Distinguished Postbaccalaureate Scholars Program

2025 NIDDK Distinguished Postbaccalaureate Scholars Program Investigators

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- Harris D. Bernstein, Ph.D.
- Carole A. Bewley, Ph.D.
- Rebecca J. Brown, M.D., M.H.Sc., Lasker Tenure Track Investigator
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Daniel H. Appella, PhD
Synthetic Bioactive Molecules Section, Laboratory of Bioorganic Chemistry, NIDDK, NIH

Keywords: Peptide Nucleic Acid, Thyclotide, Nanoparticles, Nucleic Acid Testing, HIV

Project Description:

Diagnostic testing of individuals for viral infection is essential to provide effective treatment and to prevent spreading the infection to others. There is an ongoing need to develop new methods to rapidly detect virus-derived nucleic acid sequences in a patient at the point-of-care. My lab is developing new types of molecules that can recognize and bind to DNA or RNA sequences that are associated with viruses, and we incorporate these molecules into microfluidic-based devices to study their ability to detect their target sequences. The molecules used in our work are called Peptide Nucleic Acids (PNAs). The chemical backbone of PNA consists of a synthetic polyamide, and attached to the backbone are the nucleobases of DNA. We chemically synthesize PNAs in my lab. While PNA molecules do not exist naturally, a PNA with a distinct sequence of nucleobases will bind to a complementary DNA or RNA sequence following the same Watson-Crick-Franklin hydrogen bond pairing that occurs in nature between complementary nucleic acids. My lab has developed a new method to incorporate cyclopentane rings into the PNA backbone to enhance the binding of PNA to its target nucleic acids, and we have made several cyclopentane-PNAs designed to target nucleic acid sequences of HIV-1. Recently, we have introduced tetrahydrofuran rings into the backbone to create a new class of molecules we call thyclotides. To construct a detection device prototype, we attach the PNA to the surface of a microfluidic channel and then flow a solution of a complementary nucleic acid sequence (DNA or RNA) through the channel (Figure 1). The PNA will bind to the target nucleic acid sequence, and prevent it from flowing through the exit of the channel. Once the target is retained in the channel, its presence can be detected using a combination of gold nanoparticles and silver solution. My lab is continuing to refine and improve this detection method and extend its applications.

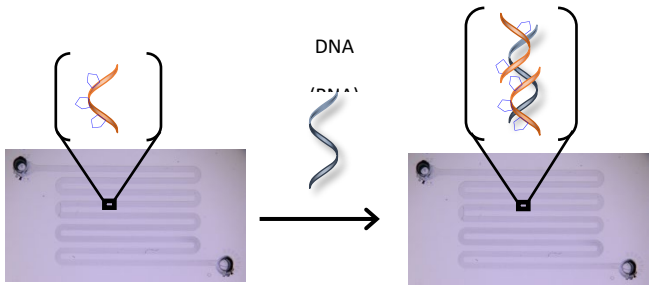


Figure 1. A cyclopentane PNA (orange strand) is attached to the surface of a microfluidic channel. When complementary DNA or RNA (blue strand) is flowed through the channel, a complex between the PNA and nucleic acid is formed which can then be detected.

Diversity Statement:

Encouraging and promoting diversity and inclusion across all genders, races, orientations, and ethnicities is critically important to promoting a healthy working environment within chemistry, biomedical research, and all scientific disciplines. Within my own lab, I strive to bring together a diverse group of individuals from different backgrounds, and I always encourage open discourse of scientific ideas as well as mutual respect between all individuals. My lab encompasses a wide range of scientific disciplines, including organic chemistry, nucleic acid biochemistry, and microfluidic engineering. We highly value the diversity of everyone's background to contribute to advancing our scientific research.

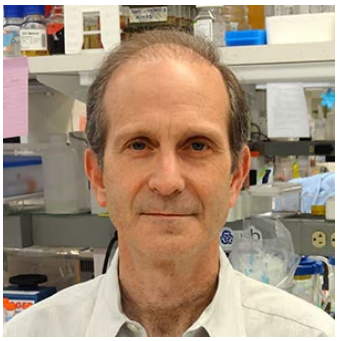
Leslie J Baier, PhD
Diabetes Molecular Genetics Section, Phoenix Epidemiology and Clinical Research Branch

Keywords: human genetics, type 2 diabetes, obesity, Indigenous populations, health disparities

Project Description:
The prevalence of type 2 diabetes and obesity varies by ethnicity. While different ethnic groups often undergo different environmental/lifestyle exposures, previous studies have shown that genetics has an important role in determining risk for these diseases. Our group has been determining which genes contribute to type 2 diabetes and obesity in an Indigenous population isolate living near Phoenix Arizona, who suffer from a particularly high prevalence of these diseases. Prior genetic studies across diverse ethnic groups have shown that both type 2 diabetes and obesity are very polygenic (more than 200 different DNA variants can increase risk); many of these variants increase risk in all ethnic groups while others are ethnic specific. Our group has identified several DNA variants that uniquely affect risk for type 2 diabetes and/or obesity in our Indigenous population (N=8000 participants) and our current goal is to understand how these novel variants function within a cell to ultimately affect metabolic pathways that underlie these diseases. Some of our studies use *in vitro* model systems where we determine whether a disease risk DNA variant affects expression of a specific gene or alters protein structure. However, we also created a model system using induced pluripotent stem cells (iPSCs) that are differentiated into pancreatic beta cells to study *in vivo* how a variant affects development of beta cells which produce and secret insulin, a key hormone in diabetes. Once we understand how and when a specific genetic variant alters key metabolic pathways leading to type 2 diabetes, we assess various drugs to determine if a specific drug can be identified that can perform better in individuals who have a specific genetic variant.

