their electives, may participate in the ORSP's Summer Research Fellowship Program.

A M4 and P4 student must have written documentation of the time permitted to complete the summer project.

If the project is to cross-over into any elective time, the student must obtain written approval of the elective director indicating the time frame that will be allotted to the fellowship project.

The project investigator will have to approve the plan.

Special requests will be considered if it is arranged and approved in advance.

PROGRAM REQUIREMENTS

Prior research experience is not required for research projects. However, research experience may be a factor for selection for a specific project and will be up to the discretion of the individual project investigator.

Students are required to complete all applicable training prior to beginning their research projects. Required training will be determined by the project investigator.

All students are required to complete the online Collaborative Institute Training Initiative (CITI) Human Subjects Research – Social-Behavioral-Educational Module Certificate. (See page 3 for details.) If you have completed this training during the past three years you do not have to repeat it. You can provide a certificate of completion if you are selected for a fellowship.

Fellowship Stipends and Commitment
Through the Office of Research and Sponsored Programs

1. All students agree to fulfill a commitment with the project investigator for completion of a research fellowship. Each project investigator is volunteering their time and expertise to train the fellow. It is the student's responsibility to be prompt, available for the project for the contracted time and attend to all requirements of the fellowship.

2. The total stipend for the research fellowship will be $3,000. Student research fellows are contracted employees and will be paid in two equal installments: the first payment will be issued at the midpoint of the fellowship and the second payment will be issued upon successful completion of the fellowship.

NOTE: When a student and the principal investigator of a specific student research fellowship opportunity have - through mutual discussion - determined a match exists and the student "commits" to work on that specific project with the principal investigator, that "commitment" is firm. The decision by a student to revoke their prior commitment in order to accept another fellowship opportunity is considered a professionalism issue and may result in a professionalism concern note (PCN) being filed in the student record.

Collaborative Institute Training Initiative (CITI) at the University of Miami
Human Subjects Research – Social-Behavioral-Educational Module Certificate

1. All students who are selected for a summer research fellowship will be required to take the computerized on-line researcher course at:

   https://www.citiprogram.org

   If you have taken this training within the past year you do not need to repeat it. Please provide a copy of the completion certificate to Nona Hose in the Office of Research and Sponsored Programs, Office G-235 if you are selected for a fellowship.

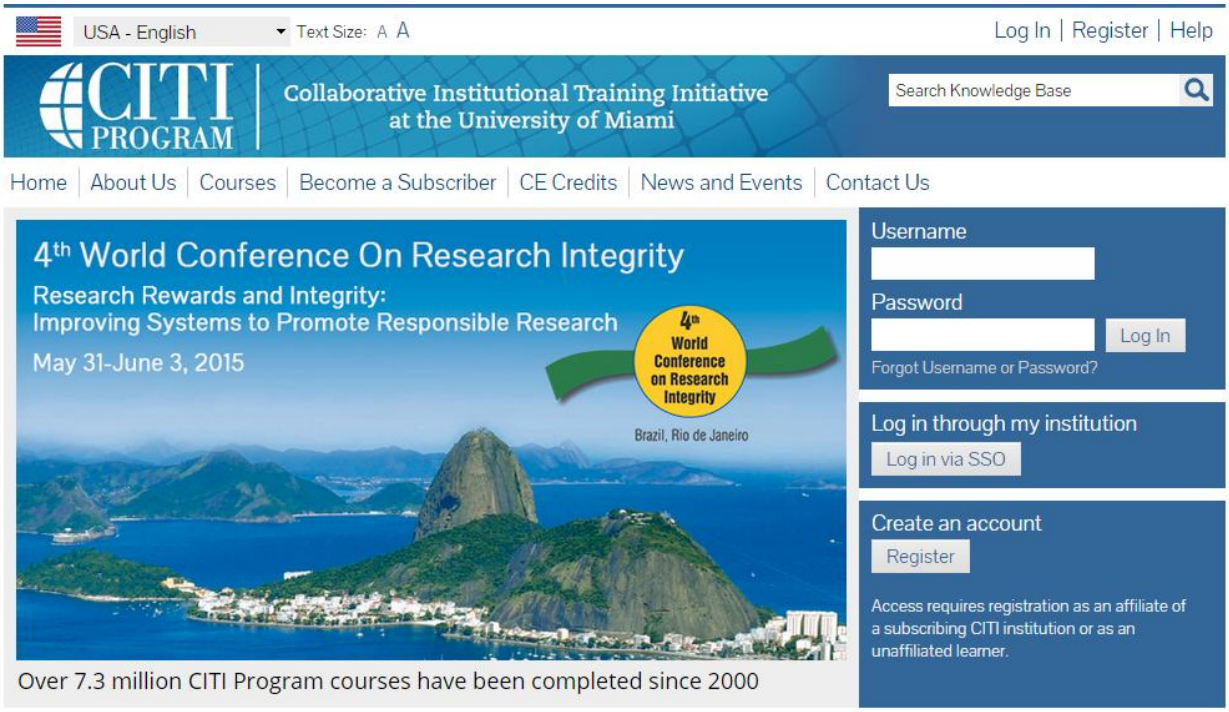
2. Description of course from the CITI Program:

   "Basic HSR modules are suitable for all persons involved in research studies involving human subjects, or who have responsibilities for setting policies and procedures with respect to such research, including IRBs. These modules are typically assembled into a basic course, which is the learner's first exposure to the content. Refresher modules, which can be assembled into refresher courses presented to learners at intervals defined by the institution, are designed to provide continuing education in human subject research issues. The standalone courses are intended for institutional/signatory officials, IRB administration (administrators, directors, coordinators, and other support staff), and IRB chairs.

   HSR module topics include: basics of IRB regulations and the review process, assessing risk to subjects, avoiding group harms, conflicts of interest, cultural competence, FDA-regulated research, genetic research, HIPAA-regulated research, informed consent, international research, Internet research, IRB member responsibilities, IRB chair responsibilities, records-based research, research in schools, research with protected populations, research with vulnerable subjects, the role of the community member, unanticipated problems and reporting, and students in research."

3. A certificate of completion will be awarded. Send this certificate to Nona Hose, Executive Administrative Assistant, Office of Research and Sponsored Programs, NEOMED

4. You will not be permitted to participate in any research without this certification.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CITI PROGRAM
Collaborative Institutional Training Initiative at the University of Miami
Search Knowledge Base
Home | About Us | Courses | Become a Subscriber | CE Credits | News and Events | Contact Us
4th World Conference On Research Integrity
Research Rewards and Integrity:
Improving Systems to Promote Responsible Research
May 31-June 3, 2015
4th World Conference on Research Integrity
Brazil, Rio de Janeiro
Over 7.3 million CITI Program courses have been completed since 2000
Username
Password
Log In
Forgot Username or Password?
Log in through my institution
Log in via SSO
Create an account
Register
Access requires registration as an affiliate of a subscribing CITI institution or as an unaffiliated learner.

Student Research Symposium

Friday, November 20, 2026

All ORSP sponsored fellows are **required** to participate in the Student Research Symposium.

Details as to preparation, deadline, etc., for poster presentations will be provided at a later date.

NEOMED
Office of Research & Sponsored Programs

Student Research Fellowship Program

APPLICATION MATERIALS

APPLICATION AND HIRING PROCEDURES

PLEASE NOTE: The application and interview process begins as soon as the project catalog is distributed. Please submit your applications as soon as possible.
The deadline to apply is Friday, February 6, 2026.

1. Students who are required to complete a summer course remediation are strongly discouraged from participating in any student research fellowship program that overlaps with the remediation exam study period. Please contact Craig Theissen, Director of Academic Support at **ctheissen@neomed.edu** or (330) 325-6758 for additional information.

2. Application/Interview process:
   a. Complete the application form online.
   b. Submit a *curriculum vitae* along with your application online.

3. Hiring Process:

   Students and project investigators should approach the fellowships as job opportunities. Students are asked to submit an application and curriculum vitae to the project investigator(s) of their choice. The project investigators will then contact the student(s) in which they are interested and set up an interview. After interviews are conducted, the project investigator will make his/her selection and offer the position to the student of his/her choice. Once a student has accepted the offer of a fellowship, the project investigator will notify Nona Hose in the Office of Research and Sponsored Programs.

   The project investigators will be asked to fill out a NEOMED Training Checklist form indicating any safety training that will be required (lab safety, animal care and use, etc.). This checklist will be provided to the student and to NEOMED's Safety Office.

   All onboarding paperwork and applicable safety training must be done before the student can begin working on a project.

   You may contact Nona if you have any questions or need additional information.
   Nona Hose, Executive Administrative Assistant
   Office of Research & Sponsored Programs, Room G-235
   Phone: 330-325-6499
   E-Mail: nhose@neomed.edu

CONTACT LIST FOR PROJECT APPLICATIONS

Project Investigator contact information:

Area Health Education Center (AHEC) at NEOMED

Maureen Drummond, MSM, SLM, VCM and Rebecca Brabander, M.S., M.Ed.
Emails: mdrummond@neomed.edu and rbrabander@neomed.edu

Bitonte College of Dentistry

Ehsanul Hoque Apu, Ph.D.
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David Kay, Ph.D.
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Nazeeba Siddika, BDS, MPH, Ph.D.
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Pharmacy Practice department's main office is located in E-28A

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Pharmaceutical Sciences department's main office is located in RGE-400

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Psychiatry department's main office is located in B-226

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Additional fellowship opportunities – please see individual project descriptions for locations of these fellowship

UH/NEOMED Hearing Group Partnership

Viral Tejani, Au.D., Ph.D.
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Jennifer Villwock, MD, FAAOA
Email: jennifer.villwock@uhhospitals.org

NEOMED

Office of Research & Sponsored Program's Student Research Fellowship Program

Project Descriptions

Submit your application to Dr. Maureen Drummond

Project Description
Title: "Strengthening Health Professions Education: How AHEC Scholar Alumni Integrate Regional AHEC Learning in Their NEOMED Graduate Programs"

Location: Area Health Education Center at NEOMED (Suite G-133) PI Name	Title	Responsibility	Contact Information
Maureen Drummond	**Principal Investigator**	**Will be responsible for population sampling, act as a study advisor, assist in data presentation and study design.**	**mdrummond@neomed.edu (330) 325-6585**
Rebecca Brabander	**Co-Investigator**	**Will be responsible for study design and survey synthesis.**	**rjohnson4@neomed.edu (330) 325-6584**

Title: Differentiating enantiomeric potency for the activity of a small drug-like novel FAK activating molecule
PI: Marc D. Basson, MD, PhD
Location: RGE 100

Abstract
The Basson laboratory has recently identified a series of small non-toxic drug-like molecules that specifically activate Focal Adhesion Kinase and promote GI mucosal healing in multiple different models in mice and rats. Data developed by students over the summer last year and subsequent mathematical modeling suggests that the lead molecule has two major enantiomers and that only one of these is likely to bind and activate FAK well. This is important because the current formulation includes both enantiomers. A pure preparation might be substantially more potent since the inactive enantiomer will at least dilute the efficacy and may in fact competitively inhibit the activity of the active enantiomer. We now need to test this hypothesis. The student will compare each enantiomer with the parent compound mixture, to determine their ability to promote monolayer wound healing and FAK activity in human Caco-2 intestinal epithelial cells.

Significance
This work will lead to the development of a first-in-class novel agent to promote GI mucosal repair. Currently there is nothing in the pharmacopeia that does this We can only neutralize injurious factors like acid or inflammation and hope the GI tract will heal. Such agents could eventually be used to treat diseases as diverse as gastritis, peptic ulcer disease, Crohn's disease, ulcerative colitis, NSAID-toxicity, and necrotizing enterocolitis.

Research methods that will be learned by the student
Mammalian cell culture
Monolayer wound assay
Protein assay
Western blotting
Statistical analysis

Proposed methods of data analysis
Standard statistical techniques including t-tests and outlier analysis

How will the anticipated findings contribute to the success of the overall research?
Successful completion of this work will identify a new lead molecule that can be validated in mice and rats and then eventually used as the basis of an IND application to the FDA for human trials.

Student fellow mentoring plan
The student will be assigned to work 1:1 with a member of the Basson laboratory for daily guidance and will participate in weekly two-hour laboratory meetings that both focus on data and emphasize discussion of experimental design and data analysis. Depending on the student's level of interest, there may also be opportunities to participate in other work going on in the lab, including small animal studies, as well as clinical research projects that are ongoing in the Basson research group. It is anticipated that the student will subsequently prepare a poster or oral presentation for student research day under Dr. Basson's supervision and that the data developed will be included in a publication on which the student will be a coauthor. All research will be conducted in the Basson laboratory.

Submit your application Dr. Ehsanul Hoque Apu – 1 of 4 projects

Title: Surrogate Modeling for Patient-Specific Craniofacial Reconstruction: Bridging the Gap Between High-Fidelity FEA and Real-Time Prediction

Project PI: Dr. Ehsanul Hoque Apu, Dept. of Biomedical Sciences, BCOD, Northeast Ohio Medical University (E: ehoqueapu@neomed.edu)

Project Co-PI: Dr. Nazeeba Siddika, Dept. of Specialty Dentistry, BCOD, Northeast Ohio Medical University (E: nsiddika@neomed.edu)

Abstract
Patient-specific finite element analysis (FEA) has emerged as the gold standard for characterizing the heterogeneous and anisotropic mechanical response of craniofacial structures. However, the computational burden associated with high-fidelity simulations—derived from multi-scale imaging modalities such as Cone Beam CT (CBCT) and Micro-CT—remains a significant barrier to routine clinical integration. To resolve the latency between accurate biomechanical assessment and the real-time demands of surgical planning, the field is increasingly pivoting toward surrogate modeling. This review critically examines the state-of-the-art in surrogate modeling architectures applied to craniofacial biomechanics. We delineate the end-to-end computational pipeline, traversing from image segmentation and mesh generation (e.g., 3D Slicer) to high-fidelity physics-based solution schemes (e.g., MOOSE, Abaqus). The review categorizes current strategies into data-driven machine learning approaches (e.g., Deep Neural Networks, Gaussian Processes) and projectionbased Reduced Order Models (e.g., POD-Galerkin), with specific focus on emerging hybrid paradigms like Physics-Informed Neural Networks (PINNs). We evaluate the fidelitye Viciency trade-oV inherent in these models, particularly regarding their capacity to handle complex topology changes during osteotomy and reconstruction. Furthermore, we discuss the pivotal role of open-source frameworks in democratizing access to these technologies and facilitating reproducible workflows for generating predictive Digital Twins. We conclude that combining high-quality validation with reliable surrogate inference is essential for the development of the next generation of clinical decision support systems.

Keywords: Craniofacial Biomechanics, Surrogate Modeling, Finite Element Analysis (FEA), Machine Learning (ML), Reduced Order Modeling (ROM), Physics-Informed Neural Networks (PINNs), Digital Twins, Micro-CT / CBCT, Surgical Planning, Computational Medicine.

The specific aims are to:
1. Synthesize existing literature on surrogate models for mimicking human craniofacial hard tissues.
2. Identify and categorize the models, based on their characteristics and supporting multi-scale imaging modalities such as Cone Beam CT (CBCT) and Micro-CT.
3. From literature, we will evaluate the models, particularly regarding their capacity to handle complex topology changes during osteotomy and reconstruction.
4. Draft a review manuscript and plan for an original study based on the findings.

What is the specific research question being addressed by the research project?
- What is the current evidence on variations of existing surrogate models for craniofacial hard tissue regeneration and reconstruction

Submit your application to Dr. Ehsanul Hoque Apu – 2 of 4 projects

Title: Toward the Dental Digital Twin: Integrating Image-Based Finite Element Modeling and Machine Learning for Predicting Peri-Implant Disease Progression.

Project PI: Dr. Ehsanul Hoque Apu, Dept. of Biomedical Sciences, BCOD, Northeast Ohio Medical University (E: ehoqueapu@neomed.edu)

Project Co-PI: Dr. Nazeeba Siddika, Dept. of Specialty Dentistry, BCOD, Northeast Ohio Medical University (E: nsiddika@neomed.edu)

Other NEOMED Faculty Investigators:
- Prof. Sorin Teich, Dean of BCOD, NEOMED.
- Dr. Ahmed Abdelkarim, Dept. of Specialty Dentistry, BCOD, NEOMED.
- Dr. Mohammad Ansari, Assistant Professor of Anatomy and Neurobiology

Abstract:
Failure of dental implant failure is a complex process caused by the interplay of mechanical stresses and biological issues such as peri-implantitis. While conventional diagnostics mainly respond to problems, computer modeling provides a proactive way to predict failure mechanisms. Nonetheless, traditional Finite Element Analysis (FEA) has primarily been confined to static, linear-elastic models, which do not adequately capture the evolving, time-dependent nature of oral health conditions. This review explores the latest computational strategies for predicting implant failures, highlighting the evolution from basic models to sophisticated, dynamic simulations, with particular emphasis on the progression from medical imaging to predictive analytics. It details the utilization of Imageto-Mesh pipelines, multiphysics simulations, and surrogate modeling techniques. The review also explains how CBCT and Micro-CT scans—via tools such as 3D Slicer—are employed to develop patient-specific tissue models and describes the application of opensource platforms like MOOSE to integrate mechanical stress calculations with biological processes, thus simulating bone remodeling over time. Additionally, it underscores the role of Machine Learning in expediting complex FEA computations, thereby enabling near realtime predictive capabilities. The concept of “Virtual Laboratory" is introduced, wherein parameters are optimized and analyzed through computational simulations. Special attention is given to open-source workflows that link physical models to data-driven algorithms, using Python and MATLAB. The integration of high-quality imaging, multiphysics FEA, and artificial intelligence is propelling the development of the Dental Digital Twin—a comprehensive digital model of a patient’s oral health status. The authors believe that nextgeneration models will not only show current stress distributions but also forecast progressive bone loss, thereby enhancing surgical planning and proactive intervention.

Keywords: Dental Implants, Digital Twin, Finite Element Analysis (FEA), Multiphysics Simulation, Machine Learning, Bone Remodeling, Peri-implantitis, Patient-Specific Modeling.

The specific aims are to:

1. Search and analyze existing literature.
2. Identify and categorize the computational models for Digital Twin, such as Finite Element Analysis (FEA), Multiphysics Simulation and Machine Learning.
3. From literature, we will evaluate the models, particularly regarding their capacity to predict the progression of Bone Remodeling and Peri-implantitis.
4. Draft a review manuscript and plan for an original study based on the findings.

What is the specific research question being addressed by the research project?

- What is the current evidence on variations of existing computational models for predicting the progression of Bone Remodeling and Peri-implantitis

Submit your application to Dr. Ehsanul Hoque Apu – 3 of 4 projects

Title: Computational Strategies for Real-Time Biomechanical Prediction in Craniofacial Injuries Using Physics-Informed Neural Networks: A Mini-Review.

Project PI: Dr. Ehsanul Hoque Apu, Dept. of Biomedical Sciences, BCOD, Northeast Ohio Medical University (E: ehoqueapu@neomed.edu)

Project Co-PI: Dr. Nazeeba Siddika, Dept. of Specialty Dentistry, BCOD, Northeast Ohio Medical University (E: nsiddika@neomed.edu)

Other NEOMED Faculty Investigators:
- Dr. Ahmed Abdelkarim, Dept. of Specialty Dentistry, BCOD, NEOMED.
- Dr. Mohammad Ansari, Assistant Professor of Anatomy and Neurobiology

Abstract:
Traditional assessment of complex craniofacial trauma lacks the quantitative accuracy needed for optimal treatment planning. While the Finite Element Method (FEM) provides high-fidelity biomechanical analysis, its computational cost limits clinical use in timesensitive situations. Physics-based machine learning overcomes this by creating eEicient surrogate models that incorporate the governing laws of mechanics, allowing near real-time prediction of fracture patterns and post-operative outcomes with high physical accuracy. This paper discusses key computational methods for combining FEM and physics-informed machine learning (ML), presenting a schematic for a clinical workflow and examining the current limitations of this approach. This work emphasizes a crucial step toward translating advanced computational tools from research into personalized, real-time surgical planning.

The specific aims are to:
1. Search and analyze existing literature.
2. Identify and categorize the computational models, Finite Element Analysis (FEA), Multiphysics Simulation and Machine Learning.
3. From literature, we will evaluate the models, particularly regarding their capacity to predict the progression of hard and soft tissue injuries.
4. Draft a review manuscript and plan for an original study based on the findings.

What is the specific research question being addressed by the research project?
- What is the current evidence on variations of existing computational models for predicting the progression of hard and soft tissue injuries.

Submit your application to Dr. Ehsanul Hoque Apu – 4 of 4 projects

Title: Preclinical Imaging of Temporomandibular Joint Microarchitecture.

Project PI: Dr. Ehsanul Hoque Apu, Dept. of Biomedical Sciences, BCOD, Northeast Ohio Medical University (E: ehoqueapu@neomed.edu)

Project Co-PI: Dr. Nazeeba Siddika, Dept. of Specialty Dentistry, BCOD, Northeast Ohio Medical University (E: nsiddika@neomed.edu)

Other NEOMED Faculty Investigators:
- Dr. Ahmed Abdelkarim, Dept. of Specialty Dentistry, BCOD, NEOMED.
- Dr. Mohammad Ansari, Assistant Professor of Anatomy and Neurobiology

Abstract:
The temporomandibular joint (TMJ) is a complex load-bearing articulation comprising the mandibular condyle, temporal bone, and an interposed fibrocartilaginous disc. Its intricate microstructure and biomechanical demands make it particularly susceptible to temporomandibular disorders (TMDs), which aCect a significant portion of the population and often lead to chronic orofacial pain and functional limitations. Despite decades of research, the internal architecture of the TMJ—especially the disc and osteochondral interface—remains insuCiciently characterized due to its deep anatomical location and heterogeneous tissue composition. Recent advances in high resolution imaging modalities, particularly micro-computed tomography (microCT), have enabled detailed three-dimensional (3D) visualization of mineralized and soft tissues within the TMJ. When integrated with complementary techniques such as high-resolution magnetic resonance imaging (MRI) and histological validation, these approaches oCer unprecedented insights into the spatial organization, mineral density, and structural integrity of the joint. This review highlights the potential of preclinical imaging to quantitatively assess TMJ microstructure, paving the way for improved understanding of TMD pathophysiology and the development of targeted therapeutic strategies.

The specific aims are to:
1. Search and analyze existing literature on the biology of temporomandibular joint (TMJ) and the relation with TMJ osteoarthritis (OA).
2. Identify and categorize the recent advances in high-resolution imaging modalities for 3D visualizing of TMJ and TMJ-OA.
3. From literature, we will evaluate the stages of osteochondral junction lesions in TMJ and evaluate the existing pre-clinical models to study TMJ-OA.
4. Draft a review manuscript and plan for an original study based on the findings.

What is the specific research question being addressed by the research project?
- What is the current evidence on stages of osteochondral junction lesions in TMJ by existing computational models for predicting the progression of hard and soft tissue injuries.

Submit your application to Dr. David Kay

Project title: Tooth shape across ontogeny in crocodylian species with varying degrees of heterodonty

PI: David Kay; Assistant Professor, Department of Biomedical Science, Bitonte College of Dentistry

Research location: NEOMED (Rootstown campus)

Abstract

In some vertebrates with socketed dentitions, alveoli (sockets) and tooth cusps are unusually related. For example, tooth cusp offset in some muroid rodents is the result of tooth bud-jaw interactions: parallel or offset cusps can be induced to vary developmentally based on experimentally manipulated lateral alveolar thickness in mice and voles. This research emphasized the jaw and teeth as a directly integrated developmental unit. Previously, I have also shown that tooth crown shape and alveolar shape are significantly related in adult *Alligator mississippiensis,* suggesting that a similar mechanically constraining mechanism found in rodents may extend to crocodylians as well. Further, crocodylians are uniquely polyphyodont with tooth sockets formed iteratively during ontogeny, implicating this integration as a means of generating heterodont or homodont dentition over the course of their lifespan. Preliminary investigations into alveolar mechanical constraint driving heterodonty in crocodylians suggests that iteratively growing alveolar septa generate a mesiodistal constraint to each developing crown and alveolar walls generate a buccolingual constraint. While this implies the alveoli mechanically shape teeth to produce heterodonty in crocodylians, the study did not take into account a quantification of tooth shape itself. This current project aims to investigate this by measuring tooth shape across ontogeny in crocodylian species with relatively more heterodont (differently shaped teeth) or homodont (similar shaped teeth) dentitions, by testing *Alligator mississipiensis* and *Crocodylus acutus*, respectively using a 3D digital anatomical approach.

Significance

My research program strives to deepen the understanding of socket-crown relationships, with the eventual goal of understanding its role in the evolution of complex dentitions. This then would provide a possible proof-of-concept for the use of extant crocodylians as a possible model system for tooth replacement in humans.

Research objectives/goals

Overall, the goal of my research is to investigate the relationship between alveoli and tooth shape in thecodont dentitions, comparing crocodylians and mammals to eventually understand the influence of tooth sockets on the evolution of complex dentitions. This project's goals are to 1) quantify alligator and crocodile tooth shape across ontogeny to better understand the amount of shape change from hatching to adulthood, and 2) compare the shapes between the

two species to quantify the degree of heterodonty between them and how that shifts across ontogeny. This understanding will be placed within the context of alveolar growth patterns to investigate a possible alveolar-tooth relationship driving heterodonty in extant crocodylians.