Diversity Statement:
As routine medical care moves towards Precision Medicine (determining which treatment, drug, or dosage is optimal for a particular patient based on their ethnicity/genetics) it is important that people of all ethnicities participate in genomic research. If not, health disparities will only worsen. Yet conducting research equally among people of all races is complicated by a wide range of issues including funding of research in minority populations, access to patients who are not near major medical centers, etc. However, in the United States, a major issue that prevents some ethnic groups from participating in genomic studies is distrust of researchers and the U.S. government. It is important that we as researchers understand the history and basis of mistrust while seeking to strengthen our partnership/relationship with diverse communities. For the past 30 years my research has focused on an Indigenous community living near Phoenix Arizona who have a disproportionately high rate of type 2 diabetes and obesity. While it is exciting to make progress in understanding the genetic underpinnings of diseases that are prevalent in this community, it is important for me, and my trainees, to find ways to better partner with members of this Indigenous community to be able to communicate our findings to

individuals with a wide range of scientific backgrounds, some of whom may not trust in medical research. It is also important for me and my trainees to understand the stereotypes that can develop from long term studies of a specific population where a disease is common. I believe the best way to ensure that people of all ethnicities receive the best healthcare possible is to ensure that people of all ethnicities are represented in cohorts of medical and research professionals. While I fully embrace all kinds of diversity (religious, cultural, gender, health, etc.), given my research, I particularly try to recruit Indigenous trainees into my group such that they can become involved in research that affects their communities, interact with members of their families or communities to allay fears that arise from genomic terms or concepts, while at the same time I can learn about their culture, history, and perceptions to allow me to be a more compassionate and insightful scientist.



Harris Bernstein, PhD
Genetics and Biochemistry Branch

Keywords: bacteria, bacterial pathogenesis, biofilms, outer membrane proteins

Project Description:
For over a century bacteria have been divided two groups: Gram-positive, which have only a single cell membrane, and Gram-negative, which have two cell membranes called the inner membrane (IM) and the outer membrane (OM). The OM of Gram-negative bacteria serves as a first line of defense by preventing the uptake of hydrophobic molecules, including many antibiotics that are currently used to treat infections caused by Gram-positive bacteria. Most of the bacteria that have acquired multi-drug resistance are Gram-negative, and as a consequence there is now a serious need to develop new antibiotics that can be used to cure diseases caused by these "superbugs".

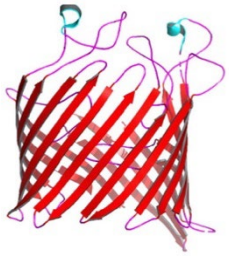


Figure 1. Transmembrane β barrel

My research group has a long-standing interest in understanding the structure, function, and assembly (folding and membrane insertion) of proteins that reside in the OM of Gram-negative bacteria. These proteins are of particular interest both because they have an unusual structure and because two of them have proven to be excellent targets for novel antibiotics (one of which is now in clinical trials) that do not have to cross the OM barrier to work effectively. Unlike almost all other integral membrane proteins that contain 1-12 α-helical transmembrane segments, bacterial outer membrane proteins (OMPs) contain a single "β barrel" (Figure 1), which is essentially a β sheet folded into a closed cylindrical structure, that serves as a membrane spanning segment. In the last several years my group has focused on a highly conserved protein complex called the "β barrel assembly machine" (BAM) and has made considerable progress in elucidating the mechanism by which it catalyzes the assembly of OMPs in *E. coli*. Very recently, we have also obtained strong evidence that a related protein dimer called the "translocation and assembly module" (TAM) has a similar function.

The goal of the project is to identify and characterize small molecules that inhibit the activity of an important *E. coli* OMP called PgaA. PgaA functions together with proteins that reside in the IM and the space between the two membranes (i.e., the periplasm) to secrete polysaccharides into the environment that are critical components of biofilms. Inhibitors of PgaA would potentially be of great value because the pathogenicity of virulent strains of *E. coli* (e.g., uropathogenic strains) as well as other organisms that produce PgaA homologs is dependent on their ability to form biofilms. In the first part of the project, a Distinguished Postbaccalaureate Scholar who joins the laboratory would express and purify PgaA for use in a screen for molecules that bind to the protein as part of a pre-arranged

collaborative effort. The second stage of the project would be devoted to optimizing and using an established assay to identify the compounds that not only bind to PgaA but that also inhibit its activity. The binding sites of the inhibitors would then be identified using structural methods. If time is available It should also be possible to use the structural data to test hypotheses about the mechanism of polysaccharide export and to identify residues in PgaA that play important roles in the export reaction.

Diversity Statement:

Since I arrived at the NIH as an independent investigator 31 years ago, I have always tried to recruit candidates who are highly qualified regardless of their race, ethnicity, religion, cultural practices, gender or sexual orientation. I am always looking for candidates who are "diamonds in the rough" who might ultimately follow in the footsteps of distinguished scientists who came from disadvantaged backgrounds or underrepresented communities. As a consequence of my commitment to DEI, I have hired two African-American fellows who were born in Kenya and Liberia, respectively, trained a postdoctoral fellow and a summer intern who were admitted to the NIH Undergraduate Scholarship Program (a program designed to help members of underrepresented minority groups pursue careers in biomedical research) and hired a summer intern who was accepted into another campus-wide program designed to provide educational opportunities for students who come from disadvantaged backgrounds. All of these individuals have gone on to successful careers that are built on their scientific training or into advanced scientific training programs. Furthermore, the majority of my lab members have been women.

I should also note that In 2021-2022 I served as co-chair of the NIDDK Fellowship Office and Training Enhancements Working Group, which suggested measures to promote diversity at the trainee level (including increasing representation of individuals from historically underrepresented groups) to the NIDDK Executive Committee. I hope to serve on other committees that promote diversity should the opportunity arise in the future.

Carole Bewley, PhD
Natural Products Chemistry Section, Laboratory of Bioorganic Chemistry

Keywords: bioorganic chemistry, small molecules, antibiotic discovery, natural product biosynthesis

Project Description:
More than half of our antibiotic and anticancer therapeutics come from or are inspired by 'natural products'. Research in the Natural Products Chemistry Section in LBC, NIDDK focuses primarily on the discovery and development of novel antibiotics, as well as the engineering of protein-drug conjugates for the prevention and treatment of HIV infection. Relevant to antibiotic discovery, we have several exciting projects and questions we are currently tackling in the lab. Natural products (NPs) are primarily produced by and discovered from environmental bacteria such as the actinomycetes. Although bacterial genomes are relatively small, averaging 8-10 megabases for the actinomycetes, some strains have the genetic capacity to produce upwards of 30 different small molecule NPs and antibiotics. The genes that encode enzymes responsible for producing NPs are clustered on the bacterial chromosome in regions known as biosynthetic gene clusters (BGCs). Thanks to whole genome sequencing, these evolutionarily conserved features can be identified. This has several important implications in NP discovery. First, we are now able to use bioinformatics to detect and identify the presence of BGCs that produce antibiotics; second, we can bioinformatically 'mine' genomes to select for specific classes of molecules and their producing strains; and third, having genomic information can help us to study transcription factors and regulators that might control the production of antibiotics, an area that is greatly understudied. Thus, several important questions in the broad field of natural products research that we are trying to answer and possible projects that a postbac scholar would work on include the following.

1. The chemical diversity of peptide-based natural products, commonly referred to as RiPPS, is vast, and the precision-based, post-translational modifications that change a linear peptide to a single multi-cyclic core are not well characterized. We use chemical and structural biology techniques to determine the structural basis of enzymatic reactions. Using X-ray crystallography, we have been able to obtain high-resolution snapshots of peptide 'tayloring' enzymes in action and to understand how such highly-specific reactions are taking place. In turn, this work paves the way for synthetic and chemical biology approaches to make unnatural peptide NPs that can be tested for enhanced biological activities in disease-relevant assays.
2a. If a given actinomycete strain is capable of producing 30 or more natural products, why in culture do we only detect a few to several? How is their production being regulated, and using genetic approaches, how might we control the production through activation or silencing of BGCs and enzymes? We are taking a multi-tiered approach to answer these questions. We are using robotic high-throughput growth conditions to alter the metabolism and chemical output of chemically rich actinomycete strains. Coupled with bioassays, NMR and high-resolution Mass Spectrometry, we can identify growth conditions that act

as elicitors to turn on production of ‘silent’ natural products. This is a powerful platform for new antibiotic discovery.
2b. In addition to screening, we are studying the role of regulators in antibiotic production. From whole genome sequences, we can identify BGCs and their putative regulators, express these proteins recombinantly, and determine their DNA binding specifity. Once determined in vitro, genetic approaches can be used to test hypotheses about secondary metabolite production and its regulation. This is an extremely important but overlooked area in the field of natural products, and can be challenging to address. With current technologies, we are poised to begin to answer some of these long-standing questions in the field.