Research methods

The methods for this project rely heavily on using computational tools to measure 3D digital datasets in the form of micro-computed tomography scans of crocodilian heads and skulls.

Data analysis method

Tooth shape data from specimens will be analyzed using a specific set of methods from geometric morphometrics (statistical study of shape) called outline analysis using the program R. This methodology avoids the need for homologous landmarks but requires manual alignment of images to properly remove orientation, location and scale. Once quantified, shape data will then be ordinated, and specific statistical hypotheses will be tested and tied back to the overall objectives. I have developed the basic statistical workflow for this project, so R expertise is not necessary, but is a great learning experience for how to curate, analyze, and discuss complex data.

Fellowship research role

The research fellowship recipient will be tasked with processing, procurement, and analysis of tooth shape data. These insights on tooth shape differences between species and across ontogeny will play a critical role in my larger research program investigating the possible relationship between tooth sockets and tooth shape. The shape data provide the specific empirical evidence of how teeth change shape across tooth generations and vary between crocodylians. Currently my research only compares generalized whole-dentition levels of heterodonty, and lacks the specific information needed to synthesize this portion of my research program.

Student Fellow Training/Mentoring Plan

Training of the research fellowship recipient will take the form of scheduled meetings to discuss literature and progress, hands-on training modules, and informal meetings as data are gathered and analyzed. The first week or two (student schedule dependent) will be focused solely on introducing relevant primary background literature and completing an Avizo training module. The literature will largely surround the concepts of dental anatomy, alveolar-tooth interactions, and digital anatomical approaches. The Avizo training module will address the specific methods for processing a 3D dataset for measurement, segmentation, and rendering. Once these are completed, the student will be tasked with procuring the data needed for outline analysis. During this time, we will continue to discuss primary literature that is related to data analysis (e.g., geometric morphometrics) as well as further dental research. Depending on other students' interest, the literature discussions could take the form of a journal group that meets weekly.

The resources that will be involved in this research mostly revolve around the processing, measurement, and analysis of digital anatomical data. Processing and measurement of digital anatomical datasets will be carried out using the software suites Avizo and Fiji. Processed tooth outlines will be analyzed using a pre-developed analytical framework in R. Depending on specimen availability, there could be usage of NEOMED's in-house micro-computed tomography scanner to gather additional scan data. This would then include a more hands-on training regarding machine usage and safety. The current plan of this research will be centered on NEOMED's Rootstown campus. As the computing equipment is largely shared, scheduling for time on machines will require cooperation with other labs.

Submit your application to Dr. Nazeeba Siddika – 1 of 2 projects

Title: Airborne Contaminants in Dentistry: A Comprehensive Review of Microbial, Chemical, and Environmental Emissions During Clinical Procedures

Principal Investigator (PI) name: Dr. Nazeeba Siddika, Assistant Professor of Epidemiology.

Co-PI: Dr. Ehsanul Hoque Apu, Assistant Professor of Biomedical Sciences.

Other Investigator: Dr. Sorin Teich, Dean of Bitonte College of Dentistry.

Location: Bitonte College of Dentistry, NEOMED

Abstract of project – Aerosol generation in dental settings has long been recognized as a central concern for occupational and patient safety. Dental procedures involving high-speed handpieces, ultrasonic scalers, air–water syringes, and air-polishing devices produce complex mixtures of airborne contaminants, including microbial bioaerosols, chemical emissions, and particulate pollutants. These aerosols consist of droplets and particles of varying sizes that can remain suspended in the air, disperse throughout the operatory, and be inhaled by dental personnel or patients.

The COVID-19 pandemic amplified global attention to dental aerosols, highlighting the potential role of airborne transmission in clinical environments. Although numerous studies have investigated aerosol generation during specific dental procedures, findings remain highly variable due to methodological inconsistencies, differences in measurement technologies, and heterogeneity across clinical environments. Furthermore, recent investigations indicate that aerosols generated in dentistry may contain not only microorganisms from the patient's oral cavity but also particles derived from dental materials, waterline systems, cleaning agents, and environmental dust. These components contribute to a complex exposure mixture with uncertain health implications.

Many investigations address only microbial contamination or aerosol quantity, neglecting the chemical and particulate components that also contribute to exposure. Despite the substantial interest in aerosol-related risks, a comprehensive understanding of the sources, composition, and behavior of aerosols and pollutants generated during dental procedures is still lacking. This gap hinders the development of evidence-based guidelines to optimize ventilation, personal protective equipment (PPE), material selection, and procedural workflows. A rigorous synthesis of the available evidence is therefore needed to support future occupational safety recommendations and infection-control policies.

The goals and objectives for the research project; what aspect of the overall research will be the focus of the student's research experience?

The primary aim of this research proposal is to conduct a comprehensive review of the available evidence on microbial, chemical, and particulate pollutants generated during dental procedures, with an emphasis on identifying their sources, composition, and potential health implications.

The specific aims are to:

1. Synthesize existing literature on aerosol production during dental procedures, focusing on microbial, chemical, and particulate emission profiles.
2. Identify and categorize the sources of these contaminants, including patient-derived, procedure-specific, equipment-based, and environmental origins.
3. Evaluate reported exposure levels, including particle size distributions, microbial loads, and chemical concentrations across different dental procedures and settings.

The student will gain the ability to understand the purpose and value of conducting a comprehensive review in research and how to summarize the evidence.

What is the specific research question being addressed by the research project?
What is the current evidence on the quantity, size distribution, and composition of aerosols generated during common dental procedures, and what are their primary sources?

The significance of the overall research
This comprehensive review will provide a much-needed synthesis of the diverse evidence related to aerosolized contaminants in dental settings. By integrating data on microbial, chemical, and particulate emissions, the study will offer a holistic understanding of dental aerosol composition, sources and its determinants. The findings will:

- Support the development of evidence-based infection-control policies, particularly in the wake of emerging respiratory diseases for both healthcare provider and the patient.
- Inform occupational health guidelines by clarifying the risks faced by dental personnel and identifying high-emission procedures.
- Guide improvements in clinic ventilation, procedural workflows, and equipment selection, ultimately enhancing indoor air quality.

By providing a robust scientific foundation, this review will contribute meaningfully to the advancement of safer, more resilient, and better-informed dental clinical environments.

The research methods that will be used/learned by the student during the fellowship to address the question/problem being asked.
The students will learn how to formulate a clear and focused research question. They will learn to identify appropriate search terms, perform literature searches, and extract relevant and essential information from selected articles. The students will also develop skills in organizing and recording extracted data, synthesizing the available evidence, identifying gaps in the current literature, and proposing informed recommendations for future research directions.

The proposed methods of data analysis: Not applicable

A statement of how the anticipated findings from the fellow contribute to the success of the overall research being investigated.
The fellow's review will directly support the broader research program by providing a consolidated, methodologically rigorous foundation upon which future experimental investigations and risk-mitigation strategies can be built. Their work will help illuminate gaps in current knowledge, highlight underexplored exposure pathways, and inform the development of

evidence-based recommendations for ventilation optimization, PPE design, operatory workflows, material selection, and infection-control policies. Ultimately, the fellow's findings will strengthen the scientific rationale guiding the project and enhance its impact on dental public health and occupational safety.

Submit your application to Dr. Nazeeba Siddika – 2 of 2 projects

Title: Knowledge, Attitude and Practice on Dental Care, and Oral Health Status among Pregnant Women in Bangladesh.
Principal Investigator (PI) name: Dr. Nazeeba Siddika, Assistant Professor of Epidemiology.
Co-PI: Dr. Ehsanul Hoque Apu, Assistant Professor of Biomedical Sciences.
Location: Bitonte College of Dentistry, NEOMED

Abstract:
Oral health is a critical component of overall well-being, yet pregnant women face heightened risks of gingivitis, periodontitis, and dental caries due to hormonal fluctuations, dietary changes, altered saliva composition, and decreased immune function. These oral conditions have been associated with adverse pregnancy outcomes, including low birth weight and preterm delivery. Despite the recognized importance of maternal oral health, many pregnant women, specifically from Low- and Middle-Income Countries (LMICs) like Bangladesh avoid dental care because of socioeconomic and cultural barriers, limited knowledge, and misconceptions about the safety of dental procedures during pregnancy. Healthcare providers including dentists, midwives, and prenatal care professionals also frequently lack adequate training and confidence in providing or recommending dental care during pregnancy, resulting in missed opportunities for early intervention. The World Health Organization advocates for integrated health service delivery, especially in resource-constrained settings, yet collaboration between medical and dental professionals remains insufficient. This gap underscores the need for strengthened interdisciplinary approaches, improved provider education, and increased awareness among pregnant women. Addressing these challenges is essential for reducing preventable oral diseases in pregnancy and lowering the risk of early childhood caries linked to maternal transmission of cariogenic bacteria.

Goals and Objectives of the Research Project
The overarching goal of this research project is to examine the knowledge, attitudes, and practices related to prenatal oral healthcare among pregnant women and healthcare providers, and to identify barriers in Bangladesh.

The specific objectives are:
To assess the oral health knowledge, attitude, and hygiene practices of pregnant women in Bangladesh.

To measure the oral health status of pregnant women in Bangladesh.

To identify factors associated with oral hygiene and dental health status of pregnant women in Bangladesh.

Specific Research Question
Primary Research Question: What are the key knowledge gaps, attitudes, and perceived barriers that prevent pregnant women and prenatal healthcare providers from seeking or recommending appropriate dental care during pregnancy?
Supporting sub-questions may include:

- How do misconceptions about the safety of dental procedures during pregnancy influence care-seeking behavior?
- What sociocultural or socioeconomic factors contribute to reluctance in seeking dental care?
- What are the barriers to accessing or visiting dental care during pregnancy?

Significance of Overall Research

Poor maternal oral health has been associated with adverse pregnancy outcomes such as preterm birth and low birth weight, as well as early childhood caries due to vertical transmission of *Streptococcus mutans*. Despite all the known adverse effects of poor oral hygiene during pregnancy on maternal and child health, many pregnant women do not access dental services in LMICs, and healthcare providers often lack clarity or confidence regarding oral health recommendations.

This research is significant because it:

- Addresses preventable oral and systemic health complications in LMICs like Bangladesh.
- Supports WHO's call for integrated health service delivery, particularly in low-resource settings.
- Identifies modifiable barriers that can guide policy changes, provider training, and public health interventions.
- Contributes to improving maternal health outcomes and long-term child oral health.

Research Methods the Student Will Use/Learn

This will be an observational, cross-sectional and hospital-based study. We have already collected preliminary data by surveying pregnant women in the capital city of Bangladesh. During the fellowship, the student will learn about multiple qualitative and quantitative research methods, including: Reviewing existing research on prenatal oral health, periodontal disease during pregnancy, and healthcare provider roles.
Data cleaning, organizing datasets, and maintaining confidentiality and research integrity.
Writing initial draft of the manuscript, journal selection and preparing the manuscript for publication.

Contribution of Anticipated Student Findings to the Overall Research

The student's findings will play a crucial role in identifying key barriers and misconceptions that contribute to the low utilization of dental services during pregnancy in LMICs. These insights will:

- Inform the development of targeted educational interventions for both pregnant women and healthcare providers.
- Help shape recommendations for integrated prenatal–dental healthcare models.
- Contribute to evidence-based strategies aimed at reducing adverse pregnancy outcomes related to poor oral health.
- Support future training modules for midwives, physicians, and dentists regarding the importance and safety of dental care during pregnancy.

Ultimately, the student's work will strengthen the evidence base needed to advocate for improved oral healthcare integration within prenatal services and promote better maternal and child health outcomes in LMICs.

Submit your application to Dr. Hope Ball

Project Description:

***Title**:* Pediatric Cancer Research: Determining the Role of Cellular Metabolism in Therapeutic Resistance

Principle Investigator: Hope C. Ball, Ph.D.; Associate Research Scientist (Akron Children's Hospital); Assistant Professor Department of Biomedical Sciences (NEOMED)

Abstract: Cancer is the second leading cause of death in the pediatric population. While adult cancers arise from genetic instability caused by repeated carcinogenic exposure, most pediatric cancers are caused by mutations or dysregulations in pathways governing normal development. Pediatric mutations are unique and demonstrate significant differences from their adult same-cancer counterparts. Because of this, findings from adult malignancies cannot be directly translated into effective pediatric therapies. While improvements in diagnostic and treatment strategies have improved patient outcomes, a significant number of cases are still compromised by therapeutic resistance. Therapy development is hampered both by unique pediatric mutations and because the underlying mechanisms of therapy resistance remain poorly understood.

***Significance**:* Improvements in care have improved overall survival rates for many common childhood cancers, but overall survival for patients with bone and CNS tumors have not changed significantly. One reason for this is that patients with recurrent and/or metastatic disease often have tumors resistant to standard-of-care chemotherapies. These realities underscore the critical need for research to better understand therapy resistant mechanisms towards the goal of identifying novel targets for therapy, prevent metastatic spread, and improve chemotherapeutic efficacy.

Goals/Objectives: The goals of my research laboratory are to determine the underlying mechanisms that contribute to chemotherapeutic resistance in several common pediatric solid tumors (medulloblastoma, neuroblastoma, and osteosarcoma). Cellular metabolism in one way in which cancer cells hijack host resources and escape immune detection. These pathways are of particular interest for the development of novel therapeutics, and my goals are to elucidate cancer-specific mechanisms and/or biomarkers to further these research avenues.
Methods/Data Analysis: My laboratory utilizes both *in vitro* and *in vivo* methods. Fellows can expect to learn cell culture, RNA/DNA/protein isolation, gene expression (qPCR), Western blot, pathway modulation (by RNAi, overexpression vectors, and/or pharmacology), proliferation/viability assays, and data analysis (ANOVA, t-tests, relative expression (delta-delta Ct)).

Fellow's Contributions to Research: The data collected will be vital to improving the scientific understanding of the mechanisms underlying chemotherapeutic resistance in pediatric solid cancers. The Fellow will work alongside the PI and the Senior Technician to learn all necessary laboratory techniques towards the goal of becoming proficient and independent in these tasks. The Fellow will be directly involved with data collection and analysis, and will be responsible for

preparing and presenting a poster at the annual NEOMED Student Research Fellowship Symposium. Additionally, the Fellow will be included on all posters, presentations, and publications that result from the work conducted in the laboratory during the Fellowship.

Student Fellow Training and Mentoring Plan:

Training/Mentoring Plan: Mentoring is an important part of any internship program. The training the Fellow will receive in the laboratory will advance their understanding of basic/translational research study design (including methodology, implementation, and data analysis) and improve their ability to write/critically evaluate published peer reviewed research, an ability critical not only to this fellowship, but to their future profession as a physician. To foster these skills, the Fellow will attend and participate in weekly lab meetings and journal clubs and may be asked to contribute to manuscripts in preparation for publication in peer reviewed journals.

Resources: The Fellow will have access to the PI and Senior technician who are skilled in molecular techniques and have experience teaching these techniques. The Fellow will also have access to hospital research meetings, access to clinical journals, and scientific and data analysis software.

Location: Research will take place in the Akron Children's Hospital Hematology/Oncology Molecular Research Laboratory located on the second floor of the RGE building at NEOMED.

Submit your application to Marc Basson – project 1 of 2

Project title: Mechanistic Drivers of SLFN12-Mediated Chemotherapy Sensitization in Lung Adenocarcinoma

PI: Marc D. Basson, MD, PhD

Location: RGE 100

Abstract
The Basson Lab has been investigating the role of SLFN12, an intermediate member of the Schlafen protein family, in the biology and drug responsiveness of several cancer types. Prior work from the laboratory showed that high SLFN12 expression is associated with improved prognosis and increased chemotherapy sensitivity in cancers such as triple-negative breast cancer. Our ongoing research in lung adenocarcinoma has demonstrated similar trends, where SLFN12 overexpression enhances sensitivity to specific cytotoxic drugs in some cell lines. However, other lung adenocarcinoma cell lines remain resistant or display only minimal changes in drug response despite SLFN12 overexpression. To understand these differences, we analyzed proteomic profiles from SLFN12-overexpressing sensitive and resistant lung adenocarcinoma cell lines. Several proteins were significantly upregulated in the sensitive line compared with the resistant line, while other proteins were downregulated in the sensitive cells but elevated in the resistant ones. These findings suggest that downstream effectors of SLFN12 may determine whether a cell line becomes sensitized or remains resistant. We are generating stable lentiviral cell lines that either overexpress SLFN12 or contain an empty vector control in one sensitive and one resistant lung adenocarcinoma model. The proposed project will manipulate proteins identified from proteomic analysis by knocking down proteins that are upregulated in the sensitive line and overexpressing proteins that are downregulated. The goal is to determine whether altering these targets can convert sensitive lines into resistant ones and, conversely, make resistant lines more sensitive to chemotherapy.

Significance
This study will help define the molecular mechanisms that govern SLFN12-mediated chemotherapy sensitization in lung adenocarcinoma. By identifying and validating the key downstream proteins that distinguish sensitivity from resistance in SLFN12-overexpressing cells, the project may identify new biomarkers that predict chemotherapy response. These findings may also reveal new therapeutic targets that could be modulated to overcome drug resistance. A clearer understanding of how SLFN12 interacts with downstream pathways could ultimately contribute to developing more effective treatment strategies for lung adenocarcinoma patients.

Research methods that will be learned by the student

- Mammalian cell culture
- Lentiviral transduction and stable cell line maintenance
- Gene knockdown and gene overexpression methods
- Crystal violet cell viability assays
- Drug preparation and dose response curve generation
- Q PCR

- Western blotting
- Interpretation of proteomic data
- Data analysis

Proposed methods of data analysis: Standard statistical techniques, including t-tests and outlier analysis

How will the anticipated findings contribute to the success of the overall research?
If altering the expression of SLFN12-associated downstream proteins changes chemotherapy sensitivity, this will help confirm the pathways that regulate SLFN12's effect in lung adenocarcinoma. These results will support the development of predictive markers for chemotherapy responsiveness and may guide the design of therapeutic strategies that resensitize resistant tumors. Positive findings would justify additional validation in mouse models and could inform future translational efforts, including the preparation of an IND application for human studies.

Student fellow mentoring plan
The student will work with a trained member of the Basson laboratory, receiving daily guidance and support throughout the project. The students will also participate in weekly two-hour laboratory meetings focused on data presentation, experimental design, troubleshooting, and scientific discussion. Depending on the student's interest, there may be opportunities to engage in additional projects in the laboratory, including small animal work or clinical research initiatives within the Basson research group. The student will prepare a poster or oral presentation for the student research day under Dr. Basson's supervision, and the data generated may contribute to a manuscript on which the student will be a coauthor. All research activities will take place in the Basson laboratory.

Submit your application to Dr. Marc Basson – project 2 of 2

Project title: SLFN12 sensitizes Colorectal cancer to certain chemotherapy drugs

PI: Marc D. Basson, MD, PhD

Location: RGE 100

Abstract
The Basson Lab has been investigating the effects of SLFN12, an intermediate protein of the Schlafen family linked to better prognosis in aggressive and resistant cancer types, such as triple-negative breast cancer and lung adenocarcinoma. The Basson lab published an article showing that the improved prognosis observed in triple-negative breast cancer cells with high SLFN12 expression is attributed not only to the tumor's intrinsic biology when SLFN12 is expressed, but also to the sensitization of certain chemotherapy drugs. Our work on lung adenocarcinoma, which is still ongoing, confirmed this. In colon cancer, high levels of SLFN12 expression are often linked to a better prognosis, implying that elevated SLFN12 could be a positive outcome indicator, possibly because it helps suppress tumor cell growth and promotes differentiation. We look forward to testing how different chemotherapy drugs affect the cell viability of HT-29 and HCT 116, two colon adenocarcinoma cell lines, when we overexpress SLFN12, compared to the baseline SLFN12 expression in the same cell lines.

Significance
This study will provide a deeper understanding of SLFN12's role in colon adenocarcinoma, including whether its impact on prognosis is related to the tumor's intrinsic biology or its response to chemotherapy agents when SLFN12 is overexpressed. If proven to impact cells' response to chemotherapy, SLFN12 levels may one day help determine the most effective chemotherapeutic strategy for patients with colon adenocarcinoma. Additionally, targeting and activating the SLFN12 pathway might have a synergistic effect when combined with conventional cytotoxic chemotherapy in colon adenocarcinoma with low SLFN12 levels.

Research methods that will be learned by the student

- Mammalian cell culture
- Crystal violet cell viability assay
- Drug preparation
- Q-PCR
- Western blotting
- Data analysis

Proposed methods of data analysis: Standard statistical techniques, including t-tests and outlier analysis

How will the anticipated findings contribute to the success of the overall research?
Should SLFN12 levels be shown to influence cellular responses to chemotherapy, they could eventually be used to guide the selection of the most effective chemotherapy regimen for colon

adenocarcinoma patients. This can be validated in mice and rats and eventually used as the basis for an IND application to the FDA for human trials.

Student fellow mentoring plan

The student will be assigned to work with a member of the Basson laboratory for daily guidance and will participate in weekly two-hour laboratory meetings that both focus on data and emphasize discussion of experimental design and data analysis. Depending on the student's level of interest, there may also be opportunities to participate in other work going on in the lab, including small animal studies, as well as clinical research projects that are ongoing in the Basson research group. It is anticipated that the student will subsequently prepare a poster or oral presentation for student research day under Dr. Basson's supervision and that the data developed will be included in a publication in which the student will be a co-author. All research will be conducted in the Basson laboratory.

Submit your application to Dr. Yeong-Renn Chen

1. Project Title

CB-839 Targets Cardiac Mitochondrial Glutaminolysis to Mitigate Acute Myocardial Injury

Principal Investigator: Yeong-Renn Chen, Ph.D.
Title/Location: Professor, RGE344

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2. Abstract of Project

The objective of this research project is to investigate how mitochondrial health influences cardiac adaptation to acute myocardial injury, with a long-term goal of reducing the progression to heart failure. Using a murine model of ischemia–reperfusion (I/R) injury, we will examine the role of mitochondrial glutaminase (GLS1), a key enzyme mediating glutamine oxidation (glutaminolysis), which may compromise myocardial resilience under pathological stress.

Glutamine-dependent anaplerosis is activated during oxidative stress in acute myocardial injury. Although this response may provide short-term metabolic support, increased GLS1 activity is also associated with maladaptive remodeling and fibrosis. We hypothesize that in vivo GLS1 inhibition will reduce I/R-induced damage and attenuate adverse cardiac remodeling. Despite the clinical importance of this pathway, the mechanistic contributions of glutaminolysis to myocardial infarction remain insufficiently defined.

To test this hypothesis, we will use CB-839 (telaglenastat), a highly selective, orally available GLS1 inhibitor that targets both GAC and KGA isoforms. CB-839 suppresses mitochondrial glutamine metabolism and has demonstrated excellent tolerability in early oncology trials, with up to 96% inhibition of tumor glutaminase activity. Its predecessor, BPTES, has been shown to attenuate pressure overload–induced cardiac hypertrophy, supporting GLS1 inhibition as a cardioprotective strategy.

FBV mice (8–9 weeks old) will receive CB-839 (200 mg/kg, oral gavage) or vehicle control for 6–18 days. I/R injury will be induced by transient occlusion of the left anterior descending (LAD) coronary artery for 30 minutes, followed by 24 hours of reperfusion.

We will evaluate whether CB-839 enhances myocardial adaptation to I/R by improving mitochondrial respiration, preserving mitochondrial integrity, and suppressing pathological glutaminolysis. Mitochondrial respiration will be measured using oxygen polarography, and cardiac function will be assessed by echocardiography.

The findings are expected to offer mechanistic insights into how glutaminolysis regulates cardiac adaptation to injury and may identify GLS1 inhibition as a therapeutic strategy for myocardial infarction and heart failure. This work has the potential to contribute toward improving human healthspan through novel approaches to cardioprotection.

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3. Significance of the Research

Myocardial infarction affects more than 800,000 Americans annually and carries a 20% mortality rate. Aging amplifies susceptibility to ischemia–reperfusion injury, a major driver of heart failure. Mitochondrial dysfunction—manifested by impaired energy production and redox imbalance—is central to heart failure pathogenesis.

Glutaminolysis increases markedly in post-ischemic myocardium and is implicated in:

- redox dysregulation
- inefficient energy coupling
- impaired myocardial recovery
- progressive cardiac fibrosis and dysfunction

This project tests the hypothesis that pharmacological GLS1 inhibition with CB-839 can improve myocardial resilience to acute myocardial injury and reduce the risk of subsequent heart failure. Using CB-839 as the therapeutic model, this study will help establish whether targeting dysregulated glutaminolysis provides a novel cardioprotective strategy.

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4. Goals and Objectives

This project aims to train medical students in biomedical research while exploring how GLS1-mediated glutaminolysis and mitochondrial health influence the heart's response to acute injury. The objectives are:

- To evaluate how in vivo GLS1 inhibition affects myocardial adaptation to acute I/R injury
- To assess changes in mitochondrial bioenergetics and cardiac function
- To provide hands-on training in echocardiography, mitochondrial isolation, spectroscopic assays, and data analysis

To ensure feasibility within an eight-week summer fellowship, the study will focus on characterizing cardiac and mitochondrial phenotypes in a pharmacological acute I/R model.

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5. Research Methods

A. In Vivo Mouse Model of Myocardial I/R

- The myocardial I/R protocol will follow previously published methods.
- FBV mice treated with CB-839 or vehicle will undergo 30 minutes of LAD ligation followed by 24 hours of reperfusion.
- Cardiac function will be assessed under anesthesia using echocardiography.
- Hearts will then be excised for TTC staining to delineate infarct size and risk region.
- Tissue from the risk region will be used for mitochondrial isolation.

B. Mitochondrial Isolation and Respiration Analysis

- Mitochondria will be isolated from non-ischemic and post-ischemic tissue via differential centrifugation.
- Respiration will be assessed at 30°C using a Clark-type oxygen electrode.
- NADH-linked (malate/glutamate) and succinate-linked respiration will be measured.
- Enzymatic activities of ETC complexes will be quantified as previously described.
- GLS1 activity will be measured by glutamine-to-glutamate conversion coupled to glutamate dehydrogenase.

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6. Data Analysis

1. **Echocardiography:**
    - Ejection fraction, fractional shortening
    - LV internal diameters (systole/diastole)
    - LV volumes
    - Relative wall thickness

- Heart weight/body weight ratio
- Mitral valve E/A ratio

2. **Mitochondrial assays:**
   - OCR first-derivative kinetics
   - Complex I activity via NADH oxidation. Complex II activity via DCPIP reduction
   - Complex III and Complex IV activities via ferricytochrome c reduction and ferrocytochrome c oxidation
3. **Statistics:**
   - Data reported as mean ± SEM
   - Between-group comparisons using one-way ANOVA

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7. Contribution to the Overall Research Program

By integrating echocardiographic analysis, mitochondrial bioenergetics, and pharmacological GLS1 modulation, this pilot project will expand our understanding of how mitochondrial glutaminolysis influences cardiac recovery after I/R injury. These studies are expected to:

- Reveal new insights into mitochondrial determinants of cardiac resilience
- Identify GLS1 as a potential therapeutic target
- Provide foundational data for future grant applications
- Support long-term investigations into cardioprotection and heart failure prevention

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Summer Research Fellow Training and Monitoring Plan

1. **Student Requirements and Procedures**

a. Students will begin by reviewing key publications from Dr. Chen's group and the 2025 summer research poster. They will receive training on acute myocardial injury models, echocardiography, mitochondrial isolation, spectroscopic assays, and data interpretation.

b. Echocardiography training will be supervised by Dr. Vahagn Ohanyan.

c. Students will participate in regular 1:1 meetings with Dr. Chen and joint meetings with Dr. Chen and Dr. Ohanyan.

d. Training schedule:

- Weeks 1–3: animal model and pharmacological treatment
- Weeks 4–6: mitochondrial biology and polarographic analysis
- Weeks 7–8: data analysis and interpretation

e. Students will attend weekly Cardiovascular Interest Group meetings and present research updates.

f. Students will participate in the summer research journal club.

g. Students will present a research poster at Summer Research Day.

2. **Protocol Availability**
   Protocols for CB-839 and BPTES treatment are established in the PI's laboratory. All required equipment and personnel are available.
3. **Research Location**
   Research activities will be conducted in RGE laboratories and the echocardiography facility in the C-building on the NEOMED campus.

Submit your application to Dr. Lisa Cooper

Project Description

1) **Title**: Neuron counts in the unusually large brains of whales
PI: Lisa Cooper, Department of Biomedical Sciences
LOCATION: NEOMED, C-156

2) **Abstract**: Within mammals, dolphins and beluga whales are known to have a large brain size relative to body size. However, little is known of the composition of these brains. To increase our understanding of the different cells that make up the brains of terrestrial vs. marine mammals, this study aims to establish a fundamental understanding of the number of neurons in the brains of an echolocating and agile beluga whale compared to a slow move and non-echolocating bowhead whale. This study will use fluorescent labels to stain the neurons in the brains of both animals. Numbers of neurons will be counted using a confocal microscope. We hypothesize that the cerebellum of both animals will be roughly equal in their neuron density, but the cortex of the beluga brain will display a greater neuron density. Results will be compared with published accounts of neuron densities within terrestrial mammals (i.e., bats, elephants, carnivores, and ungulates). We expect our results will add a critical understanding of the architecture of big brains in cetaceans as well as elucidate the evolution of brains within aquatic and terrestrial mammals.

3) **Significance of the Research:** The brains of cetaceans (whales, dolphins, and porpoises) are unusual among mammals in that they process different locomotor and sensory information. We expect the life in an aquatic habitat has altered brain function. Comparative studies of the brains of cetaceans have so far shown that massive increases in brain size are found in dolphins and their close relatives, but baleen whales retain relative brain sizes similar to that of terrestrial mammals. Critical to our understanding of the architecture of these brains is understanding the cellular architecture of the brains. This study will increase our understanding of the evolutionary origins by quantifying cell type within the brains of a large-brained beluga compared to that of a small-brained bowhead whale. By comparing neuron counts, our data will elucidate whether the large brain of some cetaceans is the result of an expansion in the number of neurons, or supportive glial cells, or both. Fresh tissues of these arctic species are exceptionally rare. We conduct field work in the Arctic and has collected brains of each species that are currently fixes and ready for analysis.

Our contribution is expected to further the goal of understanding the unique architecture of the brains of echolocating and non-echolocating whales compared to terrestrial mammals. Our contribution will be significant because the data will assist in developing a nuanced understanding of the cellular evolution leading to the expanded brain size in modern whales. It is also likely that our results will vertically advance our understanding of neural plasticity within the mammalian brain associated with life in novel habitats.

4) Goals and Objectives of the Research: By comparing neuron counts, our data will elucidate whether the large brain of some cetaceans is the result of an expansion in the number of neurons, or supportive glial cells, or both.

5) Research Methods Learned by the Summer Fellow: First, the researcher will be trained to participate in every phase of project research, including specimen preparation and analyses. Opportunities for students to gain experience with unusual model organisms are rare, and the skills gained through involvement with this project should substantially broaden the researcher's skill sets. The student will learn to homogenize and stain brain tissue, count neurons, and analyze data.

6) Research Methods and Data Analysis – The brains of one beluga and bowhead are fixed. The brains will be cut into 5-gram sections, and these sections will then be homogenized, stained, and counted for neurons. DAPI stain will be used to stain all nuclei, while an anti-NeuN antibody stain will stain neurons. This protocol is already established the lab of the PIs. Using a confocal microscope, we will count number of positively DAPI and anti-NeuN nuclei throughout homologous regions in both taxa. We will compare neuron densities of these parts to those of terrestrial mammals through use of ANOVA.

7) Expected Outcomes – Three possible outcomes are anticipated for this study. Our null hypothesis is that neuron densities will be similar between the two whales. If the beluga cerebellum has greater neuron density, this is likely associated with its agile swimming style relative to the slow-moving bowhead. Our findings, regardless of outcome, will lay the foundation for future work quantifying total brain neuron counts between the two taxa. We expect the cerebellum work to be the first of several publications.

Student Fellow Training/Mentoring Plan: Funding is requested to support one summer research fellow. PI's Cooper, Smith and Thewissen are committed to fostering the researcher's development for the summer. This goal will be achieved through a structured mentoring program, as described below.

Research will be conducted in Cooper's lab (C-156) using fixed brains that are ready for analysis. Protocols are already established, and all necessary laboratory equipment and disposables are already in use as this is an ongoing project.

Besides benefiting from working alongside the PI's, the student will be required to attend and present once at weekly laboratory meetings. The Musculoskeletal Research Focus Area - a joint effort of the Department of Anatomy and Neurobiology and the Department of Integrated Medical Sciences at NEOMED – also sponsors a weekly journal club on the general topic of "Evolutionary Morphology", where the fellow would have the opportunity to share and discuss ongoing research findings and pertinent scientific publications. Finally, the student will design and present a poster for the end-of-program poster symposium at NEOMED.

Submit your application to Dr. Feng Dong

Project title: Molecular and Cellular Mechanisms Driving the Development of Aortic Stenosis
Principal Investigator: Feng Dong, Associate Professor, RGE 234

Abstract of project:

Previously, we identified a blunted stromal cell–derived factor-1 (SDF-1)/CXCR4 signaling axis in diabetes, and our preliminary data indicate that chronic CXCR4 expression is increased in cardiac myocytes from diabetic mice. Although CXCR4 activation in the diabetic heart produces a pronounced negative inotropic effect, we believe this seemingly counterintuitive response represents a key adaptive mechanism. Importantly, our initial studies show that diabetic mice (high-fat, high-sugar diet) lacking CXCR4 specifically in cardiac myocytes exhibit markedly higher mortality than diet-matched wild-type controls. More recently, using our endothelial cell–specific CXCR4 knockout mice, we discovered that loss of CXCR4 in endothelial cells leads to the development of aortic stenosis. This proposal builds on these novel models of CXCR4 deficiency to investigate the role of CXCR4 in aortic valve stenosis and to define the mechanisms by which CXCR4 loss disrupts endothelial and cardiac function.

4. The significance of the overall research:

Upon completion of these studies, we will define the critical contribution of the SDF-1/CXCR4 axis to the pathogenesis of aortic stenosis. This work will establish a mechanistic foundation for identifying novel physiological insights and developing new therapeutic strategies targeting the pathways that drive valve disease.

5. The goals and objectives for the summer research project what aspect of the overall research will be the focus of the student's summer research experience? What is the specific research question being addressed by the summer research project?

The goal of our proposed studies is to elucidate the molecular mechanisms and physiological processes that drive the development of aortic stenosis. The student's summer research experience will focus on learning and applying scientific principles and experimental approaches relevant to aortic stenosis research.

The specific research question for the summer project is to determine how loss of CXCR4 affects cardiac function using our endothelial cell–specific CXCR4 knockout mouse models.

6. The research methods that will be used/learned by the student:

The experiments will provide students with hands-on experience in a range of cellular, molecular, and biochemical techniques, including cell culture, Western blotting, and quantitative PCR. Students will also gain exposure to microscopy and in vivo methodologies, such as confocal imaging and echocardiography, as part of their training in interdisciplinary cardiovascular research.

7. The proposed methods of data analysis:

Comparisons between two groups will be assessed using a two-tailed Student's t-test. For analyses involving multiple groups, we will use two-way ANOVA followed by Tukey's post hoc test.

8. A statement of how the anticipated findings from the summer research fellow contribute to the success of the overall research being investigated?

The summer research project is part of an ongoing investigation in the lab. Our preliminary data indicate that deletion of CXCR4 in endothelial cells promotes the development of aortic stenosis. The anticipated outcomes of the summer project will address a key question: how does endothelial cell–specific CXCR4 loss influence aortic stenosis and overall cardiac function?

Student Fellow Training/Mentoring Plan

Plan for training/mentoring the summer research fellow – individual, group, lab meetings, journal clubs, seminars, etc.

After receiving appropriate training, students will engage in a variety of experiments spanning cell biology, molecular biology, and microscopy, with each student assigned unique tasks that contribute directly to the overall project. They will be trained in troubleshooting techniques and encouraged to develop alternative strategies and hypotheses based on their experimental findings. Students will regularly present their results and project updates both formally, during lab meetings, and informally to the PI. These meetings will include discussions of relevant literature to enhance critical thinking and oral presentation skills. At the conclusion of the program, students will present their research at the NEOMED Research Symposium.

Description of resources available.

The PI's laboratory is located within the department's 4,000 sq. ft. open laboratory space, providing students with a well-equipped and collaborative research environment. In addition, the PI has access to comprehensive core facilities, including an animal surgery suite with ventilators, surgical instruments, and echocardiography systems, as well as a station for tissue processing and paraffin embedding. The laboratory also includes fully equipped tissue culture facilities, dark rooms, FACS, RT-PCR, gel imaging, and analytical software. The lab is situated within a modern complex that houses the Departments of Integrative Medical Sciences and Pharmaceutical Sciences.

Site where the research will be conducted.

The majority of the work will be conducted in RGE 200, with additional experiments performed in RGE 217 and RGE 218

Submit your application to Dr. Alex Galazyuk

Project Title: Neural mechanisms underlying age-related hearing loss
PI Name: Alex Galazyuk
Location: NEOMED

Abstract: Age-related hearing loss remains one of the most common chronic conditions of aging. It begins from the gradual loss or impairment of the inner and outer hair cells in the cochlea. This loss leads to the development of deficits in the central auditory system which eventually cause difficulties in processing temporally complex sounds such as speech, especially in noisy environments. Typically, individuals experience a notable decline in their hearing abilities after the age of 65, whereas cochlea degradation begins much earlier in life. Within the field, there exists a consensus that central plasticity, often referred to as central gain enhancement, serves as a compensatory mechanism to counterbalance the loss of input from the cochlea to the central auditory system due to aging. The postsynaptic mechanism underlying this compensation is largely unknown. It has been hypothesized that alterations in the balance between excitation and inhibition may play the key role. The goal of this project is to elucidate the postsynaptic mechanisms that contribute to the central gain and to identify pharmacological therapy to improve hearing performance in aged individuals.

Significance: Age-related hearing loss remains one of the most common chronic conditions of aging. Older listeners experience difficulties understanding speech, particularly in noisy environments. While audibility partially accounts for these functional deficits, elderly listeners with normal hearing and intact cognitive function still have poorer speech recognition ability in noise compared to young listeners. Central auditory processing has been shown to play a key role in compensation for the loss of cochlea function with age. This compensation has been hypothesized to rely on altered balance between excitation and inhibition and often referred as central gain enhancement. At present, little is known about postsynaptic mechanism(s) underlying central gain alteration. Deep knowledge about changes in both the excitatory and inhibitory components of this mechanism can help us to better understand the cellular basis for aging. The proposed study will improve our knowledge of the central mechanisms responsible for auditory aging and provide a foundation for the development of treatment strategies.

Goals and Objectives: The student will identify changes in sound-evoked responses of inferior colliculus neurons in different age groups of unanesthetized mice.

Methods: The student will learn how to record single neuron electrical activity of neurons in the inferior colliculus in response to different sound frequency and intensity. The student will learn to use electrophysiological setup to stimulate mice with sounds and record action potentials of auditory neurons in response to these stimuli. The student will also have an opportunity to observe other techniques in the lab, including fabrication of glass recording microelectrodes and generation of automated sound stimulation protocol.

Data Analysis: Data collected by the student will be analyzed using custom-made software. For each recorded neuron its so-called frequency response area based on more than 3,000 sounds with different combinations of sound frequency and intensity will be constructed and analyzed.

Anticipated Findings: The anticipated findings from this project will identify the differences in sound processing with age.

Student Fellow Training/Mentoring Plan

The student will have the opportunity to meet individually with the PI regularly. In addition to working directly with the PI, the student's training will be continuously monitored by a postdoctoral fellow. Research will be conducted at NEOMED. All resources necessary for the described experiments are available. We work as part of the NEOMED Hearing Research Group, and students in the lab will have the opportunity to interact with the other group members.

Submit your application to Dr. Adam Goodwill – 1 of 2 projects

Project Title:
GLP 1 Mediated Cardioprotection During Anthracycline Exposure in a Large Animal Physiology Model

Principal Investigator:
Adam G. Goodwill, PhD, FCVS; Assistant Professor Integrative Medical Sciences

Research Location:
Northeast Ohio Medical University College of Medicine
RGE-300
RGE-308
Comparative Medicine Unit

Abstract:
Anthracycline chemotherapy is highly effective in cancer treatment, but cumulative exposure produces predictable cardiac injury. The early stages of toxicity involve shifts in oxygen handling, impaired mitochondrial efficiency, and progressive mechanical dysfunction that ultimately progress to heart failure. Therapies that reduce metabolic stress and preserve contractile mechanics may allow greater cumulative dosing without cardiac collapse.

GLP 1 receptor agonists have shown clear cardiovascular benefit in clinical populations. Several groups have reported improved mitochondrial efficiency, improved ATP linked respiration, reduced lipid oxidation and reduced apoptotic signaling with GLP 1 treatment. Retrospective human data also suggest a reduction in heart failure events of roughly fifty percent when GLP 1 therapy is present during anthracycline exposure. These findings indicate that GLP 1 may offset mitochondrial stress, protect the microvasculature, and maintain contractile reserve under toxic load.

This study will quantify cardioprotection using NEOMEDs large animal model. The student will evaluate myocardial oxygen consumption and metabolic efficiency, measure coronary flow reserve, and analyze pressure volume loops for early divergence of contractile mechanics. Results are expected to define an integrated physiological profile that indicates whether GLP 1 slows deterioration or permits higher safe dosing thresholds.

Significance:
Anthracycline toxicity limits the lifetime dose patients are allowed to receive. We believe GLP 1 has the potential to mitigate toxicity and increase lifetime dosing limits. If metabolic efficiency is preserved and coronary reserve remains intact, the heart may tolerate significantly more chemotherapy exposure before failure. Because GLP 1 therapies are widely available and well tolerated, this work has immediate translational value. Any protective phenotype identified in this project could serve as a clinical monitoring target for cardiotoxicity surveillance and for designing future interventional studies.

Goals and Objectives for the Research Project

The overarching goal of this work is to determine whether GLP 1 therapy protects the heart during anthracycline exposure through preservation of metabolic efficiency, coronary reserve, and mechanical performance.

The student will complete the following objectives.

1. Measure myocardial oxygen consumption during treatment exposure and determine whether GLP 1 reduces oxygen cost per unit stroke work.
2. Quantify coronary flow reserve and evaluate whether GLP 1 maintains hyperemic capacity as cumulative drug exposure increases.
3. Process and analyze pressure volume loops to detect the earliest point at which GLP 1 treated hearts maintain contractile function longer than untreated hearts.
4. Optional mechanistic objective, performed only if primary aims are complete. Isolate mitochondria post mortem and measure oxygen consumption rate, respiratory control ratio and ATP linked respiration to establish mechanistic support for observed physiological protection.

Research Methods

All work will be completed in a fully instrumented large animal model. Under general anesthesia, animals will undergo left lateral thoracotomy. Perivascular coronary flow probes will be placed around the left anterior descending and circumflex arteries. Arterial and coronary venous catheters will enable sampling for oxygen content and metabolic substrates. A high fidelity pressure volume catheter may be inserted to allow multi beat characterization of systolic and diastolic mechanics.

Animals will receive serial anthracycline treatments with or without GLP 1 therapy. Data will be collected at and between treatments. This allows direct comparison of metabolic demand, microvascular performance, and contractile function across progressive exposure.

Myocardial oxygen consumption will be calculated from arterial venous gradients and measured coronary flow. Coronary reserve will be assessed by brief LAD occlusion and analysis of peak hyperemia and flow debt repayment. Pressure volume loops will be processed for elastance, preload recruitable stroke work, diastolic stiffness constants and pressure volume area.

If optional mitochondrial analysis is performed, left ventricular tissue will be used to isolate mitochondria and measure oxygen consumption, respiratory control ratio and ATP linked flux using high resolution respirometry.

Methods of Data Analysis

Data will be analyzed using SigmaPlot or GraphPad. Repeated measures ANOVA will be used for longitudinal comparisons. Regression analyses will examine relationships among efficiency, flow reserve and mechanical preservation. Graphs will be constructed to visualize treatment divergence over time and to determine whether GLP 1 delays the onset of dysfunction.

Anticipated Findings

We anticipate that GLP 1 treated hearts will demonstrate lower oxygen cost per unit stroke work, more stable coronary flow reserve during hyperemia, and slower deterioration of pressure volume loop derived contractile indices. Identification of any of these protective responses would provide strong evidence that GLP 1 can reduce anthracycline toxicity and may support revised lifetime dosing limits in future clinical application.

If GLP 1 does not protect across these domains, the result will still be highly informative. The findings will identify the precise stage where toxicity overcomes compensation, which will guide future mechanistic studies and dosing strategies.

This work will produce a high value physiologic dataset that supports the next phase of therapeutic development.

Training Plan

All learners will complete required CITI certification and CMU orientation prior to participating in animal work and all procedures will follow approved IACUC protocols. Large animal studies will be performed with direct instruction and supervision from Dr. Goodwill. Students will be encouraged to participate in every stage of the project, including animal preparation, physiological monitoring, sample collection, analytic processing, data interpretation, and final presentation of results.

Cross training will be used to ensure that each learner gains experience in instrument setup, real time acquisition, metabolic and hemodynamic calculations, and visual data analysis. Dr. Goodwill intends to work with students daily to provide guidance, answer questions, and assist with technical and conceptual development. Brief daily check ins will assist with planning, troubleshooting, and maintaining research momentum.

Weekly laboratory meetings will serve as the primary venue for structured discussion and review of ongoing work. Students will also attend the cardiovascular research journal club associated with the research focus area to strengthen their ability to read primary literature and evaluate scientific conclusions. Presentation skills will be developed through staged practice sessions. Each student will present preliminary findings to the laboratory team, revise slides with feedback, and then deliver a refined version to the cardiovascular research group prior to any external symposium or abstract submission.

Data analysis software and computational tools will be available for all trainees. A see one, do one, teach one progression will be used whenever appropriate. Students will observe a workflow first, repeat it independently, and demonstrate competency by guiding another team member through the same process. All figures and analytic results will be reviewed with Dr. Goodwill prior to public presentation.

Finally, students will be encouraged to maintain work life balance. The laboratory values scientific productivity but also believes that mental health supports clarity, creativity, and long-term success. Trainees will be encouraged to disconnect at the end of the workday knowing that the research will still be there tomorrow.

Available Resources

- Assorted Surgical Equipment
- ADInstruments Powerlab C with 16 inputs
- Dell XPS Computer for data acquisition
- Grass amplifier (Multiple)
- Harvard Apparatus Perfusion Servo Controller (2)
- Harvard Apparatus Syringe Pumps (Multiple)
- Harvard Apparatus Transductor Amplifier (8)
- Haake K20 Heated/Cooled Circulating Water Bath
- iWorx Biopotential Amplifier for ECG
- Lifepak 20 Defibrillator with Internal/External Paddles
- Masterflex L/S Peristaltic Pumps (2)
- Stryker 810 Autopsy Saw
- Transonic ADV-550 Admittance Pressure Volume System
- Transonic TS410 Tubing Flow System
- Transonic TS420 Transit Time Perivascular Flow Module (3)
- Werfen Gem Premier 5000 Blood Gas Analyzer

Submit your application to Dr. Adam Goodwill – 2 of 2 projects

Project Title:
Ischemia Dependent Cardioprotection by SGLT2 Inhibitors Mechanistic and Metabolomic Evaluation in a Large Animal Preparation
Principal Investigator:
Adam G. Goodwill, PhD, FCVS; Assistant Professor Integrative Medical Sciences
Research Location:
Northeast Ohio Medical University College of Medicine
RGE-300 RGE-308 Comparative Medicine Unit

Abstract:
SGLT2 inhibitors reduce heart failure events across many clinical populations, and this benefit cannot be explained by glucose lowering or canonical endocrine signaling pathways. Our laboratory has established that cardioprotection by SGLT2 inhibitors is strictly dependent on the presence of myocardial ischemia. In a large animal model, we previously demonstrated that the improvement in diastolic relaxation, quantified by the time constant tau, scales with the severity of ischemia. Protection was observed with both canagliflozin and empagliflozin which indicates a class mediated effect rather than a compound specific artifact.

Our group has also developed and published an extracorporeal coronary perfusion preparation in open chest swine that maintains a fully beating, load bearing heart while allowing servo controlled perfusion of the LAD across a wide hemodynamic range. In this model coronary pressure and flow are adjustable from approximately 140 to 40 mmHg and coronary venous sampling provides a direct index of oxygen delivery and extraction. This platform allows controlled induction of ischemia, continuous pressure volume monitoring, measurement of tau, and real time sampling of extracellular fluid from the myocardium.

The purpose of the 2026 student project is to determine whether SGLT2 mediated cardioprotection is driven by direct myocardial drug action or requires systemic signals. We will perform intracoronary infusions of SGLT2 inhibitor into ischemic and non ischemic territories while perfusion is varied across and beyond the autoregulatory range. During each condition we will record pressure volume relations, measure tau, quantify coronary flow, and collect extracellular and coronary venous samples for metabolomic and proteomic analysis in collaboration with Cedars Sinai Medical Center. By integrating physiologic response with biochemical signatures, this work will identify mechanistic pathways responsible for ischemia linked cardioprotection.

Significance:
SGLT2 inhibitors provide robust protection in settings of cardiovascular stress, yet the mechanism remains unresolved. Our data indicate that protection emerges only during ischemia and increases with ischemic intensity. Determining whether this protection arises from direct myocardial effects or through circulating mediators has substantial clinical and scientific value. If a local mechanism dominates, intracoronary or targeted dosing strategies may improve therapy. If protection is mediated through metabolic or humoral pathways, monitoring and modulation of these signals may enhance safety and efficacy. The metabolomic and proteomic dataset

generated here will serve as foundational evidence for future R level funding, manuscript publication, and conference presentation.