Diversity Statement:

Ecologists often use the saying ‘Nature abhors a monoculture’ when speaking about biological, agricultural and environmental systems. I and my co-workers share that view when thinking about the culture and representation we strive to attain in my group and in the laboratory setting. Science is about discovery and proving hypotheses and it works best and most productively when group members openly share ideas, learn from one another, actively seek feedback and constructive critique on their work, and strive to help everyone develop into outstanding, independent and collaborative scientists. My experience demonstrates that these goals are best achieved when diversifying in all ways the staff and trainees. Diversification includes differences in backgrounds, upbringing, ethnic and cultural experiences, education, and the list goes on. As a product of public schools, being of mixed race, and taking a ‘non-traditional’ path to land at the NIH, I enjoy the commitment and responsibility of mentoring all students, postbacs and postdocs and providing a welcoming environment. In addition, the scientists in our group have earned undergraduate and doctoral degrees in different subject areas ranging from organic chemistry, natural products discovery, structural biology, biochemistry and biotechnology, to name a few. This makes our research group and environment highly interdisciplinary and thriving. I believe that that energy comes both from the excitement of constantly learning, and likewise, the shared struggles or challenges we all face in a research setting. I and my group members would welcome the opportunity to mentor a postbac scholar through the NIDDK Distinguished Postbaccalaureate Scholars Program.

Rebecca J. Brown, MD
Diabetes, Endocrinology, and Obesity Branch

Keywords: Metabolic syndrome, diabetes, cardiovascular disease, insulin resistance, obesity

Project Description:
Metabolic syndrome, a cluster of risk factors linked to cardiovascular disease, is a global epidemic, with a prevalence of approximately 35% in the United States, and close to 50% after age 60 (1). Pathophysiologically, metabolic syndrome is caused by insulin resistance, which is in turn usually driven by obesity. The goals of my lab are to 1) Understand insulin signaling and insulin resistance by studying patients with rare disorders of severe insulin resistance; 2) Apply what we learn about pathophysiology to develop therapies for these rare and life-threatening diseases; and 3) Use what we learn from rare diseases to elucidate drug targets for more common disorders of insulin resistance, such as obesity and type 2 diabetes (T2D). Our patients include those with lipodystrophy, characterized by generalized or partial deficiency of body fat, and mutations of the insulin receptor gene (*INSR*).

Postbac IRTAs in my lab will take on one or more independent projects, thus gaining experience with reviewing scientific literature, generating hypotheses, study design, database management, statistical analysis, scientific writing, and oral presentations. Independent research in the lab is supported by bi-weekly one-on-one meetings, weekly lab meetings, and journal clubs. Postbac IRTAs also work on clinical and translational research protocols studying the natural history and effects of pharmacologic interventions in patients with severe forms of insulin resistance. During these projects, postbacs learn numerous metabolic research techniques, including how to measure insulin resistance using the hyperinsulinemic, euglycemic clamp studies, stable isotope tracer techniques, measurement of energy expenditure using indirect calorimetry, measurement of body composition, and assessment of blood vessel (endothelial) function. Postbacs will learn to work as part of an interdisciplinary healthcare team including other postbacs, physicians, nurses, nurse practitioners, and patients. Postbacs are also provided ample opportunity to shadow physicians within and outside our team.

Below are proposed projects to assess the role of insulin resistance in cardiovascular disease:

1. *Effects of insulin resistance on in vivo endothelial function (Clinical Project).*

Methods: The postbac will assist in running a clinical study in patients with lipodystrophy, *INSR*, and healthy controls before and during hyperinsulinemia induced by oral glucose, and serially measure nitric oxide (NO), endothelin-1 (ET-1), and vasodilation. The postbac will work with lab members and collaborators to recruit subjects, conduct studies, and analyze data. In this role, the postbac will learn about clinical trial design and conduct, including regulatory aspects of human subjects research, working with patients to conduct complex physiology studies, and collecting and analyzing data.

2. *Effects of insulin resistance on clotting and inflammation (Basic Science Project).*

Methods: In collaboration with George Washington University, the postbac will isolate endothelial progenitor cells from blood samples obtained from the same patients with lipodystrophy, *INSR*, and healthy controls who are studied in the clinical project, above. The postbac will phenotype these cells using measures of cell migration, colony formation, clotting, and inflammation. These measures will be correlated with the clinical phenotyping, above.

In both projects, the postbac will gain experience reviewing the scientific literature, database management, statistical analysis, scientific writing, and oral presentation skills.

Diversity Statement:

My group studies insulin resistance and metabolic syndrome, conditions that disproportionately affect communities of color and socioeconomically disadvantaged populations, and thus will be of interest to trainees who want to find solutions to health disparities in metabolic disease. I endeavor to promote diversity in my hiring practices and actively promote the career development of trainees of diverse backgrounds. Trainees will find a welcoming and respectful environment in a diverse group in which all voices are heard. In addition, I encourage my trainees to engage in research projects that specifically address issues of diversity and inclusion (see example abstract, below, from the Endocrine Society annual meeting, 2021):

1. Brent S. Abel; Elaine K. Cochran; Megan Startzell; Rebecca J. Brown. Racial Disparities Among Clinical Trials for Inherited Forms of Lipodystrophy. Poster presentation at Endocrine Society Annual Meeting, 2021.