Goals and Objectives for the Research Project

The primary goal of this project is to define molecular and physiological signatures of SGLT2 mediated cardioprotection under graded ischemia.

The student will complete the following objectives:

1. Reproduce the ischemia dependent relaxation response associated with SGLT2 inhibitors across a more severe ischemic range.
2. Quantify the relationship between ischemia intensity and tau preservation to refine the protection curve.
3. Use intracoronary infusion to test whether drug effect occurs independently of systemic circulation.
4. Collect extracellular and coronary venous fluid samples during each ischemic stage for metabolomic and proteomic analysis.
5. Integrate biochemical signatures with relaxation mechanics to identify mechanistic drivers of protection.

Research Methods

Experiments will be performed in our established swine preparation. Animals will undergo left thoracotomy for instrumentation. The LAD will be cannulated and perfused through an extracorporeal servo controlled pump. Coronary flow will be titrated across and beyond the autoregulatory range to induce graded ischemia. Pressure volume catheters will allow direct measurement of systolic and diastolic mechanics including tau, preload recruitable stroke work, and end diastolic pressure volume relations. Coronary venous blood will be collected from the anterior interventricular vein for oxygen content and metabolite quantification.
SGLT2 inhibitor or vehicle will be infused by intracoronary route into ischemic or normally perfused territories. Myocardial extracellular fluid will be sampled through our interstitial microperfusion system during each perfusion condition. Samples will be frozen, cataloged, and submitted for metabolomic and proteomic analysis. Data acquisition will occur continuously with time alignment between physiology and biochemical sampling.

Methods of Data Analysis

Longitudinal outcomes will be evaluated using repeated measures ANOVA. Tau, oxygen extraction, and flow response will be modeled against ischemia severity. Metabolomic output will be dimensionally reduced to identify treatment specific clusters. Differential metabolite and protein abundance analysis will be used to identify candidate pathways. Integration plots will compare metabolomic signatures to tau preservation to determine which pathways correspond most strongly with cardioprotection.

Anticipated Findings

We expect SGLT2 inhibitors to improve tau at high ischemic severity and to produce metabolomic divergence that tracks with protection. If direct infusion in non ischemic regions does not produce benefit, this will support a requirement for ischemic signaling. If metabolomic

signatures predict functional preservation regardless of region, circulating mediators are likely involved. Either outcome will clarify mechanism and inform next phase experimental design. This work directly advances an active line of research, expands our dataset, and is expected to produce abstract and manuscript level findings within the training interval.

STUDENT FELLOW TRAINING/MENTORING PLAN

Training Plan

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- Transonic TS420 Transit Time Perivascular Flow Module (3)
- Werfen Gem Premier 5000 Blood Gas Analyzer

Submit your application to Dr. Neysa Grider-Potter

Title: Bat craniovertebral morphology across dietary regimes
Neysa Grider-Potter, D-103

Abstract
The semicircular canals and vestibule sense angular and linear accelerations of the head and facilitate visual stability and whole-body coordination. Size, shape and orientation of these canals has long been associated with sensitivity to head motion and locomotor agility. As a clade, bats are among the most agile of mammals practicing astounding feats of aerial agility in order to capture flying prey. However, there is variation in locomotor capabilities within bats that tend to fall along dietary regimes with insectivorous species being more agile than their frugivorous relatives. Further, there is extreme variation in cervical morphology that is largely lack functional explanation. Because the cervical spine balances and moves the head, the stability requirements of the inner ear should influence vertebral morphology. The goal of this work is to understand how inner ear morphology varies among bats of diverse dietary habits and if inner ear morphology is, in turn, shaping the cervical spine.

Significance
Bats are the only mammalian group to have evolved power flight. This unique mode of locomotion, as well as their echolocation abilities, has significantly shaped their anatomy and allowed them to radiate into a diverse array of dietary niches. Understanding how inner ear morphology both is influenced by dietary habits and covaries with vertebral morphology expand our knowledge about mammalian functional anatomy. These relationships between form and function have the potential to be applied to the fossil record to understand more about bat evolution.

Objectives
Here we aim test the hypotheses that 1) semicircular canal and vestibular morphology varies among bat taxa alongside dietary habits and 2) bats with more agile morphologies (i.e. larger canal radii of curvature, more orthogonally-oriented canals, enlarged vestibule) will have more gracile cervical vertebrae (e.g. thinner laminae, shorter transverse and spinous processes).

Methods and student responsibilities

The student will be primarily responsible for measuring and scanning bat specimens. Scan data will primarily be analyzed in 3D Slicer and Rhinoceros. The student will be trained in these programs along with the use of the microCT scanner. Hypotheses will be tested using relevant statistical analyses (ANOVA, linear regression). Coding
experience is encouraged but not required. Results of this study have the potential to be published as a student-led peer-reviewed journal article and contribute to other ongoing projects.

Training and Mentoring Plan

Training in project methods will be provided by the PI as needed throughout the duration of the fellowship. Students are welcome to attend the weekly Musculoskeletal Research Focus Area journal club. Research will be primarily conducted on campus with the potential for occasional remote work depending upon computer power and availability.

Submit your application to Dr. Tobin Hieronymus

Title: Muscular and Fascial Instrumentation and Anatomy Using Reflected Light Polarimetry and Contrast-Enhanced MicroCT
PI: Tobin Hieronymus, Associate Professor of Anatomy & Neurobiology
Research Location: NEOMED

Abstract: Smooth muscle plays a critical role in the function of many organ systems, but our ability to understand the effects of smooth muscle contraction are limited by our current inability to directly record smooth muscle activity *in-vivo*. Unlike skeletal muscle, smooth muscle does not depend on cell-membrane depolarization to coordinate contraction, so standard techniques such as electromyography (EMG) will not work. Current research in Hieronymus lab is focused on two major aims: (1) developing new methods of measuring peripheral smooth muscle optical properties to record activity, and (2) developing selective, localized, and reversible interventions to manipulate smooth muscle contraction for functional studies. This summer research project has two available tracks: one track will prototype and test components of a direct polarimetric probe system with the aim of developing *in vivo* instrumentation; the other will make use of recent advances in microCT imaging to characterize the architecture of smooth muscle tissue in bird skin (our lab's experimental model system for smooth muscle polarimetry and manipulation), with particular attention to its relationship to the superficial and deep fascia of the human-comparable musculoskeletal elements of the forelimb.

Significance: In addition to the smooth muscle lining the GI tract, airways, and vasculature, avian skin contains bundles of smooth muscle responsible for moving the feathers, similar to the arrector pili muscles in human skin. Because they are abundant and comparatively large, these muscles form a readily accessible experimental model for studies of smooth muscle physiology. My lab is developing a contact polarimetry instrument to record smooth muscle activity *in vivo* and investigating means to locally and reversibly knock down smooth muscle function—both of these aims feed into the broader goal of testing hypotheses of smooth muscle function *in vivo* during normal behavior. Current electrophysiology-based methods do not allow for direct measurement of smooth muscle contraction, and instead rely on indirect measures of correlated skeletal muscle contraction, which are only present in some systems. The ability to directly measure and reversibly manipulate smooth muscle function *in vivo* has implications across urogenital, gastrointestinal, and cardiopulmonary physiology.

Goals & Objectives: The goals of these paired studies are to develop new instrumentation components for measuring smooth muscle activity, and to provide the first tomographic characterization of smooth muscle bundles in avian skin. Students' research experience in the first track will focus on prototyping and testing optical and electronic instrumentation. The specific question to be addressed in this track is whether expected variation in optical properties of smooth muscle can be detected by reflected light polarimetry. Students' research experience in the second track will focus on assessing interconnections between dermal smooth muscle bundles, superficial fascia, and underlying deep fascia and skeletal muscle of the forelimb. The specific question to be addressed is whether the unusual connections of dermal smooth muscle to underlying bone in the avian forelimb are mediated by deep fascia and associated muscular tissue.

Research Methods: For prototyping, the student will use basic small electronics etching and soldering techniques, together with basic biocompatible materials approaches such as PDMS casting. For imaging, the student will apply Diffusable Iodine Contrast Enhancement (DICE) and Selectively Perfused Iodine Contrast Enhancement (SPICE), both recently developed techniques for imaging normally radiolucent tissues with X-ray computed tomography (CT). These techniques employ the radiodensity of iodine as a contrast agent for CT imaging, and are thus comparable to the use of injectable iodinated contrast media for angiography. Paraffin histology of focal samples will be used to confirm tissue relationships in areas of interest.

Data Analysis: Analysis for this project will include signal processing in R and RStudio to assess instrument function and segmentation using Avizo CT analysis software to generate computer models of the musculature and surrounding tissues.

Contribution to Overall Research Effort: Completion of this project will augment continuing experiments with avian feather muscles. This work will also produce stand-alone methods and anatomical results suitable for student-led publication.

Student Fellow Mentoring Plan: Student fellows will take part in weekly lab meetings with all lab members to identify and address lab-wide issues and tasks. If both tracks are filled, students will have the opportunity to work collaboratively on all phases of both projects. Student fellows will also be expected to attend the weekly journal club for the Musculoskeletal Research Focus Area, providing exposure to a broad range of research topics as well as a chance to interact with researchers at different career stages—typical attendance in summer includes 2-4 summer fellows, 2-3 technicians, 1-4 graduate students, 3 postdocs, and 3-4 faculty PIs. Timely completion and reporting of the student fellows' projects will be ensured by biweekly one-on-one meetings with the PI, not only to organize work but also to work through main tasks side by side (*e.g.,* worked examples of analysis, drafting, editing and presentation) both during the summer and through the following year as needed. Materials and equipment for the proposed research are currently available in the PIs lab.

Submit your application to Dr. Louis Kwantwi

Project title, Principal Investigator name, title and location where the research will take place
Principal Investigator: Louis Kwantwi **Title: "Evaluating Whether M64HCl Can Reverse Liver Injury Caused by the Toxic Metabolite of Tylenol in an In-Vitro Hepatic Cell Model."**
Institution: Northeast Ohio Medical University **Department:** Biomedical Sciences **Location:** NEOMED Biomedical Sciences Research Laboratories

Abstract of project

Acetaminophen (Tylenol) overdose causes liver injury when the drug is converted into a harmful metabolite that damages hepatocytes. This project uses a liver cell line to determine whether **M64HCl** can promote recovery after exposure to this toxic metabolite. By comparing cellular responses in injured cells treated with M64HCl versus untreated controls, the student will evaluate the compound's potential protective or restorative effects. The project provides hands-on experience with cell-based injury models and introduces the student to how candidate compounds are assessed for therapeutic promise.

The significance of the overall research

Acetaminophen toxicity is one of the most common causes of acute liver failure. Identifying compounds that counteract injury from its toxic metabolite could improve patient outcomes and inform new therapeutic strategies. If M64HCl demonstrates beneficial effects in this model, the findings would support further mechanistic studies and contribute to efforts to understand and mitigate metabolite-driven hepatotoxicity.

4. The goals and objectives for the research project; what aspect of the overall research will be the focus of the student's research experience? What is the specific research question being addressed by the research project?

- Assess whether metabolite-injured hepatocytes show reduced indicators of stress or damage when treated with M64HCl.
- Compare outcomes between injured cells with and without M64HCl exposure.
- Interpret whether any observed improvements suggest that M64HCl enhances recovery.

Research Methods
The project uses a liver-derived cell line to model toxic injury from the acetaminophen metabolite. The student will learn how cell lines are used as simplified systems for studying hepatocyte responses, how to interpret conceptual indicators of cellular injury or recovery, and how to compare results across conditions (injury alone vs. injury + M64HCl). All work follows established, supervised laboratory practices, with emphasis on data interpretation rather than technical optimization. Students will learn and use mammalian cell culture, Western blot, ELISA.

The proposed methods of data analysis
The student will evaluate differences in injury-related indicators across treatment groups, identify whether M64HCl-treated cells show signs of improved health, and apply basic statistical reasoning to interpret trends. The focus is on understanding biological meaning rather than

complex analyses. T test, outlier tests, tests of normality, non-parametric tests if the data are not normally distributed will be used.

A statement of how the anticipated findings from the fellow contribute to the success of the overall research being investigated

This work will eventually contribute to an overall plan to apply to the FDA for human testing and lives saved.

Student Fellow Training/Mentoring Plan
Students will meet the PI at least 3x weekly and will participate as well in weekly 2-hour lab meetings of the Kwantwi/Liu/Basson lab group at which they will present their work and receive feedback from all three faculty. It is expected that the student will present their work at next year's Student Research Day and be mentored by Drs. Kwantwi and Basson in the preparation and rehearsal of this presentation. It is expected that the data that the student will generate will also be part of a publication on which the student will be a coauthor

Resources Supervised access to cell-culture facilities, standard laboratory equipment, data-analysis tools, and mentoring from experienced research personnel.

Research Site: All activities will be conducted in the **Biomedical Sciences Research Laboratories at NEOMED**, which provides a supportive environment for undergraduate research training

Submit your application to Dr. Guiming Liu

Project title: Role of FAK in Human Urothelial Cell Migration and Proliferation
PI: Guiming Liu, PhD, Associate Professor, Department of Biomedical Sciences
Location: RGE 100

Abstract of Project.
Ulcerative cystitis is a debilitating condition characterized by ulcerative lesions within the bladder lining, including Hunner-type interstitial cystitis (IC) and hemorrhagic chemical (cyclophosphamide, ifosfamide, or ketamine–induced) or radiation cystitis. Damage to the superficial urothelial layer exposes underlying tissues to urine, solutes, and toxins, triggering inflammation and hematuria. This results in significant pain and a spectrum of lower urinary tract symptoms (LUTS)—including frequency, urgency, incontinence, dysuria, suprapubic pain, hematuria, and incomplete bladder emptying—that severely impair quality of life. Although the incidence of ulcerative cystitis continues to rise, effective treatments remain limited.

Focal Adhesion Kinase (FAK) is a protein tyrosine kinase that functions as a scaffold linking the cytoskeleton to the extracellular matrix through focal adhesions. We have demonstrated that a newly developed FAK activator, M64HCl, accelerates mucosal healing in a rat model of acetic acid–induced intestinal injury (*BMC Gastroenterol.* 2025, 25:347). We hypothesize that M64HCl can be repurposed to address the critical unmet need in ulcerative cystitis by promoting urothelial repair through FAK activation. To test this hypothesis, we conducted a pilot in vivo study showing that subcutaneous administration of M64HCl before intraperitoneal cyclophosphamide (CYP) significantly reduced hemorrhage and urothelial denudation four days after CYP administration in mice. To translate these findings toward clinical application, our next step is to determine whether M64HCl increases p-FAK levels and enhances adhesion, migration, and proliferation in primary human bladder urothelial cells, as well as to elucidate its underlying molecular mechanisms. This will be the focus of the summer student fellow's project. The student will culture primary human bladder urothelial cells, measure FAK and p-FAK expression, and assess cell adhesion, migration, and proliferation following FAK inhibition/gene knockdown or activation/gene overexpression. Additionally, gene expression profiles of focal adhesion and cytoskeletal regulators will be analyzed, and phosphoproteomic profiling will be performed to identify mechanistic pathways. Key target molecules will be further validated through gain- and loss-of-function experiments.

Significance.
Despite the increasing incidence of ulcerative cystitis, treatment options remain inadequate. Common therapies - such as systemic amitriptyline, prednisolone, and cyclosporine A, or intravesical agents like dimethyl sulfoxide, hyaluronic acid, and lidocaine - are used particularly for Hunner-type IC. However, these treatments are primarily symptomatic, often lack robust evidence, show limited efficacy, and may cause significant side effects. In severe or refractory cases, cystectomy with urinary diversion is considered a last-resort option. Many patients report profound dissatisfaction with current medical care. Our preclinical pilot results are highly encouraging, demonstrating that the novel FAK activator M64HCl can alleviate CYP-induced ulcerative cystitis in mice. The long-term objective is to translate these findings into a first-in-human clinical trial. Rigorous evaluation of M64HCl's effects and mechanisms in human bladder

urothelial cells is therefore a critical next step. This work will significantly accelerate translational progress and has the potential to provide a much-needed therapeutic option for patients with ulcerative cystitis.

Research methods that will be learned by the student.

- Cell culture
- Adhesion, migration, and proliferation assays
- RNA isolation, cDNA synthesis, PCR
- Protein quantification
- Western blotting
- Statistical analysis

Proposed methods of data analysis.

Statistical analyses will be performed using GraphPad Prism (GraphPad Software, La Jolla, CA). Normally distributed data will be presented as mean ± standard deviation (SD). Comparisons among multiple groups will be analyzed using ANOVA followed by the Tukey-Kramer post hoc test. Comparisons between two groups will be conducted using an unpaired, two-tailed t-test. P-values < 0.05 will be considered statistically significant.

How will the anticipated findings contribute to the success of the overall research?

If successful, this will accelerate the translation of a promising preclinical result into a future clinical trial. This treatment represents a fundamentally novel therapeutic strategy compared to existing approaches. In addition, the data generated could serve as important preliminary evidence to support future grant applications.

STUDENT FELLOW TRAINING/MENTORING PLAN

The student will receive daily guidance from Dr. Liu and members of the Basson - Liu Laboratory. They will participate in weekly laboratory meetings focused on experimental design and data analysis and will present their progress regularly. Depending on the student's interests, opportunities may be available to engage in additional ongoing projects, including rodent studies. The student will also participate in seminars offered by the Department, College, and University. It is anticipated that the student will prepare a poster or oral presentation for Student Research Day and that the data generated will contribute to a future publication on which the student will be included as a co-author

Submit your application to Dr. Priya Raman - 1 of 2 projects

PROJECT TITLE Role of smooth muscle O-GlcNAcylation in regulation of cognitive dysfunction in Type 2 diabetes
PRINCIPAL INVESTIGATOR Priya Raman, Ph.D., Associate Professor, Biomedical Sciences
LOCATION NEOMED, Rootstown

ABSTRACT OF PROJECT

Type 2 diabetes (T2D) negatively impacts cerebrovascular function and increases the risk of developing Alzheimer's disease-related dementia (ADRD). Growing literature supports the notion that dysregulated function of vascular smooth muscle cells (VSMC), a major cell type found in blood vessels that regulate cerebrovascular function, is a putative player in AD-related pathology and neurodegeneration. Hyperglycemia, a hallmark feature of T2D, increases O-GlcNAc transferase (OGT) signaling, a key regulator of protein O-GlcNAcylation. Increased O-GlcNAcylation, a ubiquitous posttranslational modification, correlates with adverse vascular remodeling and vascular dysfunction in T2D. However, it is unknown whether increased cerebrovascular O-GlcNAcylation contributes to cognitive dysfunction and AD pathology in T2D. The proposed project provides a unique platform to determine whether loss of VSMC-specific OGT-mediated O-GlcNAcylation inhibits cognitive dysfunction in T2D. For this, conditional VSMC-specific OGT knockout mice and wild-type controls (both sexes) on a high-fat high-sugar diet will be aged to 6 months, followed by a battery of behavioral tests to measure their cognitive, emotional, and sensorimotor behavior. The summer student working on this project will learn murine behavior phenotyping, including scoring of the behavioral tests, data analysis and data interpretation. The proposed studies will advance our understanding of how T2D contributes to cognitive dysfunction, with a focus on the regulatory role of cerebrovascular OGT-mediated O-GlcNAcylation, paving the way for the discovery of novel therapies to treat ADRD in diabetes.

BACKGROUND AND SIGNIFICANCE

Vascular pathology occurs in up to 50% of individuals with Alzheimer's disease-related dementia (ADRD) and frequently co-exists with AD-related neurodegenerative changes. Emerging evidence indicates that cerebrovascular dysfunction often precedes the onset of clinical symptoms and is a significant risk factor for the development of AD. Despite the importance of cerebrovascular dynamics in brain function, the molecular mechanism(s) that mediate cerebrovascular deficits that may lead to cognitive decline and AD pathology are poorly understood. Vascular smooth muscle cell (VSMC) is a major cell type found in blood vessels that regulate the vascular tone of the cerebral artery and are the primary controllers of cerebrovascular dynamics. Increasing evidence indicates that VSMCs have remarkable plasticity and readily transform into diseased phenotypes in response to pathogenic stimuli.

Type 2 diabetes (T2D) negatively impacts vascular function, which in turn may adversely affect brain health. T2D patients have an increased propensity for VSMC de-differentiation from 'quiescent' contractile to 'synthetic' proliferative phenotypes. Such proliferative VSMC phenotypes are linked to vascular disease progression and upregulation of multiple AD-related pathways. This supports the notion that dysregulated VSMC function may be a putative player in AD-related pathology and neurodegeneration in T2D. Hyperglycemia, a hallmark feature of T2D, increases protein O-GlcNAcylation, a ubiquitous post-translational modification (PTM) that plays

a crucial role in cellular signaling and metabolism. Increased O-GlcNAcylation correlates with adverse vascular remodeling and vascular dysfunction in T2D. However, whether increased cerebrovascular O-GlcNAcylation contributes to cognitive dysfunction and AD pathology in T2D is unknown.

Using a novel transgenic mouse model lacking VSMC-specific OGT (a key regulator of O-GlcNAcylation), the proposed work is part of a larger research initiative to test the overarching hypothesis that elevated cerebrovascular O-GlcNAcylation promotes cerebral VSMC fate switch to diseased phenotypes, prompting cerebrovascular dysfunction, AD-related pathology, and cognitive dysfunction in T2D.

GOALS AND OBJECTIVES

Goal: We will investigate whether loss of VSMC-specific OGT-mediated O-GlcNAcylation inhibits cognitive dysfunction in high-fat, high-sugar diet-induced diabetic mice.

Objectives:

1) To compare the sensorimotor function and emotional reactivity of diabetic mice with intact OGT (smOgtWT) vs. diabetic mice with VSMC-specific OGT loss-of-function (smOgtKO).

2) To compare the attention and memory of diabetic smOgtWT mice (with intact OGT) vs. diabetic smOgtKO mice (with VSMC-specific OGT deletion).

Experimental Design: We will use conditional VSMC-specific Ogt knockout mice developed in our lab by crossing Ogt-floxed mice with a tamoxifen-inducible VSMC-restricted Cre driver mouse (Itga8-CreERT2), expressing CreERT2 under the control of the mouse alpha integrin 8 (Itga8) promoter; all mice will be on C57Bl6 background. Here, tamoxifen-induced Cre recombination triggers conditional VSMC-restricted Ogt deletion. Age and sex-matched smOgtWT and smOgtKO mice will be placed on a high-fat, high-sugar (HFHS) diet to induce diabetes and aged to 6 months. For the study duration, body weight and non-fasted blood glucose levels will be measured monthly. Two weeks before the study endpoint, mice will be subjected to Intraperitoneal Glucose Tolerance and Insulin Tolerance Tests (IPGTT, IPITT) at one-week intervals. At 6 months of age (study endpoint), mice will be used for behavioral studies as outlined below. This will be followed by animal harvests for blood and tissue collection for molecular studies.

The above-described animal experiments are currently ongoing in our lab and we anticipate completion of the HFHS diet feeding, body weight and blood glucose monitoring as well as GTT and ITT measurements, prior to initiation of the summer fellowship. Due to the restricted time frame of this fellowship, the summer student will focus on behavioral tests outlined below in a subset of mice, and will conduct scoring of the behavioral data, followed by data analysis. The summer student will also participate in animal harvest procedures, including the collection of blood and tissue samples for future analysis.

INVESTIGATIVE METHODS TO BE USED

A battery of behavioral tests will be used to measure cognitive function, including the Barnes maze that measures spatial memory, an Object Recognition test that measures both attention

and memory, and the Y-maze that measures habituation and working memory. In addition, basic tests of sensorimotor function (beam traversal and spontaneous activity) and emotional reactivity (elevated plus maze) will be used to ensure that any detected differences in the cognitive tests are not due to motor impairments and/or enhanced fear. Tests will be implemented in the same order (**challenging beam, spontaneous activity, elevated plus maze, Y-maze, object recognition, and Barnes maze**) for each cohort of mice and at the same time of day. No more than two tests will be performed in one day and male and female testing will be performed separately to prevent potential interference with behavioral performance by pheromones. Videos taken during testing will be scored by experimenters blinded to genotype information and when multiple scorers are needed, they will have an inter-rater reliability of ~95%.

We will collaborate with Dr. Sheila Fleming on these studies. Dr. Fleming has considerable experience with murine behavior phenotyping and currently has these tests set up and available in her laboratory with established protocols. My lab has been working with Dr. Fleming for the past 5 years, and we have a senior graduate student who is routinely conducting murine behavioral studies.

PROPOSED METHOD OF DATA ANALYSIS

All data sets will be checked for normality and homogeneity of variance, followed by appropriate statistical analyses (parametric or non-parametric). For parametric data, statistical significance will be analyzed by one-way or two-way ANOVA followed by Tukey HSD pos-hoc or unpaired two-tailed Student's t-test, as appropriate. For non-parametric data, Kruskal-Wallis followed by Dunn's post-hoc or Mann Whitney U/Wilcoxon Sign Rank tests will be used, as appropriate; $p \leq 0.05$ is considered statistically significant.

SIGNIFICANCE OF ANTICIPATED FINDINGS

Expected Outcome. We predict that VSMC-specific loss of Ogt and O-GlcNAcylation will halt cognitive dysfunction in diabetic smOgtKO vs. smOgtWT mice (with intact Ogt).
Impact. The proposed studies will provide key pilot data in support of our hypothesis and validate the experimental feasibility of studies planned in a future R01 application, aiming to explore the mechanism(s) by which metabolic syndrome contributes to AD-related cognitive decline and cerebrovascular dysfunction.

SUMMER RESEARCH FELLOW TRAINING/MENTORING PLAN

The proposed study will offer research and training opportunities for two students, and we anticipate that these students will work concurrently on this project. Therefore, we request support for two summer students for this study.

Plan for Training/Mentoring: The summer research fellow(s) will be supervised and mentored by Dr. Priya Raman. During the first 2-3 weeks of the program, the students will receive hands-on training from Dr. Raman's graduate student, who is skilled in murine behavior phenotyping. Upon demonstration of adequate independence, the summer fellows will be expected to run independent experiments under close supervision by Dr. Raman and her team. Dr. Raman will meet with the summer students weekly to discuss the proposed research question, relevant scientific literature, and progression of experiments and data and will also provide necessary

guidance on the approaches proposed in the project. Dr. Raman will be responsible for student training in all aspects of this project, including data analysis, graphical presentations, interpretation of data and poster preparation and presentation. The summer fellows will also receive training in reading the scientific literature relevant to the project. Dr. Raman is a member of the HBVD and DOM RFAs and the summer students will be expected to participate in weekly group meetings organized by the HBVD and DOM RFAs. These meetings will develop the student's research horizons and enhance his/her scientific presentation and perception skills. At the end of the training period, the students will be expected to submit a brief report summarizing the project and results and present their data during NEOMED's Annual Poster Day.

Description of Resources available: The summer students will have access to Dr. Raman's laboratory, Dr. Fleming's behavioral test equipment and other departmental core facilities, as needed for completion of the proposed studies. The summer fellows will also have access to graphing and imaging software, as needed.

Site where the research will be conducted: This project will be conducted in Dr. Raman's laboratory and Dr. Fleming's behavioral suite at NEOMED.

Submit your application to Dr. Priya Raman – 2 of 2 projects

PROJECT TITLE Crosstalk of Aging and Metabolic Syndrome in Atherosclerosis
PRINCIPAL INVESTIGATOR Priya Raman, Ph.D., Associate Professor, Biomedical Sciences
LOCATION NEOMED, Rootstown

ABSTRACT OF PROJECT

Metabolic syndrome (MetS), a cluster of modifiable cardiovascular (CV) risk factors including hyperglycemia, visceral obesity, and dyslipidemia, significantly accelerates atherosclerosis, amplifying the risk of cardiovascular morbidity and mortality in older adults with MetS. Aging and MetS share overlapping pathogenic mechanisms that can synergistically accelerate atherosclerosis. Despite its clinical importance, the molecular mechanisms by which MetS drives age-related vasculopathy are incompletely understood. The proposed project is part of a larger research initiative to uncover novel molecular pathways and protein networks that drive accelerated atherosclerosis in MetS as a function of age. Using a mouse model of combined MetS and atherosclerosis developed in our lab, we will study the interaction of aging with MetS on atherosclerotic lesion formation. Specifically, MetS and non-MetS mice (both sexes) on standard laboratory diet will be aged to 6 months and 1 year, followed by animal harvests for collection of plasma, heart and aortic vessels. The summer student working on this project will perform histological staining of aortic root sections to assess the severity of atherosclerotic lesions in our mice genotypes, including data analysis and data interpretation. The student will also attain familiarity with the relevant scientific literature in the field.

BACKGROUND AND SIGNIFICANCE

Cardiovascular disease (CVD) is the leading cause of mortality worldwide, accounting for 19.9 million global deaths in 2021. Mortality rates due to CVD increase exponentially with age, accounting for >40% deaths in individuals aged 65–74 and nearly 60% in those aged 85 and older. Metabolic syndrome (MetS), defined by a cluster of conditions that include central obesity, hyperglycemia and dyslipidemia, significantly increases the risk of atherosclerotic cardiovascular disease. MetS patients have 2-4-fold greater risks of developing atherosclerotic complications.

Aging and MetS share overlapping pathogenic mechanisms that synergistically accelerate atherosclerosis. Aging promotes vascular cell senescence and immune dysregulation, creating a pro-inflammatory milieu that destabilizes plaques. Hyperglycemia and insulin resistance, characteristic of MetS, exacerbate these processes, creating a highly pro-atherogenic environment. Both MetS and aging amplify oxidative stress, impair endothelial function and reduce nitric oxide bioavailability. This interplay leads to accelerated plaque growth, calcification, and plaque instability, significantly increasing the cardiovascular risk in older adults with MetS. Despite the clinical significance of this intersection, the molecular pathways linking aging and MetS in atherosclerosis remain incompletely understood, highlighting a critical gap for targeted interventions.

The proposed work is part of a larger research initiative to elucidate the molecular mechanisms by which aging accelerates atherosclerosis in MetS.

GOALS AND OBJECTIVES

Goal: To determine the impact of aging on atherosclerotic lesion formation in a mouse model of combined MetS and atherosclerosis (KKAy+/-ApoE-/-) vs. non-MetS atherosclerotic mice (KKAy-/-ApoE-/-).

Objectives:

1. To compare body weight, blood glucose, plasma cholesterol and triglyceride levels in MetS atherosclerotic vs non-MetS atherosclerotic mice at 6 months and 1 year of age.
2. To compare and quantify atherosclerotic lesions in MetS atherosclerotic vs non-MetS atherosclerotic mice at 6 months and 1 year of age.

Experimental design: We will use a mouse model of combined MetS and atherosclerosis developed in our lab by crossing male agouti KKAy+/- (a murine model of MetS) with female ApoE-/- mice (a murine model of atherosclerosis). Upon weaning (4-wks-age), mice will be randomly allocated to experimental groups: a) 6-month-old MetS KKAy+/-ApoE-/-, b) 6-month-old non-MetS KKAy-/-ApoE-/-, c) 1-year-old MetS KKAy+/-ApoE-/- and d) 1-year-old non-MetS KKAy-/-ApoE-/-. Mice will be maintained on a standard laboratory diet for the duration of the study. Body weight and non-fasted blood glucose levels will be monitored monthly. At study endpoints (6 months and 1 year of age), mice will be euthanized following overnight fasting; blood, heart and aortic vessels will be collected for molecular studies. Both male and female mice will be utilized in this study.

We have already completed the animal experiments described above and all tissue samples collected from our mouse genotypes are already in hand. Due to the limited time frame of this fellowship, the summer student will focus on the analysis of blood and tissue samples previously collected from our mouse genotypes.

INVESTIGATIVE METHODS TO BE USED

Analyses of Plasma samples: Plasma triglycerides and total cholesterol levels will be measured using standard enzymatic kits (purchased from Fisher, Biovision, Sigma).

Aortic root morphometry*:* Aortic root sections (8–10-micron thickness) of formalin-fixed, OCT-embedded frozen hearts will be cut at the point where valve leaflets are first evident. Tissue sections will be stained with Oil Red O, H&E and Masson Trichrome to measure lipid burden, plaque area and collagen content, respectively. Image capture will be accomplished using an automated Slide Scanner.

Immunofluorescent staining of aortic root sections: will be conducted to detect lesion SMC abundance, immune cell infiltration and cell proliferation, per established protocols. Briefly, sections will be co-stained with i) ACTA-2 and Galectin-3 to detect inflammatory VSMCs and ii) ACTA-2 and Ki67 to detect proliferative VSMCs. Images will be captured via confocal microscopy.

PROPOSED METHOD OF DATA ANALYSIS

Morphometric and immunofluorescent images will be analyzed using ImageJ software. We will obtain multiple images from tissues collected from 3-5 mice per genotype for each sex and age

group, which should be sufficient to visualize changes between the groups and determine whether the expected differences are evident. Data from each group will be compiled, plotted and compared across all conditions. All data sets will be checked for normality and homogeneity of variance, followed by appropriate statistical analyses (parametric or non-parametric). For parametric data, statistical significance will be analyzed by one-way or two-way ANOVA followed by Tukey HSD pos-hoc or unpaired two-tailed Student's t-test, as appropriate. For non-parametric data, Kruskal-Wallis followed by Dunn's post-hoc or Mann Whitney U/Wilcoxon Sign Rank tests will be used, as appropriate; $p \leq 0.05$ is considered statistically significant.

SIGNIFICANCE OF ANTICIPATED FINDINGS

Expected Outcome. We predict that aging will significantly accelerate the development and progression of atherosclerotic lesions in MetS mice. If time and resources permit, aortic vessels derived from our mice genotypes will be used in proteomics profiling to determine the link between lesion formation and differentially expressed proteins in MetS vs non-MetS mice as a function of age.

Impact. The overarching goal of this study is to uncover novel molecular pathways and protein networks, including protein-protein interactions, that associate with accelerated atherosclerosis in MetS as a function of age. Findings from this study will inform our future research directions and lay a foundation for additional mechanistic studies to delineate the molecular interplay between aging and MetS in atherosclerotic vascular disease.

SUMMER RESEARCH FELLOW TRAINING/MENTORING PLAN

The proposed study will offer research and training opportunities for two students, and we anticipate that these students will work concurrently on this project. Therefore, we request support for two summer students for this study.

Plan for Training/Mentoring: The summer research fellows will be supervised and mentored by Dr. Priya Raman. The students will receive hands-on training from Dr. Raman and her laboratory personnel during the first 2-3 weeks of the program. Upon demonstration of adequate independence, the summer fellows will be expected to run independent experiments under close supervision by Dr. Raman and her team. Dr. Raman will meet with the summer students weekly to discuss the proposed research question, relevant scientific literature, and progression of experiments and data and will also provide necessary guidance on the approaches proposed in the project. Dr. Raman will be responsible for student training in all aspects of this project, including data analysis, graphical presentations, interpretation of data and poster preparation and presentation. The summer fellows will also receive training in critically reading the scientific literature relevant to the project. Dr. Raman is a member of the HBVD and DOM RFAs and the summer students will be expected to participate in weekly group meetings organized by the HBVD and DOM RFAs. These meetings will develop the student's research horizons and enhance his/her scientific presentation and perception skills. At the end of the training period, the students will be expected to submit a brief report summarizing the project and results and present their data during NEOMED's Annual Poster Day.

Description of Resources available: The summer students will have access to Dr. Raman's laboratory, histology core, microscopes, necessary supplies and other department core facilities, as needed.

Site where the research will be conducted: This project will be conducted in Dr. Raman's laboratory at NEOMED.

Submit your application to Dr. Jeffrey Wenstrup

1. Project information:

Title: Brain Circuitry Underlying Hearing and Emotions
Principal Investigator: Jeffrey Wenstrup, Ph.D., Professor
Co-Investigator: Sharad Shanbhag, Ph.D., Research Associate Professor
Location: Department of Biomedical Sciences, NEOMED

2. Abstract

Our work investigates neural mechanisms underlying the process by which emotional centers in the brain assign meaning to social vocalizations. Past experiments in our lab have found neurons in the amygdala that respond selectively to social vocalizations. We have examined how contextual cues associated with a social vocalization alter the interpretation of that vocalization by the individual and by neurons in the amygdala. We have shown that the behavioral and amygdalar response to a vocalization is differentially altered by exposure to olfactory cues associated with either mating or predators, and by internal levels of brain chemicals. We now propose to examine the mechanisms of selectivity for vocalizations as well as the source of contextual cues in the amygdala. Using electrical recording of nerve cell activity in the amygdala in response to mouse vocalizations, we will describe how different neurons of the amygdala respond to social vocalizations. Using gene insertion, optical imaging, and histological techniques, we will relate the response to vocalizations of amygdala cells to their connections to other brain regions. Using acoustic methods, we record and analyze mouse vocalizations to study how they change with behaviors.

3. Background and rationale

Our long-term goal is to improve the understanding of neural mechanisms that underlie acoustic communication. This project focuses on the amygdala, a structure known for its role in auditory fear conditioning. For this role, it receives auditory input from the thalamus and cortex, contributes to identifying a stimulus as aversive, and provides for appropriate output connections to control emotional responses (e.g., autonomic responses, freezing, affiliative responses). Our view is that the amygdala plays a critical role in acoustic communication through participation in several processes. Dysfunction in the amygdala may be involved in abnormal relationships between acoustic inputs and emotional responses in conditions such as autism, schizophrenia, post-traumatic stress, and tinnitus. We are interested in how the amygdala combines vocalization-specific and contextual information necessary for interpretation of acoustic, and then connects to brain centers that control behavior. This is the next step in understanding how these neural inputs act on amygdalar neurons to influence behavior.

4. Goals and objectives

Our long-term goal is to improve the understanding of neural mechanisms that underlie acoustic communication. This summer project aims to identify and quantify the mechanisms of vocalization-selective responses. We hypothesize that discrimination and selectivity in response to social vocalizations arises from projections of secondary auditory cortical areas. We further hypothesize that inputs from the prefrontal cortex, ventral tegmental area and hippocampus underlie contextual modulation of auditory responses.

5. Investigative methods to be used

To study how information about social communication sounds is analyzed by the basolateral amygdala, we combine vocalization recordings, neurophysiological and imaging analyses of brain activity with histological analysis the brain. Vocalizations and associated behaviors are recorded with both audio and video techniques. Neurophysiological recordings utilize multi-electrode arrays to record vocalization responses simultaneously from many neurons. Imaging depends on the injection of recombinant adeno-associated virus (rAAV) coding for a calcium sensing protein that fluoresces when a neuron is active. We use this to measure brain activity over several days and as the result of experience and changes in hormonal state. At the completion of recordings, histological preparation and analysis of brain sections will reveal labeled neurons that connect with the amygdala and the location of neurophysiological and imaging recording sites in the amygdala.

6. Proposed method of data analysis

Neurophysiology: Electrophysiological responses will be plotted and quantified off-line. Initial steps will include exporting of raw data for spike sorting, processing of data using spike sorting software and then integration of sorted data with stimulus information.

Anatomy: Slide-mounted and cleared tissue sections will be examined using fluorescence microscopy and compared with state-of-the-art brain atlas tools from Allen Brain Institute. Sections containing fluorescently labeled neurons or fiber tracts will be digitally photographed and the images stored for further off-line analysis. Analysis will include, but not be limited to, counts of cell bodies in areas of interest and reconstruction of projection pathways from the BLA.

7. Significance of anticipated findings

- The results will describe how neural responses to social vocalizations are distributed within the amygdala, as well as how they are affected by sex, hormonal state and experience.
- The results will identify the brain centers associated with emotional expression that receive information from amygdalar neurons.
- The results will identify brain regions that project to the amygdala to modulate auditory responses. This work will explain how specific inputs to the amygdala contribute to behaviors associated with social communication by sound.

B. Summer Research Fellow Training/Mentoring

All research will be conducted in the Acoustic Communication and Emotions Laboratory, which is part of the Department of Biomedical Sciences at NEOMED. The laboratory includes two faculty, a research scientist, and a research associate. The student will work closely with Drs. Wenstrup and Shanbhag and interact extensively with other laboratory members.

The laboratory emphasizes collaborative interactions, high expectations and enthusiasm. The group meets in weekly laboratory meetings where ideas are developed, and technical issues and results discussed. Our laboratory has an extensive record of mentoring undergraduate and professional student trainees since 2009. The fellow will interact with members of the Hearing Research Group (HRG). The highly interactive HRG is composed of members of eight hearing neuroscience laboratories with a wide range of experimental approaches. The fellow would be expected to present a summary of their summer project to this group.

The fellow will be trained in many of the procedures associated with this project, commensurate with their skill and ability. If interested, the student will participate in neural recording experiments, either using electrophysiological or imaging techniques. The student will participate in histological processing and analysis to prepare brain sections for subsequent neural imaging and tracing. The student will also participate in analyzing the results of neural tracing studies and the neural recording data. Experience or expertise in programming (e.g., Python, MATLAB, Java), histology (including processing of tissue and microscopy) or CAD/CAM is desired but not required. From work in our lab, the student will gain experience in identifying brain regions, histological and electrophysiological techniques, and data analysis.

For more information on this project please contact
Jeffrey Wenstrup, Ph.D.
Professor
Department of Biomedical Sciences,
Northeast Ohio Medical University (NEOMED)
E-mail: jjw@neomed.edu
Phone: 330.325.6630

Submit your application to Dr. Bradley Winters

Project Title: Literature review of cellular diversity in the lateral superior olive
PI Name: Bradley Winters (bwinters@neomed.edu)
Location: NEOMED Rootstown Campus

Abstract: The superior olivary complex (SOC) in the brainstem of mammals integrates information from the two ears enabling sound localization. This ability underlies selective auditory attention and is disrupted by hearing loss and in children with central auditory processing disorder (CAPD). Principal neurons of the lateral superior olive (LSO PNs) are critical for these functions. The classical view of the LSO is a homogeneous block of cells that extracts ongoing interaural level differences (ILDs), however, LSO is increasingly implicated in encoding interaural time differences (ITDs) for broadband transients and amplitude modulations. Cellular properties are fundamental to how neurons extract and encode information. ILD/ITD processing places disparate demands on neuronal properties and there is cellular diversity in the LSO that is not well-understood. It is also critical to understand how different types of information may be organized in higher processing centers of the inferior colliculus (IC).
We found that LSO PNs consist of inhibitory and excitatory cell types with different projection patterns, intrinsic membrane properties, and morphology. The student project will be to work with the PI in accessing and consolidating scientific literature on cellular diversity in the lateral superior olive.

Significance: Our overarching hypothesis is that LSO PN cellular diversity supports both ILD and ITD coding and neurotransmitter system, intrinsic excitability, and projection pattern provide means to organize differentially extracted information in the IC. This project will consolidate knowledge about the cellular diversity of the LSO.

Goals and Objectives: The student will amass a comprehensive list of scientific papers associated with the LSO and catalog findings related to cellular diversity. The student will also draft a synthesis of this information in collaboration with the PI.

Methods: Online database research.

Data analysis: Scientific literature will be cataloged and analyzed for aspects of cellular diversity in the LSO.

Anticipated Findings: The anticipated findings are a comprehensive annotated bibliography and a draft synthesis of consistent and contradictory results.

Student Fellow Training/Mentoring Plan: The student will meet regularly with the PI and attend weekly lab meetings to better understand the type of research we do. The Winters lab is part of the close-knit NEOMED Hearing Research Group which the student will have the opportunity to interact with.

Submit your application to Dr. Jesse Young

Project Description
1) Title: Skeletal Muscle Development in the *Sus* Feeding & Locomotor Systems
PI: Dr. Jesse Young, Department of Biomedical Sciences
LOCATION: NEOMED,

2) Abstract: This study utilizes a well-established precocial animal model it is possible to investigate aspects of newborn physiology, specifically changes in the musculoskeletal system from birth to adulthood. Currently, changes occurring at the tissue level of locomotor and feeding system skeletal muscle during ontogeny are not fully understood. This includes aspects of developmental plasticity and the extent to which genetic and environmental factors determine muscle fiber type. To increase our understanding of the changes which occur in different systems of skeletal muscle this study established the muscle fiber-type proportions of both the feeding and locomotor systems at three points of development (birth, pre-weaning, post-weaning) in a precocial species (pigs). This will be done through standard histological staining of muscle tissues (NADH-TR enzyme staining), and immunohistochemistry to isolate and count Type-I, Type-IIa, and Type-IIb muscle fibers. We hypothesize that the two systems will show similarities in fiber-type proportions at birth, but that the feeding system will show a unique and distinct maturation pattern, influenced by the changes which occur at weaning as the animals move from suckling to mastication. We expect that our results will add a critical understanding to the maturation of skeletal muscle, showing that as new 'programs' (mastication) are onboarded through development, muscle must subsequently respond to new functional requirements by adapting its fiber-type proportion to new demands.

3) Significance of the Research: Two muscle systems exist within the vertebrate body plan, which offer valuable comparisons and insights into the development of skeletal muscle: the feeding and locomotor systems. In precocial mammals these two systems are already functional at birth but continue to mature postnatally. Given their different origins and functions, comparison between feeding and locomotive skeletal muscle offers interesting and yet to be investigated insight into the way in which muscle develops during ontogeny. It also allows for investigation of how muscle growth in these two systems may be related to changing functional needs (i.e., weaning).

Muscles responsible for jaw movement, tongue mobility, and esophageal activity act together to facilitate chewing, swallowing, and food transport through the digestive tract, beginning with the initial intake of food. These structures must be developed sufficiently at birth to allow for suckling and swallowing, and they must undergo coordinated development for the subsequent shift to chewing and swallowing of solid foods. Non-nutritive sucking and swallowing begin *in utero* around 15 weeks of gestation with continuing refinement from this time. After birth, efficiency improves throughout neonatal life due to further development of the oral and pharyngeal structures and refinement of suckling and oral coordination. The masticatory muscles must also sufficiently mature in size and sensorimotor coordination to meet new functional demands exerted by weaning for the shift to textured, solid foods. However, the specific changes happening at the tissue level of these muscles to facilitate these refinements is unclear.

The locomotor system consists of skeletal muscles which enable movement, weight-bearing, stability, and coordination. Like feeding, this system must already be functional at birth in precocial mammals. As the individual develops, refinements occur to ensure successful locomotion over a range of different conditions, whilst maintaining consistent equilibrium with proper balance and postural control.

This study will bridge gaps in our understanding of how changes in a systems' needs, in this case weaning and the shift to mastication of solid foods, affect the underlying architecture of the systems components. By comparing fiber-type proportions it is our intention to show how refinement versus establishment of new biological programs are represented at an architectural level. The study age groups are aimed to be representative of time points covering a major milestone in the feeding system, acting as a lens through which to see how new programming is adopted by skeletal muscle.

Our hope is that this study will further the understanding of how musculoskeletal systems develop and change through ontogeny, when it is imperative that the organism's tissues must be able to grow whilst maintaining existing, and onboarding new, functional properties.

4) Goals and Objectives of the Research: By comparing the skeletal muscle fiber-type proportions across muscles of the feeding and locomotor systems in a precocial species, our data will elucidate whether the feeding system must go through distinct fiber-type shifts as mastication comes online, becoming the primary mode of nutrient acquisition.

5) Research Methods Learned by the Summer Fellow: The researcher will be trained to assist in all phases of the research project, including specimen preparation and analysis. The student will gain experience in basic histology and immunohistochemistry methods, including tissue preparation, staining skeletal muscle, differentiating and counting muscle fiber types, and analyzing data.

6) Research Methods and Data Analysis: Skeletal muscle tissue from the feeding system (Masseter, Temporalis, Digastric, Sternohyoid, Thyrohyoid, Genioglossus, Geniohyoid, Mylohyoid, & Hyoglossus) and locomotor system (Long & Medial Heads of Triceps brachii, Gastrocnemius, & Soleus) are frozen in isopentane. Muscle tissue will be cut into 10µm sections using a cryostat, stained, and counted for specific fiber-type cells. NADH-TR stain will be used to stain all muscles, providing a generalized overview of Type-I and Type-II muscle fibers. Antibodies specific to Type-I, Type-IIa, and Type-IIb myosin's will stain the more specific Type-II fibers. These protocols are already established. Using bright field microscopy, images will be taken of the tissue sections, and we will count the number of each fiber-type cell. Comparisons will then be made of the fiber-type proportions between the two systems, as well as within the different muscles of the feeding system as they pertain to suckling, mastication, and swallowing.

7) Expected Outcomes: Several possible outcomes are anticipated for this study. Our null hypothesis is that fiber-type proportions will follow the same maturation pattern in both the feeding and locomotor systems. If the feeding system shows a different profile compared to the locomotor system, it is likely due to the onboarding of a new system program (mastication) at

weaning. Our findings, regardless of outcome, will lay the foundation for future work quantifying fiber-type proportions across the two systems throughout development.
Student Fellow Training/Mentoring Plan: Funding is requested to support one summer research fellow. PI Young is committed to fostering the researcher's development for the summer. This goal will be achieved through a structured mentoring program, as described below.

Research will be conducted in Young's lab using frozen muscle tissue which is ready for analysis. Protocols are already established, and all necessary laboratory equipment and disposables are already in use as this is an ongoing project.

Besides benefiting from working alongside the PI, the student will be required to attend and present once at the weekly MSRFA journal club. The Musculoskeletal Research Focus Area sponsors a weekly journal club on the general topic of "Evolutionary Morphology", where the fellow would have the opportunity to share and discuss ongoing research findings and pertinent scientific publications. Finally, the student will design and present a poster for the end-of-program poster symposium at NEOMED.