I encourage my trainees to participate in discussions related to diversity and inclusion during our weekly lab meetings, including presenting relevant journal articles or conducting training sessions. Examples of recent topics are:

1. Importance of inclusive language in medicine (Postbac presentation, January 25, 2024).
2. Slavery and the *Journal* — Reckoning with History and Complicity. N Engl J Med 2023;389:2117-2123. (Journal club, February 8, 2024)

Susan Buchanan, PhD
Laboratory of Molecular Biology

Keywords: mitochondria, outer membrane protein, protein biogenesis, protein crosstalk, structural biology

Project Description: Supercomplex assembly between mitochondrial TOM and SAM Aids Protein Biogenesis

The majority of the mitochondrial proteome is translated in the cytosol and imported into mitochondria as unfolded precursors. Mitochondrial outer membrane β-barrel proteins are imported by the translocase of the outer membrane (TOM complex) then folded and inserted into the membrane by the sorting and assembly machinery (SAM complex). We solved the first structures of the SAM complex and showed that it is composed of three subunits: a β-barrel core (Sam50) that spans the mitochondrial outer membrane, and two accessory subunits (Sam35 and Sam37) that associate on the cytosolic side of the membrane [1]. Sam50 and Sam35 are essential for cell viability and specifically interact with a conserved sequence motif on the precursor protein, called the β-signal. How the β-signal is recognized by the SAM complex, and the mechanism of precursor folding and insertion into the mitochondrial outer membrane remain unclear. Biochemical data demonstrate that SAM and TOM interact in the outer membrane, likely to facilitate protein import, folding, and insertion. We have data showing that Tom22 interacts with Sam37, and this project will further characterize the interaction, delineating the protein-protein interface. We will use this information to design a stable supercomplex consisting of the TOM core complex and the complete SAM complex [2]. Ultimately, this work will improve our mechanistic understanding of SAM complex function and mitochondrial outer membrane β-barrel biogenesis.

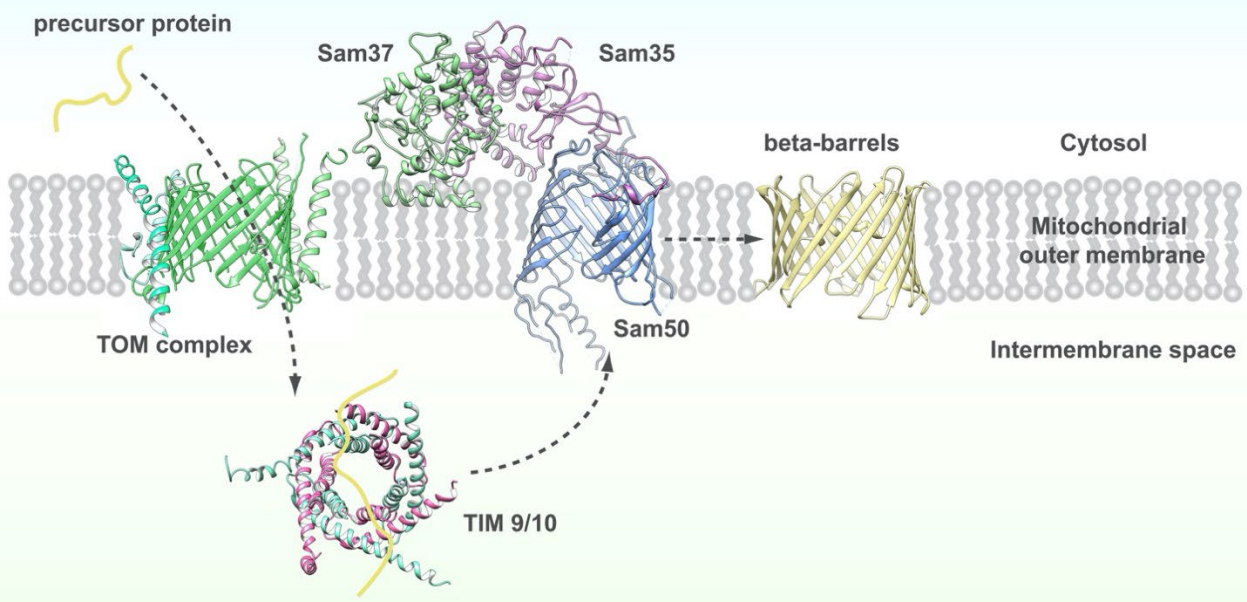


Figure 1. Schematic of β-barrel outer membrane protein biogenesis in mitochondria. Mitochondrial outer membrane β-barrel proteins are synthesized in the cytosol (yellow), then imported into the intermembrane space of the mitochondria by the translocase of the outer membrane complex (TOM complex, green). Once in the intermembrane space, the precursor protein is bound by chaperone proteins (TIM9/10, magenta/cyan) and directed to the sorting and assembly machinery complex (SAM complex, blue/pale green/orchid). The SAM complex facilitates outer membrane β-barrel precursor protein folding and insertion into the outer membrane.

[1] **Diederichs, K.A.**, Ni, X., **Rollauer, S.E.**, **Botos, I**., Tan, X., King, M.S., Kunji, E.R.S., Jiang, J. & **Buchanan, S.K.** (2020). Structural insight into mitochondrial β-barrel outer membrane protein biogenesis. *Nat Commun* 11(1): 3290. doi: 10.1038/s41467-020-17144-1. PMCID: PMC7335169
[2] **Diederichs, K.A., Buchanan, S.K. & Botos, I.** (2121) Building better barrels - β-barrel biogenesis and insertion in bacteria and mitochondria. *J Mol Biol* 433(16):166894. PMCID: PMC8292188

Diversity Statement:

Promotion of diversity and inclusion starts with the composition of my own research group. Over the course of my 20+ year career at the NIH, I have trained scientists from Belgium, Czech Republic, Dominica, Ethiopia, France, Hong Kong, Jamaica, Japan, Nigeria, Sri Lanka, UK, and USA. I believe that providing early training opportunities to fellows from diverse backgrounds produces the best cohort of young scientists to become our future leaders.

I am very active in DEIA initiatives at the NIH. As the former chair of the Women Scientist Advisors (WSA) and long-time member of the executive committee, I have been involved at the NIH-level in developing policies that foster diversity and inclusion. The WSA (and other NIH organizations) has significantly improved the NIH as a hospitable place for women to work, and the group's goal is to recruit, promote, and retain women at all levels at the NIH. Recent advances include several trans-NIH salary surveys that identified investigators (both men and women) whose salaries were below the normal level for their institutes. The WSA was also the driving force in implementing new anti-harassment policies at the NIH. In collaboration with the NIDDK Scientific Director, the NIDDK Executive Officer, and three other NIDDK WSA representatives, I worked to educate the NIDDK workforce on the new anti-harassment policy and expectations (through a poster campaign, mandatory all-hands NIDDK seminars, and in-person Conduct of Research Training that focused on various harassment scenarios).

Three years ago, I helped my graduate student start a trainee-led seminar series recognizing diversity and excellence in science: TREaDS (https://www.niddk.nih.gov/research-funding/at-niddk/training-employment/choose-niddk). This excellent program was the first of its kind at the NIH, and we are starting the fourth year of seminars. I secured funding for the program and serve on the advisory committee for the group. In addition, three years ago I co-initiated the Distinguished Postbac Scholars program to diversify our trainee population. My goal is to strengthen this program and to create a similar program for postdoctoral researchers at NIDDK.

I am committed to making the NIDDK (and NIH) a positive, inclusive place to work for all of our researchers and I welcome feedback and suggestions on changes that will make a real difference to your training experience.

Rafael Daniel Camerini-Otero MD, PHD
Genetics and Biochemistry Branch

Keywords: Meiosis, Genetic Recombination, PRDM9, genome rearrangements, genetic disease

Project Description:

Meiosis is the specialized type of cell division that gives rise to reproductive cells such as sperm and eggs. Errors in meiosis are responsible for at least half of clinically recognized miscarriages, as well as a spectrum of chromosomal birth defects in humans. Children who inherit an extra chromosome due to these errors (Down Syndrome, for example) can sometimes survive, but suffer from various congenital abnormalities and such aneuploidy is a major cause of mental retardation and neurodevelopmental disorders. Meiotic division generates four daughter cells, each of which contains half the chromosomal complement of the originating cell. This is achieved through DNA replication, followed by two meiotic divisions (meiosis I and II). Most chromosomal mis-segregation events result from errors in meiosis I (1), when genetic recombination creates crossovers (COs) to facilitate the accurate segregation of homologous chromosomes.

Recombination is initiated by the programmed formation of DNA double strand breaks (DSBs), and COs are generated from subsequent DSB repair. The vast majority of DSBs occur at a subset of genomic loci and my lab has generated the first maps of such DSB hotspots in any mammalian genome (2). We also showed that the meiosis specific histone methyltransferase protein PRDM9, defines essentially all DSB locations in mouse (3) and human (4) and it is now well established that each allele of the PRDM9 protein binds different DNA sequences to define a unique DSB hotspot landscape.

Assessment of PRDM9 diversity is important for understanding the complexity of human population genetics, the inheritance of linkage patterns, and the predisposition to genetic disease. Aberrant DSB repair can result in both benign and disease-causing structural variants (SVs), and recently, we showed that indeed, meiotic DSBs occur disproportionately frequently at SV loci (4). For this project, we propose a detailed computational analysis of the sequence determinants that predispose DSB hotspots to aberrant DSB repair during meiosis. Developing a better understanding of these events at DSB hotspots has the potential to identify loci in the human genome related to genetic disorders that arise in the germline.