Submit your application to Drs. Rachel Bracken and Jason Kolb

I. Project Description (1-2 pages)

1. Project title, Principal Investigator name, title and location

Project title: Education for Inclusion: Developing an Inclusive Communication Training Pilot for Emergency Medical Providers

Principal Investigator: Rachel Bracken, Ph.D., Assistant Professor, Department of Family and Community Medicine

Co-Investigator: Jason Kolb, MD, Clinical Faculty Educator, COM Medical Education

Location: NEOMED, Rootstown campus; Remote (via Zoom)

2. Abstract:

Recent research demonstrates the need for robust disability-focused training across all areas of health professions education (HPE), including medical, nursing, public health, and emergency medical services (EMS) curricula. Building on the results of survey and interview research conducted in 2025, the goals of this project are to identify actionable strategies and pedagogical best practices for developing and implementing disability-conscious training for prehospital emergency medical providers, such as paramedics and EMTs. Preliminary analysis of our existing survey data demonstrates the marked lack of and urgent need for EMS training specific to caring for people with disabilities, as well as the specific needs for training focused on caring for individuals with alternative or augmented communication needs, such as Deaf folks who communicate in ASL and nonverbal folks who use visual communication boards.

We hypothesize that enhanced training and resources are anticipated to improve EMS providers' competencies and the quality of care provided to patients with disabilities, thereby promoting more effective and empathetic medical interventions. We propose to test this hypothesis by developing pre- and post-intervention evaluations that will measure gains in knowledge, skills, and confidence in caring for patients with alternative communication needs in emergency, pre-hospital settings.

This project represents a crucial step to implementing disability-conscious education for EMS providers within and beyond the State of Ohio. Initial research has been supported by the Ohio Department of Public Safety, and we anticipate continued funding and support from ODPS as we move from the research to implementation stage.

We seek two Research Fellows to assist in the analysis of initial survey and interview data to identify gaps in existing approaches to disability-conscious EMS training and promising training modalities; development of learning objectives for EMS training pilot; design of EMS training pilot; and analysis of EMS training pilot. This opportunity presents mentorship in qualitative analysis, curricular development in health professions education (HPE), community collaboration, and engagement with scholarship in both disability studies and HPE.

3. Significance:

This project furthers NEOMED's focus on developing compassionate, culturally competent, and patient-centered healthcare professionals through the design and evaluation of innovation approaches to disability-conscious EMS training, an area that is significantly understudied. Student Research Fellows will hone transferrable skills in quantitative and qualitative research analysis by working with data collected online surveys and remote (Zoom-based) interviews of EMS providers and EMS educators conducted by members of the research team in 2025. SRFs will also develop skills in translational research by applying research finding to the design and evaluation of disability conscious EMS training.

This research also aims to foster a more inclusive and accessible healthcare environment through better understanding and addressing the educational needs of EMS providers.

4. Goals and Objectives:

The primary scientific objectives of this research are (1) to evaluate the effectiveness of current EMS training standards in preparing paramedics to provide comprehensive care to patients with disabilities (PWD) and (2) to develop and pilot innovative EMS training that addresses existing gaps in EMS training and practice as they relate to PWD, thereby contributing critical insights into the enhancement of EMS curricula and policy-making. Specifically, this study will:

1. Analyze survey and interview data to:
    a. Assess the perceived preparedness of EMS providers across various certification levels in managing patients with a range of disabilities including physical, sensory, and cognitive impairments.
    b. Investigate the frequency and nature of EMS encounters with PWD, focusing on the challenges and barriers EMS personnel face in these interactions.
    c. Explore the effectiveness of existing educational resources and identify areas requiring further development to ensure that EMS providers can offer equitable and effective care to all patients, regardless of disability.
    d. Determine the impact of specialized training on EMS providers' confidence in their ability to communicate effectively and manage medical emergencies related to disabilities.
    e. Evaluate the relationship between EMS providers' training and their perceived effectiveness in delivering care that meets the unique needs of PWD.
2. Develop innovative, disability-conscious training for EMS providers in the state of Ohio by:
    a. Identifying specific learning goals and objectives specific to providing emergency, pre-hospital care to patients with alternative or augmented communication needs.
    b. Collaborating with NEOMED faculty and community experts to design an inclusive educational intervention.
    c. Piloting and assessing an EMS training intervention.

Student Research Fellows will participate in completing the following objectives:

1. Complete CITI training and participate in preparation of IRB and ODPS grant applications, February – March 2026
2. Analyze survey and interview results using methods such as thematic analysis to determine paramedic / EMT training needs, April – June 2026
3. Develop learning goals and design EMS training intervention, July – August 2026
4. Pilot and evaluation EMS training intervention, September – October 2026
5. Disseminate study results at NEOMED student research conference, November 2026

5. Research Methods to be Used:

This translational study utilizes quantitative and qualitative research methods by way of online surveys and interviews. Fellows will participate in the analysis of online surveys (using Qualtrics) and online, remote (Zoom-based) interview data to develop EMS training intervention(s). This research project affords students the unique opportunity to gain familiarity with not only qualitative research design and analysis, but also educational design for health professionals.

6. Proposed method of data analysis

Student Fellows will engage in all aspects of quantitative and qualitative data analysis. Quantitative analysis will include descriptive statistics (e.g., frequencies, means, standard deviations) to summarize response patterns, as well as inferential tests (e.g., chi-square, ANOVA) to examine relationships among demographic variables, confidence ratings, and perceived barriers. Additional correlation or regression analyses may be employed to identify predictors of preparedness and teaching effectiveness. Qualitative analysis will include transcription of interviews and thematic analysis of interview data, i.e., data will be categorized using codes and emerging themes identified. Analysis of interview data will be applied to the development of learning objectives and pedagogical best practices for developing disability-conscious EMS training. Fellows will develop learning goals and participate in the design of an educational intervention for EMS providers.

Student Fellows will also participate in developing tables and figures to display findings and summarizing results. Student Fellows will prepare and present a poster for the NEOMED Research Day. If the Fellows wish to continue with the project after the conclusion of the fellowship, they will have the opportunity to participate in preparation of a manuscript for publication.

While it is possible that applicants for the student fellowship may have some experience engaging in quantitative and qualitative data analysis, prior knowledge or experience is not required. The PIs intend to provide hands-on training and instruction on how to engage in such research in a scientifically rigorous manner.

7. Significance of anticipated findings

It is well documented that people with disabilities (PWD) experience "deep and sustained inequities in health and health care access" in the United States.[1] In the emergency department, a 2023 qualitative study found evidence of "inadequate communication" negatively impacting the care received by PWD and documented both "the importance of mindful listening and patience by healthcare staff" and a need for "comprehensive training with staff about assistive devices and services."[2] In the United States, very little published research examines the training of paramedics regarding treating PWD. What literature does exist focuses mainly on the treatment of children with disabilities. Two different studies examined different implementations of an online self-study program for interacting with children with disabilities, and both found statistically significant improvements in paramedics' confidence in managing these patients.[3,4] Outside of pediatrics, one 2019 scoping review focused on paramedics' knowledge regarding mental health found a need for more research addressing, among others, paramedic "education and training of non-technical skills," such as soft skills necessary for treating PWD.[5] By identifying gaps in existing EMS training approaches; developing innovative disability-conscious EMS training, and evaluating training outcomes, this project will be the critical to developing and implementing targeted disability-conscious training for all EMS providers.

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[1] Mitra M, Long-Bellil L, Moura I, Miles A, Kaye HS. Advancing Health Equity And Reducing Health Disparities For People With Disabilities In The United States: Study examines health equity and health disparities for people with disabilities in the United States. *Health Aff (Millwood)*. 2022;41(10):1379-1386. doi:10.1377/hlthaff.2022.00499

[2] Carmichael JH, Kalagher KM, Reznek MA, Modi P. Improving Accessibility in the Emergency Department for Patients with Disabilities: A Qualitative Study. *West J Emerg Med*. 2023;24(3). doi:10.5811/WESTJEM.58406

[3] Spaite DW, Karriker KJ, Seng M, et al. Training Paramedics: Emergency Care For Children With Special Health Care Needs. *Prehosp Emerg Care*. 2000;4(2):178-185. doi:10.1080/1090312009094147

[4] Wolf-Fordham SB, Twyman JS, Hamad CD. Educating First Responders to Provide Emergency Services to Individuals with Disabilities. *Disaster Med Public Health Prep*. 2014;8(6):533-540. doi:10.1017/dmp.2014.129

[5] Emond K, O'Meara P, Bish M. Paramedic management of mental health related presentations: a scoping review. *J Ment Health*. 2019;28(1):89-96. doi:10.1080/09638237.2018.1487534

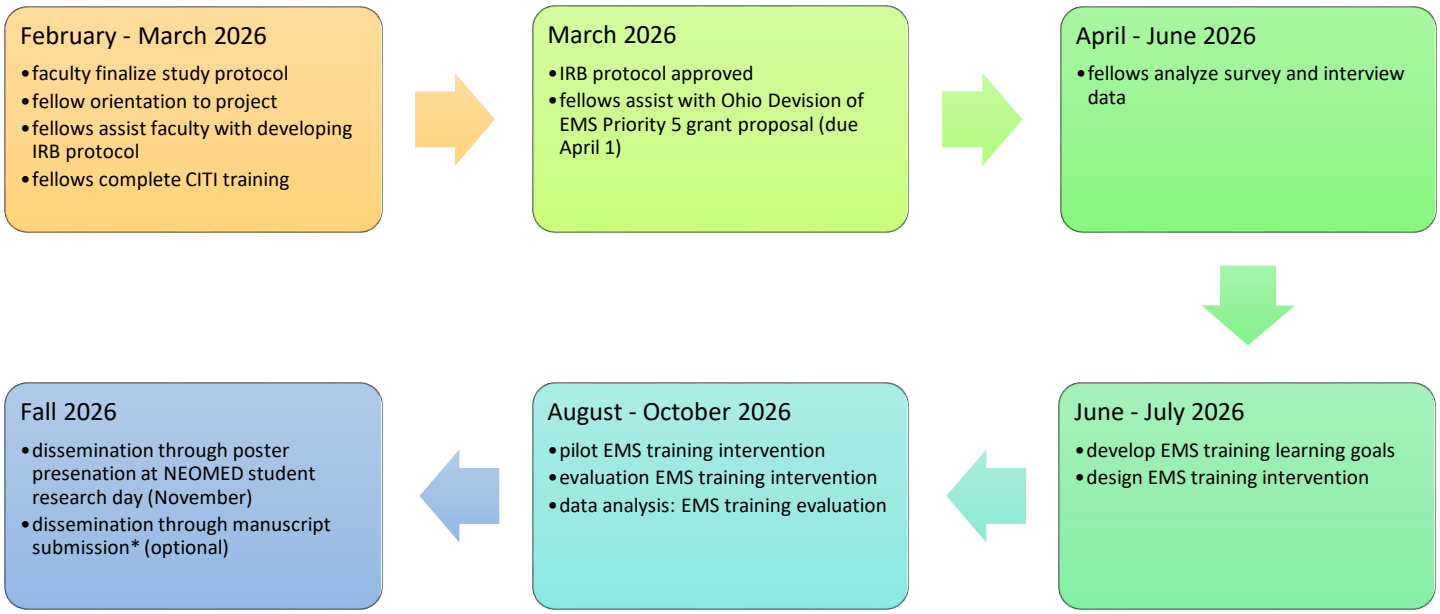
II. Student Fellow Training/Mentoring Plan (1/2 page)

Student Fellows will learn the basics of mixed-methods – survey and interview – data collection and thematic, qualitative analysis, including development of an IRB protocol, as well as translational education research in the health professions. The faculty members will provide project management, guidance, and mentoring related to their own areas of expertise while maintaining a highly collaborative, team-based approach to training and research. Students will be required to complete CITI training on human subjects research.

As a member of the national Health Humanities Consortium's Curriculum and Assessment subcommittee, Dr. Bracken will provide overall guidance to the fellows, expertise regarding the study topic (disability studies in/and health professions education) and thematic analysis of interview data, and guidance with dissemination. As a board-certified emergency medicine physician, Dr. Kolb will provide guidance on survey design, data analysis, and EMS clinical practice and training protocols.

The study faculty will have regular and frequent communication with the summer research Fellows. Given that collaborative relationships are necessary for the successful completion of this project, regular research team meetings will be scheduled throughout June – August 2025. Student Fellows will have access to workspace within the Department of Family and Community Medicine, including access to workstations with computers and appropriate data and software (e.g. Excel, Zoom, and Qualtrics Software). All data analyses will be conducted on NEOMED's campus and will adhere to IRB protocols.

III. Proposed Project and Mentoring Timeline:



Submit your application to Drs. Sara Dugan and Stacey Gardner-Buckshaw

Title: Cannabis and Pain Management Advice for Pregnant Women – Exploratory Study

Note: This project has a substantial data collection component, and could accept 3 students. Principal Investigator: Stacey Gardner-Buckshaw, Ph.D., MPA, Associate Professor and Director of Community Engagement, Department of Family and Community Medicine, NEOMED and Sara Dugan, Pharm.D., BCPP, BCPS, Associate Professor, Psychiatry, Professor, Pharmacy Practice

Location: NEOMED College of Medicine Department of Family and Community Medicine, NEOMED College of Pharmacy, and University Hospital Rainbow Babies & Children's Ahuja Center for Women & Children Midtown.

Abstract and Significance: Cannabis is the most widely used illicit substance among pregnant individuals, with reported use ranging from 3.9% to 16% in the U.S. and even higher among young adults or those using cannabis to alleviate nausea. Further, recent negative political and media attention towards Acetaminophen may motivate pregnant individuals to use cannabis as an alternative to treat pain. And as recreational cannabis legalization is growing across states, perceived risk of harm during pregnancy is declining among patients. Since THC and CBD cross the placenta—and possibly accumulate in fetal tissues—the American College of Obstetricians & Gynecologists (ACOG), CDC, and American Academy of Family Physicians (AAFP) strongly advise against cannabis use during pregnancy and lactation to protect the fetus and infant from harm and death. Yet, per patient report, dispensaries claim cannabis is safe for use during pregnancy, post-partum, and when lactating.

Goals and Objectives: The long-term goal of this project is to inform policymakers, and draft legislation, requiring cannabis dispensaries to follow protocols to reduce risk of harm to pregnant and post-partum women, and their unborn and infant children. The short-term objectives to be achieved this summer are to (1) identify and categorize the information medical and non-medical cannabis dispensaries are providing pregnant and post-partum/lactating patients, and (2) to assess and describe any safeguards already in place. To help accomplish this, the summer research fellow(s) will conduct a survey research study and policy analysis. The students will use existing data to inform study design, engaging stakeholders from the University Hospitals Rainbow Babies & Children's Ahuja Center for Women & Children Midtown. Then, the team will compile and report the information to stakeholders and policymakers responsible for the Substance Use Disorder (SUD) prevention and treatment expansion. The fellow(s) will be required to present the research project at NEOMED Scholarship Day and at an external professional meeting.
Significance of Anticipated Findings: Results of this study may inform best practices in SUD screening, intervention, and recovery, as well as public policy and protocol for distributing cannabis to pregnant, post-partum, and lactating patients, and will likely inform a forthcoming grant-funded project proposal.

Investigative Methods: The student will help design and implement an exploratory study to identify best practices in cannabis dispensing protocols and conduct survey research to document and categorize current dispensary practices look for themes.

Proposed Method of Data Analysis: This project requires simple descriptive statistics, as well as understanding of the various qualitative and quantitative methods.

Student Role: Under direction, the student(s) will take a leadership role in all parts of the research process including but not limited to: institutional review, informed consent, protocol development, data collection and analyses, and dissemination. The student(s) will meet at least bi-weekly with collaborating NEOMED faculty as needed.

Mentoring Plan:

1. Student meets with either Dr. Gardner-Buckshaw or Dr. Dugan and/or community preceptor bi-weekly.
2. Educational topics we will cover, in the context of the project:
   A. Establishing a research question
   B. Conducting a gap analysis/literature review
   C. Writing a grant proposal
   D. Protection of human subjects
   E. Data collection/management
   F. Posters and presentations
3. The student will work with advisors to submit a regional or national presentation of their work.

Resources Available: The student(s) will receive space in the DFCM, with access to computers and a telephone (as required) for research-related activities. The student will also receive research and statistical support as needed. If we receive a qualifying grant, it may be used for student travel to meetings/interviews/presentations, or for poster printing for dissemination. Student grants are available from AAFP, FMEC, and OAFP among other organizations.

Submit your application to Dr. Stacey Gardner-Buckshaw

Title: Developing a Private Practice Elective for Undergraduate Medical Education
Principal Investigator: Stacey Gardner-Buckshaw, Ph.D., MPA, Associate Professor and Director of Community Engagement, Department of Family and Community Medicine, NEOMED
Partners: Ohio Rural Health Association, American Academy of Family Physicians
Location: Department of Family and Community Medicine

Abstract and Significance: Currently, there are only three known programs that include business, management, and financial training to prepare undergraduate medical students for a career in private practice (Toledo, Thomas Jefferson, Indiana). The format for each varies greatly, ranging from a brief online elective to a 24-credit Certificate. There's strong evidence that limited business and management skills among physicians contribute to challenges in establishing and sustaining rural practices—and this deficiency is a recognized factor affecting recruitment and retention in those areas:

1. Lack of Business Acumen Affects Viability of Rural Practices: Physicians often lack foundational business training, which undermines their ability to manage revenue cycles, staffing, compliance, telehealth, and strategic planning.
2. Rural-Specific Barriers Driven by Financial & Administrative Strain: Provider burnout and turnover in rural areas stem from cost pressures, administrative burdens, and insufficient infrastructure. Qualitative studies with rural physicians highlight time/resource constraints and profitability concerns as disproportionate barriers.
3. Recruitment & Retention Decline—Business-Skill Gap as a Contributor: Financial instability of rural hospitals and practices as deterrents to physician relocation and lack of administrative confidence reduce physicians' inclination to choose or stay in rural settings.
4. Workforce Policy Acknowledges Need for Support: AAMC reports recognize that recruitment gains can be undermined by lack of preparation for real-world rural practice—factors include economics and administrative readiness. Organizational briefs (NRHA, HRSA, AMA) stress the importance of business training, financial literacy, mentorship, and operational support to build and retain rural practices.

Goals and Objectives: The objective of this study is to inquire about the essential components of a "Developing a Private Practice" curriculum, and how to prioritize the content. The results will be shared with NEOMED leadership and rural and primary care stakeholders to develop a medical school elective course.

Significance of Anticipated Findings: Results of this study may inform best practices in private medical practice development and management and will likely inform a forthcoming project proposal for either a grant, or a course textbook/toolkit that could be sold. Long-term, we intend to build comfort and confidence among physicians to open and operate a private medical practice where they feel called to do so, including rural areas.
Investigative Methods: Key informants, identified by project stakeholders, will engage in a 90-minute Concept Mapping/Pattern Matching exercise using GroupWisdom Software. This exercise will (1) identify the essential components of a "Developing a Private Practice"

curriculum, (2) group components into larger topic areas, and (3) prioritize the content based on importance and feasibility.

Proposed Method of Data Analysis: This project requires use of GroupWisdom software, and the student hired for this project will be expected to learn how to use this product in addition to collecting simple descriptive statistics, as well as understanding of the various qualitative and quantitative methods.

Student Role: Under direction, the student(s) will take a leadership role in all parts of the research process including but not limited to: institutional review, informed consent, protocol development, data collection and analyses, and dissemination. The student(s) will meet at least bi-weekly with collaborating NEOMED faculty as needed**.**

Mentoring Plan:

1. Student meets with either Dr. Gardner-Buckshaw bi-weekly.
2. Educational topics we will cover, in the context of the project:
    A. Establishing a research question
    B. Conducting a gap analysis/literature review
    C. Writing a grant proposal
    D. Protection of human subjects
    E. Data collection/management
    F. Posters and presentations
3. The student will work with advisors to submit a regional or national presentation, and may be invited to engage in writing the publication.

Resources Available: The student(s) will receive space in the DFCM, with access to computers and a telephone (as required) for research-related activities. The student will also receive research and statistical support as needed. If we receive a qualifying grant, it may be used for student travel to meetings/interviews/presentations, or for poster printing for dissemination. Student grants are available from AAFP, FMEC, and OAFP among other organizations

Submit your application to Dr. Paul LeCat – 1 of 2 projects

Project Description:

1. Dietary sugar intake: assessment and intervention for metabolic syndrome in primary care

2. Dietary sugar is clearly linked with every aspect of metabolic syndrome (obesity, hypertension, hypercholesterolemia, type 2 diabetes, and others). It has been shown to be causative in obesity, coronary artery disease, and diabetes. 50% of Americans consume 4-fold the maximum sugar intake recommended by the American Heart Association. The World Health Organization (WHO), American Academy of Pediatrics (AAP), and others have set similar limits. Some estimate that sugar related diseases could account for as much as 75% of current US medical expenditures.

There is currently no standardized method of measuring a patient's sugar intake in a primary care setting in the way that alcohol or smoking is. There is also no standardized method of intervening through education for patients who overconsume sugar. We hope to find a simple, fast, and effective way to measure sugar intake and behaviors related to sugar consumption in the outpatient setting and intervene with a simple and brief educational piece. Impacts of the education will be measured and evaluated using biometric data and labwork which is already on the patient's medical record with the patient's consent.

3.Development and implementation of a standardized, office friendly sugar intake instrument has yet to be developed. The impact of motivational interviewing on lowering sugar intake and its impact on various aspects of Metabolic Syndrome has not been studied. Metabolic syndrome involves: Hypertension, Diabetes II, Obesity, Hypercholesterolemia, metabolically associated steatohepatitis (MASH), and some would say polycystic ovarian syndrome and obstructive sleep apnea.

4. What is the direct effect of lowering sugar intake on metabolic syndrome-associated metrics? Weight, BMI, SBP, DBP, fasting glucose, Hgb A1c, ALT, cholesterol, LDL, HDL, Triglycerides will be analyzed vs. change in sugar intake for each patient and results compared.

5. Students doing the intake will assess sugar intake over a 12-month period with 16, 15-minute meetings with multiple patients.

6. Labwork and metrics as per (4.) will be gathered on EPIC and analyzed. These correlations of delta sugar intake and delta metrics will be compared and associations analyzed

7. The fellow will contribute great value by gathering and helping to analyze the data.

Student Fellow Training / Mentoring Plan:

1. The fellow will participate in organizational meetings of the students and help coordinate interactions with the site (Boardman Family Medicine and Dr. Thomas Macabobby) The fellow will be actively involved in data analysis with statistical help from NEOMED

2. There will be statistical help from Dr. Phil Turk, and interaction with the student leadership (Burkhanova, Stalnaker, and Snowden) as well as Dr. Macabobby
3. The actual data collection will occur virtually by video or phone, and the patient recruitment will occur at Boardman.

Submit your application to Dr. Paul LeCat – 2 of 2 projects

Project description:

1. Physical Exam Skills: An "invisible" fracture in the patient safety/ QI loop?
2. Physical exam is a cornerstone of medicine and provides unique information, not provided by history or even technology in many instances. It has been shown to speed intervention in crucial situations, and streamline workups, saving resources.

Conversely, it could then be expected that *gaps in physical exam skill* contribute significantly to poor patient outcomes. Studies have shown that little improvement in exam skills occurs in graduate medical education, nor afterward and many would argue there is decay in these skills, without intentionality to improve.

Complicating matters, physical exam errors are often "invisible". When a finding is missed, the exam is reported as "normal". One can argue that the finding was absent at the time of exam, but was it? How is this phenomenon being addressed?

Historically, these gaps were addressed at the bedside during rounds or at Grand Rounds, involving actual patients for exam skill demonstration. Today these activities do not usually involve the patient and more commonly involve analyzing data generated by the patient (e.g. labwork, radiology studies, etc.)

Admitting residents are often unaware of any differences in their initial diagnosis and the patient's final diagnosis, thereby cutting them out of the improvement loop, missing opportunities to learn and improve.

How can we identify poor or absent physical exam skills and address these gaps in postgraduate training? (practicing physicians?) This topic presents fertile ground for Quality and patient safety Improvement.

We aim to provide physical exam feedback and education to residents involved in the care of identified groups of patients, using physical exam documentation in the patient's chart

1. Physical exam skills and training have substantially decreased in American residencies. Standard Quality Improvement efforts generally do not focus on physical exam, nor is this process linked to improvement of deficits in this area. Examining the role of physical exam in a patient's hospital course, and implementation of efforts to address deficits, could result in improvements in patient outcomes and decreased patient morbidity and mortality.

1. Research question: Can identification of quality issues in patient care be influenced by addressing corresponding physical exam skills of residents?

1. The student will learn about the hospital Quality Improvement system and how continuous quality improvement better patient outcomes. They will participate in review of patient cases to identify quality targets involving physical exams. They will also participate in the educational efforts of residents, learning advanced physical exam applications derived from

real patient cases. They may analyze assessment videos of residents. They may participate as a Standardized Patient in these exercises and participate in bedside physical diagnosis rounds with the residents.

1. The data gathered before and after these educational efforts will be compared for statistical significance. These metrics may include hospital transfers, resuscitations, scores on assessments of residents, as well as comparisons of attitudes and knowledge of residents.

1. The student will play a crucial role in coordinating efforts to improve patient morbidity and mortality by helping to educate and analyze attitudes, skills, and knowledge of residents relative to physical diagnosis skills.