Diversity Statement:

My lab has a long-standing commitment to diversity and inclusion. Over the course of close to five decades, I've enrolled students from a wide range of backgrounds, and I consider this diversity to be the cornerstone of my group's achievements. At the same time, I recognize the systemic barriers of entry that students from underrepresented minorities encounter just to be in the running for consideration. My lab actively engages in several NIH programs like the summer programs that provides an opportunity to perform research at the NIH to individuals ranging from high school to college. This Distinguished Postbaccalaureate Scholar Program is an opportunity for both students and investigators with strong commitment to diversity to keep building a more inclusive research community.

Finally, in addition to my efforts in recruiting students I am a staunch supporter of recruiting from underrepresented groups at every stage of development up to faculty level. I am very involved in the Faculty Recruitment Turn-the-Curve Working Group (5/31/2022 onwards) which extends my previous efforts as part of our Intramural Diversity & Inclusion Working Group that was paused in anticipation of this exercise. Recently, our branch recruited the first tenure-track investigator from an underrepresented group in over thirty years in the basic sciences of the intramural program of NIDDK.

1. Ottolini, C. S. et al. Genome-wide maps of recombination and chromosome segregation in human oocytes and embryos show selection for maternal recombination rates. Nat Genet (2015)
2. Smagulova, F. et al. Genome-wide analysis reveals novel molecular features of mouse recombination hotspots. Nature (2011).
3. Brick, K., Smagulova, F., Khil, P., Camerini-Otero, R. D. & Petukhova, G. V. Genetic recombination is directed away from functional genomic elements in mice. Nature (2012).
4. Pratto, F., Brick, K. et al. Recombination initiation maps of individual human genomes. Science (2014).

Stephanie T. Chung M.B.B.S.
Section on Pediatric Endocrinology, Obesity, and Metabolism, NIDDK, NIH

Keywords: youth-onset type 2 diabetes, pediatric obesity, health disparities, transition care

Project Description:

Our Section's research and clinical goals are to improve early detection and treatment of diabetes, obesity, and cardiovascular disease in women and children, especially those from under-represented groups. We conduct clinical trials in youth and adults, advocate for our youth through community outreach in schools, and collaborator internationally to generate population-specific evidence to help shape obesity and diabetes prevention strategies. My post-bac IRTA fellows are integral team members and team leads during their 2-year fellowship. My IRTA training program provides an educational, enriching, and fun experience in clinical metabolic research that will lay the foundation for future success in medical or graduate school and beyond. My post-bac IRTAs are participant advocates, study coordinators for 2-3 clinical research protocols, early career investigators, and peer mentors. The fellows receive on-site training for all activities including basic clinical research skills, protocol implementation, and data management and statistics. In addition to performing daily tasks, it is my hope that every post-bac IRTA will contribute to our research mission by learning to write and presenting their findings at scientific meetings, teach and supervise fellow and summer students, and earn co-authorship depending on their involvement and expertise. Two examples of clinical projects are outlined below.

1. <u>The Youth-onset Type 2 Diabetes and Heart Disease Study: The Young at Heart Prospective Cohort</u>
   This study evaluates the pathophysiological features of cardiovascular disease in youth-onset type 2 diabetes using a multi-level, multi-domain approach to socio-ecological risk factors (societal, community, and individual). This prospective, observational study design in youth aged 12-25 years will compare youth with type 2 diabetes with age and BMI-matched youth with overweight or obesity and age-matched healthy lean peers. Participants will be enrolled for inpatient/ outpatient metabolic visits annually. Post-bac fellows will have multiple opportunities to engage with participants for research study visits and shadow and assist in our joint NIDDK/ Children's National Hospital multidisciplinary diabetes clinic. Fellows will master metabolic phenotyping tests including glucose tolerance testing, endothelial function testing, biopsychosocial questionnaires, and ecological momentary assessments. Selected abstract topics—for which data are already available—are "Biological ageing in youth with type 2 diabetes compared to peers".

2. Time Restricted Eating and Ketone Metabolism

This is a clinical translational study designed to evaluate ketone body biology on $CD4^+$ T cell immunoregulation in response to early time restricted eating (6-h TRE) in women. Intermittent fasting dietary interventions including TRE have anti-inflammatory effects. Although the exact metabolic mechanisms remain elusive, they may be related to ketone body metabolism that differs by biological sex and obesity status. This protocol will evaluate ketone body turnover using stable-labeled isotopes in a domiciled metabolic unit. Post-bac fellows will become proficient in administering and analyzing stable isotope methodology for the analysis of glucose and ketone pathways. Selected abstract topics include "Ketone concentrations during time restricted eating".

Diversity Statement:

Winston Churchill penned "Success is going from failure to failure without losing your enthusiasm". This simple phrase embodies the tenacity and drive that most scientists share in their pursuit of excellence. As a tenure-track investigator, a woman, a mother, and a pediatric physician-scientist, I am on a daily quest for excellence. This process of pushing myself personally and professionally has only strengthened my belief in one of the guiding principles of diversity—namely, that the ideas, approaches, and successes of medicine are strengthened when people from different backgrounds—with a variety of experiences, abilities, and world views—work together in furtherance of success. My tenacity and commitment to diversity is exemplified in my past and current research questions, the success of my trainees, and my track record of leadership in both community and national outreach programs.