Student Fellow Training / Mentoring Plan:

1. The student fellow will be involved in all aspects of the study. This will include regular meetings regarding progress, attending assessments of residents performance on assessments of standardized patients, attend bedside physical diagnosis rounds with residents, attend other residency educational opportunities related to the project, attend QI committee meetings,
2. Resources will include all faculty on the project, residents, Dr. Lecat, appropriate training in statistical analysis, training in evaluation of standardized patient encounters with residents.
3. Research will be conducted at NEOMED and St. Elizabeth's hospital, Youngstown

Submit your application to Dr. Amy Lee

Title: Increasing Breast Cancer Screening Rates at the International Community Health Center
Principal investigator: Amy Lee, MD, MPH, Professor and MPH Program Director
Location: NEOMED/International Community Health Center offices for root cause analysis sessions

Abstract: International Community Health Center is a Federally Qualified Health Center (ICHC) that has seen a decline in breast cancer screening in the past year. To increase their screening rates, quality improvement project planning will be conducted this summer, which will include a root cause analysis, impact/effort matrix, and continued tracking of breast cancer screening rates.

Significance of the overall research: The International Community Health Center is a Federally Qualified Health Center based in northeast Ohio, with sites in Cleveland and Akron. It serves thousands of patients, including Asian American Pacific Islander and immigrant/refugee populations each year in northeast Ohio. Each month, between 300-400 women are eligible for breast cancer screening. However, screening rates have decreased from around 50-60% to about 20-30%, as shown in recent quality improvement data tracking. This project will investigate the causes in a staff root cause analysis exercise in two offices and prioritizing interventions from an impact/effort matrix to boost breast cancer screening rates.

Goals and objectives: This project will be for the summer fellow will be to conduct the "planning" step of the Plan-Do-Study-Act quality improvement cycle, which will include a root cause analysis (fish bone diagram and 5 whys, as appropriate), impact/effort matrix, and continued tracking of breast cancer screening rates at the International Community Health Center offices in Akron and Cleveland.

- SMART Objective 1: By August 31, 2026, conduct a root cause analysis that will provide at least 3 root causes for the decrease in breast cancer screening at ICHC.
- SMART Objective 2: By August 31, 2026, provide at least 3 recommendations of interventions to increase breast cancer screening at ICHC, prioritizing high impact/low effort actions.

Research methods that will be used/learned: An IRB application will be submitted. The student fellow will conduct two root cause analysis and impact/effort matrix development sessions at the Akron and Cleveland sites.

Proposed methods of data analysis: The student will provide a fishbone diagram (and 5 whys analysis, as appropriate) to recommend high impact/low effort interventions to increase breast cancer screening.

How the anticipated findings from the summer research fellow contribute to the success of the overall research being investigated: The products will be used by administrators of ICHC to consider as a part of their strategy to increase their rates of breast cancer screening.

Appendix

Plan for training/mentoring the summer research fellow—individual, group, lab meetings, journal clubs, seminars, etc.

The student will do the following:

- Attend regular meetings with the faculty advisor (remote or in person).
- Demonstrate project management techniques, such as creating agendas and meeting summaries and adhering to a project timeline.
- Take the Writing for the Sciences course offered by Coursera (free version) to improve their writing skills.
- Submit a non-research determination form.
- Conduct two root cause analysis and impact/effort matrix sessions—one at the Akron office and the other at the Cleveland office. Write a report
- Submit an abstract for the NEOMED student research forum in the fall.

Description of resources available. The student will be given guidance by the faculty preceptor on organizing these sessions.

Site where the research will be conducted. The research will be conducted at NEOMED, remotely, and at the Akron and Cleveland offices of the International Community Health Center.

Submit your application to Dr. Christine Crish

1. Project Title: Early neurotransmitter deficits are associated with non-cognitive risk factors in Alzheimer's model mice
PI: Christine M. Crish, Associate Professor
Location: Dept. of Pharmaceutical Sciences, NEOMED

2. Abstract: A major goal of our laboratory is to understand some of the earliest pathological mechanisms that contribute to Alzheimer's brain pathology. Decades prior to the first signs of cognitive deficits, changes begin to occur in the brain that may be associated with deficits in sensory function, appetite, continence, and other fundamental processes known to predict increased risk for dementia. There is a critical need to identify and understand these early factors in order to develop early methods for detecting disease and potentially intervening. Our lab has preliminary data showing alterations in populations of GABA and acetylcholine producing neurons in the brains of Alzheimer's (AD) model mice that precede onset of disease. Our goal is to determine which specific subpopulations of these neurons are affected in specific regions of the hippocampus and cortex at early time points in order to identify brain circuits at greatest risk for damage. These brain circuits may involve visual system dysfunction, incontinence, or other metabolic disruptions which would enable us to establish mechanistic basis for some of these early risk indicators for dementia.

3. Significance:
Dementia is diagnosed by impairment in cognitive ability but unfortunately by the time such symptoms are manifested, irreversible loss to a substantial amount of brain cells has already occurred. Thus, our research proposes to grow the overall understanding of how early changes in neural circuits that maintain sensory or homeostatic functions could signal the onset of the dementia disease process long before cognitive deficits are manifested and the brain is irreparably damaged.

4. Goals & objectives:

Goal A. Prepare tissue for immunofluorescent assays and conduct histological immunofluorescent labeling assays on brain tissue for specific neurotransmitter and AD pathology targets. Students will learn how to section fixed mouse brain sections on a microtome, store sections properly, and select region-specific sections that will be assayed. Students will learn the necessary steps on how to conduct antibody-based immunofluorescent assays including making stock laboratory solutions, calculating assay solution needs, and preparing assay incubation solutions. Students will be required to follow all assay steps to complete assays from start to finish (often a two-day process). Students will then prepare labeled tissue on slides for microscopy analysis.

Goal B. Perform microscopy and analyze images to quantify changes in distribution of neurotransmitter-specific containing neuronal populations.
Students will use microscopy to image immunofluorescent label of different cell types and provide quantitative analysis of expression patterns in hippocampus and/or cortex.

Goal C. Dietary manipulation of choline to improve brain neurotransmitter function
Students will help manage an ongoing study where we feed a choline-rich diet to AD mice to determine the impact of this in preventing/slowing disease-related changes to brain and early symptoms. Students will be involved in weighing and monitoring mice.

5. Research methods
Immunofluorescence and Microscopy
The student will be trained to section fixed brain tissue coronally on a freezing sliding microtome. The student will then be trained to use multicolor immunofluorescence assays to visualize expression of antibody-based labels for specific neuronal types in hippocampus and brainstem regions of mice. We will compare cell type distribution between groups of age- and sex-matched Alzheimer's model mice and healthy control mice. The student will be trained to photograph brain sections using a Zeiss AxioZoom V16 epifluorescent macroscope equipped with a digital high-resolution camera and a computer guided motorized stage and Z-axis and an Axio Imager M2 epifluorescent microscope with a digital high resolution camera and Apotome structured illumination module for tissue requiring higher magnification. Each structure of interest will be imaged at under multiple channels to capture different labels from antibody staining. Images will be z-stacked, flattened with the extended depth of focus module of the Zen microscope software and converted to tiffs or jpegs for analysis. Students will then be trained how to identify brain regions and quantify integrin label using Image Pro software and prepare publication-quality micrograph images for presentation.

6. Proposed method of data analysis
We will use SPSS for IBM Statistical Software to analyze all data. The PI will directly guide the student fellow in the use of this program in order to calculate the applicable analyses if the student has no prior experience in statistical analysis. The student will also be required to generate figures and illustrations depicting important findings using Prism and Adobe Illustrator.

7. Outcomes of research findings
This project will generate fundamental data on GABAergic and acetylcholinergic neuron expression patterns in the brain, which has not been previously investigated as an early, pre-cognitive decline biomarker. Knowledge in this area is critical because it will support future research that seeks to test novel pharmacological strategies to prevent or slow progression of dementia.

2026 SUMMER RESEARCH FELLOW MENTORSHIP/TRAINING PLAN

Training and site where research will be conducted
The student will perform the research at NEOMED in the C. Crish research lab and ancillary shared lab rooms on the fourth floor of RGE. The student accepted for this project will have an initial training phase that involves both web-based lab safety (EOHS online program). Students will have the opportunity to work directly with animals, therefore they will be required to complete relevant CITI-training modules for working with live mice. Students will receive one-on-one skills-based training with lab personnel. After these requirements are met, he or she will be directly trained by the PI (C. Crish) or senior lab staff on tissue preparation, assay conducting, microscopy, and analysis.

Resources available

The C.Crish Lab has access to all the resources necessary to train the summer fellow and enable them to carry out this work plan. The PI has active breeding colonies of AD model mice and a repository of brains collected from Alzheimer's and control mice across different disease stages/ages. The C. Crish lab owns a library of antibodies relevant to the proposed work, auxillary chemicals, laboratory supplies, and basic laboratory equipment (shakers, pipetters, incubators, etc) to conduct assays. The PI has access to all the required equipment, which is either part-owned by the PI, other colleagues in Pharmaceutical Sciences, or is core equipment of the Neurodegenerative Disease and Aging (NDA) research focus area which grants the PI free and unlimited use. The PI also owns statistical analysis software (SPSS) and image processing software (Adobe Creative Suite; Prism; Image Pro). C. Crish lab has dedicated lab bench space to accommodate lab staff and a dedicated desk/computer adjacent to the lab for use by research assistants.

Mentorship plan

The PI and student will have weekly one-on-one meetings to discuss the plan for data collection and analysis as well as to ensure that the project is moving forward at the correct pace. The PI has developed a workflow for all new lab assistants that details and tracks skills learned and their proficiency level, and this workflow will be employed for the student fellow as well.

The student will also attend the weekly C.Crish Lab research meetings to present and discuss their progress. The student fellow will work with the PI to assemble a research poster to present their data at the NEOMED OPRS summer fellowship presentation day.

Submit your application to Dr. Takhar Kasumov – 1 of 2 projects

Title: ACSS2 and Acetylation Remodeling in Alcohol-Induced Tauopathy.

Principal Investigator: Takhar Kasumov, Ph.D.
Associate Professor, Department of Pharmaceutical Sciences
College of Pharmacy, NEOMED
E-mail: tkasumov@neomed.edu

Alzheimer's disease (AD), the sixth leading cause of death in the United States, increases markedly with age. Chronic alcohol consumption accelerates brain aging and heightens AD risk by disrupting pathways essential for neuronal homeostasis1. Alcohol impairs brain energy metabolism and perturbs histone acetylation, critical regulators of proteostasis, synaptic plasticity, and memory formation2, 3. Alcohol use is also associated with increased tauopathy, yet the mechanistic link between alcohol-driven metabolic dysfunction and AD progression remains poorly defined.

This proposal centers on lysine acetylation, a post-translational modification dysregulated by both aging and alcohol exposure. Aberrant tau acetylation promotes the accumulation of neurofibrillary tau aggregates, a defining feature of AD-related tauopathy. In parallel, alcohol-induced reductions in specific histone acetylation marks impair autophagy-mediated tau clearance, collectively contributing to pathological tau accumulation.

Glucose is the primary ACLY-dependent source of acetyl-CoA for histone acetylation, whereas nuclear ACSS2 activates acetate derived from exogenous sources or released from local histone "reservoir" lysines4. Alcohol impairs brain glucose uptake, increases reliance on acetate metabolism, and provides alcohol-derived acetate that competes with glucose for energy production. Using our stable-isotope–based mass spectrometry platform, we showed that alcohol not only provides carbon for histone acetylation but also reprograms acetylation dynamics by facilitating direct acetate flux from metabolic reservoir sites to transcriptionally active lysine residues5.

Here, we will define how alcohol-disrupted acetylation dynamics drive alcohol-accelerated tauopathy.

We hypothesize that alcohol-induced metabolic and oxidative stress enhances ACSS2-dependent mobilization of acetate from reservoir lysines to activating lysines, increasing chromatin accessibility and inducing aberrant transcriptional programs that impair memory and promote pathological tau accumulation.

We will quantify site-specific acetylation stoichiometry and determine acetyl-CoA sources using ethanol-d_6, [U-^{13}C]glucose, and unlabeled histone-derived acetate. These tracers will resolve alcohol-derived, glucose-derived, and inter-lysine acetate transfer. Finally, ChIP-based analyses using site-specific acetyl-lysine antibodies will characterize functional epigenetic consequences in mouse hippocampus and cortex.

Impact: This work will provide new mechanistic insight into how alcohol-induced histone acetylation remodeling disrupts proteostasis and memory, establishing a foundation for future studies targeting acetylation-driven neurodegeneration.

Background and Significance: Lysine acetylation links cellular metabolism to gene regulation and proteostasis through acetyl-CoA–dependent modification of histones, transcription factors, and tau. Nuclear acetyl-CoA pools are shaped by HAT/HDAC activity and by metabolic enzymes, including PDH, ACLY, and ACSS2. ACSS2 converts acetate to acetyl-CoA for histone acetylation during metabolic stress and facilitates direct intra-histone acetate transfer from reservoir to activating lysines, as shown in yeast quiescence exit.

Brain glucose metabolism is impaired in AD due to reduced glucose uptake and utilization. NAD^+-dependent sirtuins (SIRT1 and SIRT6) oppose acetylation by deacetylating histones, transcription factors, and tau (e.g., K174ac). Alcohol further imposes metabolic stress by inhibiting glucose metabolism, generating acetate, inducing oxidative stress, depleting NAD^+, and reducing sirtuin-dependent deacetylation. However, it remains unknown whether alcohol-induced acetate redistribution, via ACSS2-dependent mobilization, drives dysregulated histone acetylation and contributes to AD-related pathology.

Goals and Objectives: Our objective is to define how *alcohol-induced metabolic stress alters histone acetylation and accelerates brain aging and tauopathy.* We hypothesize that alcohol-induced metabolic and oxidative stress enhances *ACSS2-dependent acetate mobilization* from reservoir lysines to transcriptionally activating lysines, leading to increased chromatin accessibility, aberrant gene expression, memory impairment, and pathological tau accumulation. To test this, we will use $ACSS2^+/^+$htau and $ACSS2^-/^-$htau mice as a tauopathy model.

Aim 1: Determine the role of ACSS2 in alcohol-disrupted histone acetylation. We hypothesize that ethanol impairs systemic and brain metabolism by altering mitochondrial function, reducing glucose oxidation, and increasing reliance on ACSS2-dependent acetate utilization. In $ACSS2^+/^+$htau and $ACSS2^-/^-$htau mice, we will quantify cortical and hippocampal glucose metabolism and acetyl-CoA flux. Stable isotope MS will distinguish ACLY- vs. ACSS2-derived acetylation using glucose-, ethanol-, and histone-reservoir–derived acetate.

Aim 2: Assess the epigenetic consequences of alcohol-disrupted histone acetylation. We will determine how alcohol-induced changes in H4K16ac (proteostasis/autophagy) and H4K12ac (learning/memory) affect chromatin regulation. Using H4K16ac- and H4K12ac-specific antibodies and ChIP-qPCR/ChIP-seq, we will define transcriptional changes associated with tau accumulation and metabolic stress in hippocampus and cortex.

Student Involvement: Students will gain hands-on training in proteomics sample preparation, LC-MS/MS, isotope-tracer data analysis, ChIP methods, and Western blot–based tauopathy characterization.

Methods and Data Analysis: Female $ACSS2^-/^-$, htau, and $ACSS2^-/^-$;htau mice will receive ethanol-d_6 and [U-^{13}C]glucose. Nuclear histones will be extracted and analyzed by LC-MS/MS. Raw MS data will be processed using a SwissProt mouse database, 1% FDR, tryptic peptides with

up to two missed cleavages, 6-ppm precursor and 20-ppm fragment tolerances. We will assess mitochondrial function, glucose oxidation, and enzymatic activity in hippocampal and cortical tissues. Complementary cell culture models will evaluate how altered acetylation disrupts proteostasis.

Significance of Expected Findings: This study will clarify how alcohol-disrupted histone acetylation rewires brain metabolism and contributes to cognitive impairment and tauopathy. The integration of metabolic tracing, epigenetics, and proteostasis analyses will provide mechanistic insights into alcohol-accelerated AD progression and support future development of therapeutic strategies targeting HATs, HDACs, ACSS2, or acetyl-CoA metabolism.

Student Fellow Training/Mentoring Plan: The mentoring program aims to equip student with skills in mass spectrometry and bioinformatics. Guided by the National Academies' recommendations, the program offers structured mentoring, career planning, and training in scientific presentation and writing. Key topics include coworker interactions, work habits, and thorough documentation of research. Students will join weekly journal clubs to critique articles and learn paper submission. Professional practices instruction will cover the scientific method, hypothesis formulation, research design, and timeline creation. Progress will be monitored through interviews, weekly meetings, and a final poster presentation of summer research findings.

Submit your application to Dr. Takhar Kasumov – 2 or 2 projects

Title: Stable Isotope Tracing of Mitochondrial Proteins and mtDNA Dynamics in Alzheimer's Tauopathy.

Principal Investigator: Takhar Kasumov, Ph.D.
Associate Professor, Department of Pharmaceutical Sciences
College of Pharmacy, NEOMED
E-mail: tkasumov@neomed.edu

Alzheimer's disease (AD), the leading cause of dementia and a major global health challenge, is a progressive neurodegenerative disorder characterized by cognitive decline and memory loss [1-3]. Pathologically, AD is marked by extracellular -amyloid accumulation and intracellular neurofibrillary tangles formed from tau aggregation [4]. Mitochondrial dysfunction is a central contributor to neurodegeneration in AD. Mitochondrial DNA (mtDNA), due to its limited repair capacity and proximity to reactive oxygen species production sites, is particularly susceptible to oxidative damage [5]. Several forms of pathogenic tau impair neuronal bioenergetics and may lead to disrupted mitochondrial dynamics (fusion and fission balance), and block mitophagy, preventing clearance of defective mitochondria [6]. Using our mass spectrometry platform, we demonstrated that differentially abundant proteins in tauopathy mouse brain are predominantly associated with tau aggregation and autophagy regulation, accompanied by impaired mitochondrial integrity and function.

We hypothesize that tauopathy-related disruptions in mitochondrial dynamics alter the synthesis and turnover rates of mitochondrial proteins, with a particular impact on mtDNA-encoded subunits of the respiratory chain in the brain.

We will develop and apply a novel $2H_2O$-based stable isotope method to quantify mitochondrial proteins and mtDNA synthesis in the AD brain. Oral $2H_2O$ administration establishes a steady-state enrichment, enabling turnover measurements of proteins [7, 8] and DNA [9] using high-resolution LC-MS/MS. We have validated this approach across multiple tissues [10-12] and, in preliminary brain studies, showed similar synthesis rates for nuclear- and mtDNA-encoded proteins. Using this approach, we will define how tauopathy disrupts mitochondrial dynamics, mtDNA integrity, and proteome turnover in the brains of *htau* mice (expressing all six human tau isoforms). This project will provide the direct *in vivo* measurements of mtDNA and mitochondrial proteome turnover in tauopathy, revealing mechanisms by which tau-induced mitochondrial defects drive neurodegeneration.

Impact: This project will deliver the novel isotope-based method to quantify mtDNA and mitochondrial protein synthesis in the prefrontal cortex and hippocampus, regions critically affected in AD. By linking tauopathy-induced defects in mitophagy, fusion–fission dynamics, and mtDNA integrity to impaired proteome turnover, these studies will define mechanisms of mitochondrial failure that drive synaptic dysfunction and identify therapeutic targets for AD. Background and Significance: The brain is one of the most metabolically active organs, consuming roughly 20% of the body's total energy, primarily in the form of ATP produced in healthy and functional mitochondria. Brain aging and tauopathy disrupt the mitochondrial

respiratory complexes (ETC), imbalancing mitochondrial dynamics and biogenesis, ultimately amplifying neuronal stress and degeneration. However, it remains unknown how disrupted mitochondrial dynamics affect protein turnover with tauopathy progression.
Goals and Objectives: Our objective is to define how progressive and advanced-diseases stage tauopathy affects mitochondrial dysfunction and global mitochondrial proteome turnover in AD brain. To test this, we will use pre-symptomatic, progressive-disease-stage, and advanced-disease-stage symptomatic *htau* mice as a tauopathy model. We will use age and sex-matched *C57BL/6* wild-type mice as healthy controls.

Aim 1. Determine whether tauopathy preferentially decreases synthesis of mtDNA-encoded proteins. *Hypothesis: Tauopathy-associated mtDNA defects reduce synthesis of mtDNA-encoded proteins, driving mitochondrial dysfunction.* We will evaluate the respiratory functions of hippocampal and PFC mitochondria, and measure mtDNA and mitochondrial proteome dynamics by $2H_2O$ labeling and LC-MS/MS.

Aim 2. Define how disrupted mitochondrial dynamics affect protein turnover in tauopathy. *Hypothesis: Tauopathy and aging impair mitochondrial fusion and fission, causing dysregulated protein turnover*. We will measure mitochondrial dynamics and turnover to determine their interaction in AD.

Innovation: Our approach to mitochondrial protein DNA dynamics is novel and represents a major advance in flux studies. Using 2H2O metabolic labeling of mtDNA, proteins, and their acetylated forms, we developed a high-resolution MS method that quantifies low isotopic enrichment of peptide fragment ions. Unlike conventional tracers, this approach enables simultaneous measurement of protein, DNA, and biomolecule turnover; assessment of PTMs on protein stability and aggregation; and evaluation of the interplay between mtDNA synthesis, mitochondrial dynamics, and proteome turnover. It employs a safe, inexpensive isotope delivered in drinking water, avoiding costly high-dose i.v. 13C tracer infusions that disrupt metabolic homeostasis. This cost-effective method enables direct in vivo measurement of mtDNA and mitochondrial proteome dynamics.

Student Involvement: Students will gain hands-on training in proteomics sample preparation, LC-MS/MS, mass spectrometry software and data analysis, bioinformatics, and Western blot–based tauopathy-induced mitochondrial dysfunction characterization.

Methods and Data Analysis: We will administer $2H_2O$ to *htau* and wild-type mice and collect the cortical and hippocampal brain regions at different time points, i.e., 1, 3, 7, 14, 21 and 30 days. We will prepare the proteomics samples for LC-MS/MS analysis. Raw MS data will be processed using a SwissProt mouse database, 1% FDR, tryptic peptides with up to two missed cleavages, 6-ppm precursor and 20-ppm fragment tolerances. We will also assess mitochondrial function and enzymatic activity in hippocampal and cortical tissues. Cell culture models, i.e., N2A cells and SHY5Y cells, will be used to explore downstream mechanistic pathways and how altered mitochondrial dysfunction disrupts proteostasis.

Significance of Expected Findings: This study will define mechanisms of mitochondrial failure that drive synaptic and brain proteome dysfunction and neurodegeneration, and identify dynamic biomarkers and therapeutic targets for AD.

Submit your application to Dr. Erin Reed – 1 of 2 projects

TITLE: Characterization of innate lymphoid cells in a mouse model of Alzheimer's disease
PI: Erin Reed, Assistant Professor, Department of Pharmaceutical Sciences
SITE: NEOMED, Rootstown campus

ABSTRACT: Alzheimer's disease (AD) is the primary cause of dementia, characterized by robust inflammation within the brain that accompanies the pathological hallmarks of amyloid plaques and neurofibrillary tau tangles. Microglia, the resident innate immune cells of the brain, mediate this process, driving AD pathogenesis; however, they also signal to circulating peripheral immune cells to instruct their function and phenotype. These peripheral cells similarly contribute to the inflammatory environment of the AD brain, but how they contribute to disease processes remains unclear. We hypothesize innate lymphoid cells (ILCs) from the circulation localize at brain-border interfaces (meninges and choroid plexus) to modulate parenchymal AD pathology through their actions on B cells. We propose to determine the localization and composition of ILCs during disease onset and progression, their reliance on specific signaling pathways for their action, and their influence on B cells.

SIGNIFICANCE: Successful completion of this research project will provide critical insights to the mechanisms giving rise to immune dysregulation and neuroinflammation in AD. Understanding these processes have the potential to become the basis for new therapeutic strategies.

GOALS & OBJECTIVES: The student working on this project will participate in characterizing ILCs in the brain and at the interfaces through genetic and immunohistochemical approaches to define their location, temporal dynamics, and phenotypes.

RESEARCH METHODS: To identify ILCs, the student working on this project will use a combination of genetic and immunolabeling approaches. A mouse model of AD has been generated where specific cell populations express fluorescent proteins. Brain tissue and meninges from these transgenic mice will be collected. The student will perform immunohistochemistry and microscopy on tissue slices and meningeal wholemounts to assess cell number and location. Brains and meninges will also be analyzed by flow cytometry for labeling efficiency and cell phenotype.

DATA ANALYSIS: The student will be taught how to use the microscope for data acquisition and ImageJ for analysis. They will also be taught how to use the FACSDiva program for flow cytometry data acquisition and FlowJo for analysis. Microsoft Excel will be used to perform statistical analyses of all data generated.

STUDENT CONTRIBUTION TO OVERALL INVESTIGATION: The overall investigation of peripheral immune cell participation in AD pathogenesis will be aided immensely by successful contributions of the student in characterizing the fate and functions of immune cells in the brain and its interfaces. To date, there has been little investigation of some cell populations and studies of others has produced conflicting reports. As these peripheral immune cells function in

various disease processes, the student contribution stands to be significant in advancing the project.

STUDENT TRAINING/MENTORING PLAN

Training/mentoring: The student joining this project will be mentored and trained by the PI and the postdoc who developed and is currently working on the project. The PI will meet weekly, or more often if needed/desired, with the student and postdoc to discuss the goals and progress of the project, review data, etc. The postdoc will provide daily technical oversight and mentorship. The group (PI, postdoc, and student) will also read and discuss papers related to the project on a regular basis.

Available resources: The laboratory is fully equipped and/or has access to all the equipment necessary to carry out these experiments. The requisite IACUC and IBC approvals have been attained. Many of the mice have been generated, and some tissue for analysis has been collected. Additional animals will be available for collection and analysis in Summer 2026.

Site: This research project will be carried out within the Department of Pharmaceutical Sciences at NEOMED. The laboratory is located on the 4th floor of the RGE building

Submit your application to Dr. Erin Reed – 2 of 2 projects

TITLE: Identifying novel regulatory mechanisms behind lymphocyte contributions to a mouse model of Alzheimer's disease
PI: Erin Reed, Assistant Professor, Department of Pharmaceutical Sciences
SITE: NEOMED, Rootstown campus

ABSTRACT: Alzheimer's disease (AD) is the primary cause of dementia, characterized by robust inflammation within the brain that accompanies the pathological hallmarks of amyloid plaques and neurofibrillary tau tangles. Microglia, the resident innate immune cells of the brain, mediate this process, driving AD pathogenesis; however, they also signal to circulating peripheral immune cells to instruct their function and phenotype. These peripheral cells similarly contribute to the inflammatory environment of the AD brain, but how they contribute to disease processes remains unclear. We hypothesize the sex chromosomes and gonadal hormones drive specific aspects of lymphocyte biology, biasing their phenotype and function to promote a detrimental inflammatory milieu for the onset and progression of pathology. We propose to determine the localization and phenotype of lymphocytes in the brain and meninges based on the complement of sex chromosomes and gonadal hormones.

SIGNIFICANCE: Successful completion of this research project will provide critical insights to the mechanisms giving rise to immune dysregulation and neuroinflammation in AD. Understanding these processes have the potential to become the basis for new therapeutic strategies.

GOALS & OBJECTIVES: The student working on this project will participate in immunohistochemistry, flow cytometry, and other biochemical approaches to define the relative contributions of sex chromosomes and gonadal hormones on lymphocyte location, phenotypes, and responses.

RESEARCH METHODS: The student working on this project will use a combination of genetic and immunolabeling approaches. A mouse model of AD has been generated where the complement of sex chromosomes had been decoupled from the gonads in the context of AD. Brain tissue, meninges, blood, and spleens from these transgenic mice will be collected. The student will perform immunohistochemistry and microscopy on tissue slices and meningeal wholemounts to assess cell number and location. Brains and meninges will also be analyzed by flow cytometry for cell phenotype. ELISAs will be performed to measure antibody concentrations.

DATA ANALYSIS: The student will be taught how to use the microscope for data acquisition and ImageJ for analysis. They will also be taught how to use the FACSDiva program for flow cytometry data acquisition and FlowJo for analysis. Microsoft Excel will be used to perform statistical analyses of all data generated.

STUDENT CONTRIBUTION TO OVERALL INVESTIGATION: The overall investigation of peripheral immune cell participation in AD pathogenesis will be aided immensely by successful contributions of the student in characterizing the fate and functions of immune cells in the brain and its interfaces. To date, there has been little investigation of some cell populations and studies of others has produced conflicting reports. As these peripheral immune cells function in

various disease processes, the student contribution stands to be significant in advancing the project.

STUDENT TRAINING/MENTORING PLAN

Training/mentoring: The student joining this project will be mentored and trained by the PI and the senior PhD graduate student currently working on the project. The PI will meet weekly, or more often if needed/desired, with the summer student and PhD student to discuss the goals and progress of the project, review data, etc. The PhD student will provide daily technical oversight and mentorship. The group will also read and discuss papers related to the project on a regular basis.

Available resources: The laboratory is fully equipped and/or has access to all the equipment necessary to carry out these experiments. The requisite IACUC and IBC approvals have been attained. Many of the mice have been generated, and some tissue for analysis has been collected. Additional animals will be available for collection and analysis in Summer 2026.

Site: This research project will be carried out within the Department of Pharmaceutical Sciences at NEOMED. The laboratory is located on the 4th floor of the RGE building.

Submit your application to Dr. Matthew Smith

Metabolic and Structural Retinal Vulnerabilities Following Traumatic Brain Injury
Matthew A. Smith, PhD

Project Description:
Traumatic brain injury (TBI) frequently leads to lasting visual and circadian disturbances, implicating secondary neurodegeneration within retinal ganglion cells (RGCs) and their central projections. The retina offers a unique, accessible model to investigate neurodegenerative processes after TBI, as it mirrors central nervous system (CNS) pathology while allowing for precise visualization and molecular interrogation of axonal and synaptic alterations. Emerging evidence indicates that TBI disrupts mitochondrial metabolism, autophagy, and inflammatory signaling within retinal neurons—pathways central to both degeneration and repair. Metabolic dysregulation and impaired cellular clearance may contribute to progressive RGC loss, glial activation, and synaptic remodeling long after the initial injury. This project investigates how distinct TBI mechanisms—controlled cortical impact (CCI) and jet-flow overpressure (JFO)—differentially affect retinal structure, function, and metabolic gene expression.

Using histological, molecular, and electrophysiological assays, this study aims to define the extent and regional specificity of RGC and glial changes across dorsal–ventral retinal zones following injury. Additional experiments will evaluate the therapeutic efficacy of metabolic and autophagy-enhancing compounds in mitigating post-TBI retinal degeneration. This work seeks to elucidate shared molecular pathways linking CNS trauma, metabolic compromise, and impaired regeneration—thereby identifying potential targets for neuroprotective intervention.

Student Training and Mentoring Plan:
Students will participate in all phases of the project, including: TBI Model and Drug Administration: Assisting in controlled cortical impact or jet-flow overpressure procedures, post-surgical monitoring, and intraperitoneal/intravitreal drug delivery. Tissue Collection and Histology: Performing perfusion, retinal flat-mount preparation, immunohistochemistry, and fluorescence imaging to quantify RGC subtypes and glial activation. Molecular and Functional Analysis: Conducting Western blot, qPCR, or spatial gene expression studies; assisting in visual electrophysiology (PERG/VEP) recordings; and contributing to data curation and analysis. . All training will occur in RGE 400 at NEOMED, under the direct supervision of Dr. Smith and advanced graduate researchers. Advanced CITI and in-lab training will required for individuals wanting to be involved in animals based experiments. However, a student can still contribute greatly to advance project without engaging in animal experiments.

Scholarly Development: Students will attend weekly Smith Lab meetings, receive one-on-one mentoring with the PI, and be encouraged to present progress during BTB student seminars.

Submit your application to Dr. Xinwen Wang

Title: Impact of Catechol-O-Methyltransferase (COMT) Genetic Polymorphisms on the Effectiveness of COMT Inhibitors

Principal Investigator: Xinwen Wang, Ph.D.
Assistant Professor, Department of Pharmaceutical Sciences
College of Pharmacy, NEOMED
E-mail: xwang2@neomed.edu

Abstract
Parkinson's Disease (PD), the second most common neurodegenerative disorder worldwide, affects approximately 1% of individuals over age 60(Rizek, Kumar, & Jog, 2016). catechol-O-methyltransferase (COMT) inhibitors are widely used as adjunctive therapy to enhance levodopa therapy by blocking COMTmediated levodopa metabolism. However, patient responses to COMT inhibitors vary, a significant portion of the patients do not benefit from the combined therapy(Gray, et al., 2022). There is a critical clinical need to identify the factors may influence how effectively these drugs suppress COMT activity and thereby enhance levodopa activation. Single nucleotide polymorphisms (SNPs) within the COMT gene, particularly rs4633, rs4818, and rs4680, have been associated with poor response to levodopa therapy in PD patients (Lin, Fan, Lin, Chang, & Wu, 2018). Despite their high population frequencies, the molecular consequences of these variants and haplotypes on COMT inhibitor responsiveness remain poorly defined. This project aims to characterize how rs4633, rs4818, and rs4680 and their haplotypes influence COMT expression and activity, and consequently, the magnitude of COMT inhibitor–mediated enhancement of levodopa activation. Findings will provide crucial mechanistic insight to inform precision therapy in PD.

Goals and Objectives
The overarching goal of this proposal is to establish a scientific foundation for optimizing the use of COMT inhibitor as an adjunctive therapy with levodopa for PD patients.

Our central hypothesis: COMT variants, rs4633, rs4818, and rs4680, may alter COMT expression or enzymatic function, which in turn may modulate the pharmacodynamic effectiveness of COMT inhibitors.

Specific Aim: Characterize how COMT single variants, rs4633, rs4818, and rs4680, and haplotypes alter basal COMT activity and modulate the inhibitory effectiveness of COMT inhibitors on levodopa metabolism.

Significance
This project addresses a critical but underexplored area at the intersection of pharmacogenomics and neurotherapeutics: the impact of COMT genetic polymorphisms on the pharmacodynamic effectiveness of COMT inhibitors used in Parkinson's disease (PD). COMT inhibitors are essential adjunctive therapies designed to enhance levodopa activation by blocking COMT-mediated metabolism(Rizek, et al., 2016). However, substantial interindividual

variability in treatment response remains unexplained, posing major challenges for optimizing PD pharmacotherapy(Gray, et al., 2022).

While genetic variants in COMT have been associated with poor responses to levodopa treatment(Lin, et al., 2018), their consequences for the inhibitory effectiveness of COMT inhibitors, and ultimately for levodopa metabolism, remain poorly understood. This gap limits our ability to develop precision treatment strategies for PD patients.

The project's focus on how COMT single variants and haplotypes influence COMT susceptibility to COMT inhibitor provides new mechanistic insight into how inherited genetic differences shape response to PD treatments. This is essential for optimizing PD treatment plans, especially given the prevalence of COMT polymorphisms and the high clinical reliance on COMT inhibitors in elderly patients with complex medication regimens. A clearer understanding of variant-driven changes in COMT activity will help explain therapeutic variability, reduce treatment failures, and minimize unnecessary dose escalation or polypharmacy.

By integrating pharmacogenomics, enzymology, and quantitative proteomics, this work addresses urgent needs in refining existing PD therapies and guiding the development of genotype-informed treatment strategies. It identifies key biological barriers to effective COMT inhibitor use and introduces a framework for predicting drug response based on genetic background. The findings will shape future pharmacogenomic research in PD, offering a scientific foundation for improving the efficacy and safety of levodopa-based treatment and contributing impactful knowledge to both neurodegenerative disease research and precision pharmacotherapy.

Research Methods

Generation of COMT Variant-Expressing Cell Lines

We will generate isogenic Flp-In-293 cell lines stably expressing wild-type COMT, each COMT single variant (rs4633, rs4818, rs4680), and their five major haplotypes. DNA extracted from each cell line will be sequence-verified to confirm correct variant or haplotype incorporation. Microsomal fractions will be prepared for COMT protein quantification and activity assays. COMT protein levels will be determined using targeted proteomics or capillary Western blotting (JESS).

Evaluation of COMT Inhibitor Effectiveness Across Variants

To determine which COMT variants/haplotypes alter the pharmacodynamic effectiveness of COMT inhibitors, each microsomal preparation will be incubated with a fixed concentration range of a representative COMT inhibitor, entacapone. Inhibition curves will be generated by measuring residual methylated levodopa metabolites via mass spectrometry. COMT inhibitor effectiveness will be evaluated using inhibitor dose–response assays to generate IC_{50} and Ki values, enabling comparison of how each variant or haplotype modifies COMT inhibition by entacapone.

Data Analysis and Expected Results

- Generate Michaelis–Menten and inhibitory kinetic models to evaluate differences in catalytic efficiency (Vmax/Km) and inhibitor sensitivity (IC_{50} or Ki).
- Use one-way ANOVA to compare COMT expression, basal activity, and inhibitor potency across SNPs and haplotypes.
- Correlate expression levels with inhibitory response to determine whether and how genetic variation influences inhibitor effectiveness.

We expect COMT variants and haplotypes to show measurable differences in COMT expression and basal enzymatic activity. Variants with higher intrinsic activity will likely require higher concentrations of COMT inhibitors to achieve comparable inhibition, reflected in elevated IC_{50} or Ki values. Conversely, lower-activity variants should be more easily inhibited. Haplotype effects are expected to be more pronounced than single SNP effects, identifying specific genetic combinations that reduce the effectiveness of COMT inhibitors in suppressing levodopa metabolism.

Student Fellow Training/Mentoring Plan (Limit of one half page)
Science Mentoring Plan

With regarding to the basic science training for the proposed project, the key areas I would like to help the student improve are listed as below:

a) Area: Pharmacogenomics in Parkinson's Disease
- We have Journal Club to share research trend/development and critically evaluate published articles in the field. In the Journal Club, the student will be participating in the discussion of current development in our fields. We will critically discuss the cons & pros of the research, and how the study may be designed differently to better answer the research questions.
- We have weekly lab meeting to discuss the research progress of the summer project and guide the students for trouble shooting.

b) Skills: Transformation, Transfection, Cell culture and LC-MS/MS sample preparation
- One-on-one mentoring will be offered to help student learn how to do transformation/transfection, culture transfected cells and extract intracellular and extracellular endogenous metabolites.

Presentation skills development
- The student will present the research updates weekly in our lab meeting and present articles in our Journal Club and DOM meeting.
- The student will also have opportunity to present the whole project in our department seminar after summer.
- The student will have opportunity to present at NEOMED research symposium.

Scientific Writing
a) Read publications on scientific Journal
- Reading well-written scientific articles is the key to learn and improve scientific writing. At the beginning, student will learn to search for references of interest using Google Scholar

and PubMed, and perform literature review in relevant field. We will update the reading progress in Journal Club.

b) Practice and Revise

• Practice is necessary to improve writing skills. I find the writing-revision cycles between trainee and faculty is a very efficient and individualized way to polish writing skills. I will find opportunities for the student to improve writing skill through the personalized writing revision cycles.

Submit your application to Dr. Stacey Barrenger

1. **Project Title:** Addressing Individual and Structural Barriers to Medical and Behavioral Healthcare for Returning Citizens
Location: NEOMED, community sites in Portage County

2. **Abstract:** People leaving jails and prisons, or returning citizens, have high medical and behavioral health needs that remain unmet during their return to the community due to a fragmented service system and competing demands to meet basic needs. To better address medical and behavioral health needs among this population a community-centered, multi-level approach to coordinated care is needed. This project seeks to better understand the needs of returning citizens and develop a community collaborative approach to increasing connections to healthcare.

3. **Significance:** Returning citizens, or people who have been incarcerated in prisons and jails, experience higher rates of chronic and infectious diseases. Additionally, people who have substance use disorders or mental illnesses are overrepresented among those incarcerated. This population has a high need for medical and behavioral health care, yet it is often unmet, especially as people returning to the community from jail or prison often need to find a place to live, a place to work, and re-establish important relationships. Under multiple competing demands, healthcare often falls to the side as basic needs become the priority. The transition from incarceration is an opportunity to engage people into wraparound services that addresses both their basic and health needs, yet services and supports are often fragmented within communities. Portage County o4ers a monthly Citizens Circle which is comprised of key providers of health, behavioral health, and social services who meet directly with returning citizens to help them get connected to services. Likewise, the Circle provides an opportunity for providers to collaborate with each other to eliminate barriers to services. Yet it is not clear how the Citizen's Circle is impacting individuals' lives. Engaging with individuals directly, while also working to eliminate systemic barriers to care, has the potential to improve community health, not just for returning citizens but also for others in the community who have multiple needs and have di4iculty navigating multiple sectors. This project will seek to answer the following research questions:

A) What are the best ways to engage people in medical and behavioral health services, while also supporting basic needs, during a return to the community from jails and prisons?

B) How can communities create an active coalition of medical, behavioral health, and social service providers working together to provide wraparound services for returning citizens?

4. **Goals/Objectives:** This research fellowship is a community-engaged project examining barriers to healthcare for returning citizens. The fellow will work with the

PI and community partners to develop a community needs survey and then use the results of that survey to develop a multi-level intervention. The goals of this project are: 1) to understand the individual and systemic barriers to accessing healthcare for returning citizens; 2) develop a multi-level intervention to improve access to medical, behavioral, and social services for returning citizens.
Depending on the stage of the project, the student fellow will be involved in conducting a literature review, attending community meetings to understand the scope and reach of services in Portage County, assist in developing a survey or interview to be administered to people recently released from jail or prison, and assist with analyzing data and writing up findings. These findings will inform the development of a multi-level intervention to improve access to care for people recently released from jail or prison.

5. **Research Methods:** This is a community-engaged research project, meaning that the research is conducted in partnership with service providers and community members. Dr. Barrenger has been attending meetings in the community like the monthly Portage County Citizen's Circle and other community collaborative meetings like the Reentry Coalition and Stepping Up to meet key collaborators across multiple service sectors. By attending these meetings, she is also getting a better understanding of community needs and service barriers from the perspective of service providers and community stakeholders. The goal is to develop a community needs survey (developed in partnership with providers, peers, and those newly returned to the community) to better understand gaps in services, barriers to access, and what is working from the perspective of those needing help. Portage County has engaged in needs assessments at the community level, but this project could provide a new perspective into community needs, by including individuals who are directly impacted by incarceration.

The student fellow will engage in multiple aspects of the research process which may include a review of the literature, develop additional research question, develop a survey instrument and/or interview guide, and analyze data.

6. **Proposed Methods of Data Analysis:** Depending on the type of community needs survey developed, data analysis could include survey analyses and/or coding and theming of interviews.

7. **Significance of Anticipated Findings:** The findings of this community-engaged pilot study combined with existing community-level assessments will support an application for a larger research study to implement interventions at both the individual and systems/structural level to improve connections to care.

Student Fellow Training/Mentoring Plan
The student fellow will work closely with Dr. Barrenger on this project. At the start of the fellowship, they will develop a research plan for the fellow based on the students' interests and skills and to align with the stage of the overall research project. The fellow and Dr. Barrenger will meet weekly (at a minimum) to review progress on tasks and develop new

research goals. The student will engage in a combination of independent and collaborative tasks. The fellow may also accompany Dr. Barrenger in attending community and research meetings in Portage County. Dr. Barrenger will instruct and supervise the fellow on survey and interview development, data collection, data analysis and dissemination of findings. The fellow will have space to work in the Bonfine/Barrenger lab within the Psychiatry Department and the Health Services Research Focus Area. The fellow will also have access to computer software to aid in data analyses as needed. The fellow will receive training on the ethical conduct of human subjects' research and will be guided to ensure that all aspects of the project adhere to IRB protocols

Submit your application to Dr. Viral Tejani

Impact of Socio-Economic Status on Speech Understanding in Noise
PI: Viral Tejani, AuD, PhD
Location: University Hospitals Cleveland Medical Center

Speech understanding difficulty in the presence of background noise is a common complaint when a patient is evaluated by an audiologist. Speech testing in quiet has been part of traditional protocol from the beginning of audiology. While this test may be reflective of difficulties experienced by some patients, many patients with a significant hearing loss will score at the ceiling of this test. Only more recently has speech in noise testing been emerging as part of typical audiometric evaluation protocol to address patient concerns for hearing in the presence of background noise. Previous research by Fitzgerald et al, 2019 and Smith, et al, 2024 revealed a more linear relationship between QuickSIN speech in noise evaluation and degree of high frequency hearing loss. These same patients showing deficits on QuickSIN speech in noise performance often exhibit excellent word recognition scores in quiet, even when they have significant high-frequency sensorineural hearing loss. A replication study at UH involving 500 patients (and counting) has confirmed this relationship. However, it only takes into account the age of the patient and severity of hearing loss. Socio-economic status (SES) is long known to affect patient outcomes in general and has not been considered in this replication study.

This new study evaluates the impact of SES on speech understanding in noise. SES will be quantified via the Area Deprivation Index (ADI), which is a validated measure of how disadvantaged a neighborhood is and reflects income, education, employment, and housing quality. Using a tool housed by University of Wisconsin-Madison, the summer intern will perform a retrospective review of potentially 1000 patients to obtain zip codes and cross-reference them with the UW-Madison database to obtain the ADI. Statistical analysis (multiple regression) will then determine the contributions of SES to patient performance. This project will advance the field's understanding of SES on patient performance and offers an opportunity to analyze a large dataset the size which is rarely seen in our field.

Individualized mentoring to the research fellow will be provided, which will include reviewing experimental design and journal articles. Most of the project will be done remotely. The goal will be to complete chart review in month one and submit for publication in month two.

Submit your application to Dr. Jennifer Villwock

The association of multisensory dysfunction and fall risk in hospitalized older adults

Principle Investigator:
Jennifer A. Villwock, MD, FAAOA
Vice Chair – Research
Professor – Otolaryngology-Head and Neck Surgery
Location of Research: University Hospitals Cleveland Medical Center

Abstract:
Falls occurring in a health care setting are a significant adverse outcome. Serious injury or death is following an inpatient fall is classified as a "never event" – should never happen – by the National Quality Forum and the Centers for Medicare and Medicaid Services. In addition to the very real human cost in terms of worse patient outcomes, many insurers do no reimburse hospitals for costs associated with falls. Despite the best efforts of the health care system, inpatient falls remain a significant problem, with overall rates of 3.3. to 12.5 falls per 1000 patient-days. Screening questionnaires and inventories are commonly deployed to identify those at risk for falls. However, they are imperfect with highly variable positive and negative predictive values. Additionally, the costs of over-labeling patients as fall risks are not insignificant. For example, commonly strategies are often financially prohibitive such as assigning the patient a staff member who monitors them constantly or alert staff after-the-fact and erode patient autonomy such as bed alarms.

Sensory impairments are significantly associated with increased fall risk. Screening for these deficits can be done in a point-of-care fashion and is an underleveraged strategy for better understanding, and ameliorating, fall risk. For example, in hospitalized patients, self-reported hearing loss increases fall risk by 74%. Significant olfactory dysfunction is independently associated with increased fall risk and increases the odds of balance dysfunction 4-fold (OR=4.1, 95% CI 1.5-13.7). The presence of both olfactory and vestibular dysfunction predicts worse standing balance and 50% increased fall incidence. The limited studies that have investigated MSD show a dose-response relationship between number of concurrent sensory dysfunctions and falls. Most studies demonstrating this risk have investigated community dwelling older adults. Despite its strong associations with cognition – also an important mediator of fall risk – only a minority of studies include olfaction. Additionally, sensory dysfunction has historically been studied in isolation. As a result, there is a significant gap in the literature regarding the relationship between MSD and fall risk in inpatient populations. **Multisensory dysfunction (MSD)** – including dysfunction of the olfactory, hearing, and vestibulo-occular systems – represents **an ideal clinical biomarker of fall risk**.

The proposed research will (1) determine the prevalence and magnitude of MSD in UH CMC inpatients who have been labeled as a "fall risk" by standard of care screening metrics and (2) develop predictive models using MSD and clinical data to predict falls. We hypothesize that MSD is highly prevalent in this population (>80%). We also hypothesize that predictive models incorporating MSD data will exceed the performance characteristics of the Morse Fall Scale (sensitivity ~ 60%, specificity ~ 70%, positive predictive value ~ 2%, and negative predictive value

~ 99% with cutoff value score > 45 representing fall risk). Sensory data will be obtained via AROMA (olfaction), Shoebox Audiometry (hearing), and RightEye (vestibulo-occular function). Mini mental status exam, FRAIL (frailty questionnaire), and bedside visual acuity testing will also occur.

The proposed research is critical to the development of effective screening and risk mitigation strategies for patients whose fall risk is mediated by MSD. Beyond optimizing fall prevention resources, identifying the scope of MSD in this patient population also introduces novel opportunities of intervention. For example, patients with newly identified hearing loss can be triaged to hearing support services and expedited receipt of hearing aids. Those with vestibulopathy or vestibulo-ocuclar hypofunction can receive targeted physical therapies and visual training. Olfactory dysfunction can similarly be treated with olfactory retraining. Rehabilitating sensory function has been shown to improve sensory, cognitive, and fall outcomes. Additionally, MSD rehabilitation can be deployed at bedside and in home-based programs, making is readily scalable at a public health level.

The involved student will be responsible for patient-facing data collection, basic data analysis, and scientific writing. Through their participation, they will become experienced in the administration and interpretation of sensory tests. While this project is clinically oriented, we anticipate basic science collaborations with our colleagues in Neuroscience at Case Western Reserve University. Though not required, the student is welcome to participate in the study design and execution of these associated experiments in mouse models of MSD.

Student Fellow Training/Mentoring Plan

The student will participate in biweekly (every other week) formal lab meetings. They will also receive individualized mentorship from the project primary investigator and quality improvement faculty. Attendance at Health Services Research Seminars will be strongly encouraged. Students and their mentor(s) will complete a formal written Individual Development Plan to ensure the research experience is structured to fulfill expectations of all parties. Studies will have access to asynchronous learning via Udemy (free through the library) to gain additional skills in scientific writing and data analysis.