The goal of my post-bac training program is to help this next generation of scientists think creatively and broadly to minimize biases and promote innovation. For me, this process begins with endeavoring to be an open-minded role-model and clinician for my patients, the majority of whom are from minority or disadvantaged backgrounds. Our research and clinical programs support self-sufficiency and resilience for these youth and young adults, while simultaneously training our IRTA fellows. One of the pillars of my research program is the student learners at varying levels in their academic careers, who range from undergraduate and postbaccalaureate to post-doctoral fellows. Students from all socioeconomic and cultural backgrounds have been attracted to my Section because of my emphasis on excellence through diversity. Over the last 10 years, I have mentored over 25 fellows from diverse culturally and ethnic backgrounds. I also a long-standing mentor for the NIDDK Diversity Summer Research Training Program and The Annual Biomedical Research Conference for Minority Students. To date, over 90% of my trainees have received scientific merit-based awards during their respective NIH appointments.

My inclusive mentoring philosophy is rooted in creating an environment which fosters scientific learning through a balance of individual and team-based learning, continual self-evaluation, and mutual respect. Core to the foregoing is an acknowledgement that people from diverse backgrounds often have different learning and communication styles. By focusing on a guided learning approach—with an emphasis on each trainee's unique abilities—my Section promotes freedom of thought, open discussion, and productivity. In the spirit of Churchill, we strive for success, learn from our everyday failures, and embrace scientific rigor with enthusiasm.

Valerie L. Darcey, PhD, MS, RD
Section on Nutritional and Metabolic Neuroimaging
Diabetes, Endocrinology, & Obesity Branch

Keywords: Neuroimaging, human, diet

Project Description:

Ultra-processed foods account for over 50% of the American diet and have been demonstrated to cause excessive caloric intake and weight gain in adults (Hall et al., 2019). Overconsumption of ultra-processed foods appears to be driven in part by their energy density and hyper-palatable qualities. Hyperpalatable combinations of fat and sugar are thought to have synergistic effects on the brain's reward processing in humans and recent evidence indicates that chronic exposure to a hyperpalatable snack changes human brain reward-related activity independent of any changes in body weight. Animal models demonstrate that overconsumption of ultra-processed foods may be promoted by changes in reward related dopamine neurochemistry, but whether control over one's hyperpalatable food intake is also impaired by parallel change to other neurochemical systems is unknown.

This research will test whether an ultra-processed diet impacts human (A) reward neurochemistry as measured by striatal [^{11}C]raclopride dopamine receptor availability and (B) neurochemistry implicated in behavioral control as measured by magnetic resonance (MR) spectroscopy of GABA, the brain's main inhibitory neurotransmitter, levels of which are linked to impulse control. Adult volunteers will be enrolled in an inpatient randomized crossover, controlled feeding trial to compare the effect of two 6-day eucaloric diets matched for macronutrients and energy density on neurochemistry: one composed primarily (80%) of ultra-processed foods high in hyper-palatability and one devoid of ultra-processed, hyper-palatable foods. Participants will be adults (18-45 years old) over a wide range in BMI so that we can begin to explore how a hyperpalatable, energy dense ultra-processed diet may differentially impact neurochemistry across varying levels of adiposity. Prior to the initial diet manipulation, participants will be stabilized on a 2-day standardized diet to minimize any initial diet-induced variability in measured neurochemistry at baseline neuroimaging. Using a novel simultaneous combination of ^{1}H Magnetic Resonance Spectroscopy to measure GABA and positron emission tomography to measure dopamine receptor availability within the same individuals, we hypothesize that exposure to the ultra-processed diet will increase tonic dopamine and decrease GABA tone – a combination purported to promote both the incentive salience of highly palatable food and impair behavioral control over consumption.

Diversity Statement:

Although I am a newly-minted independent investigator, my commitment to the tenets behind diversity, equity, inclusion and accessibility are deep seated. My lived experiences as a woman of color, and as both a first-generation American, and college graduate equip me to build supportive environments for URM trainees I mentor, a practice I've long cultivated. In 2008, I co-mentored a high school junior through NIDDK's Short-Term Research Experience for Underrepresented Persons program on the topic of

Foodborne Illness, Socioeconomics and Race/Ethnicity. Like me, he was the first in his family to pursue college and I happily provided him guidance as he started his academic journey. Since starting my post-doctoral fellowship, I've continued to actively train and mentor other talented URM from Latinx, LGBTQ+, and African American backgrounds. Recently, I've expanded my influence to promote recruitment and hiring of URM trainees. I successfully lobbied my mentor to join the pool of NIDDK investigators participating in our institute's Distinguished Postbaccalaureate Scholars Program to support enhancing diversity among NIDDK trainees. Of the mentoring I've done as a post-doctoral fellow, one of the most rewarding experiences was mentoring an African American high school student as she performed her pre-junior summer internship and developed her senior honors thesis. Through my mentorship, she gained valuable research experience. Through my *proactive sponsorship*, her contributions were recognized via co-authorship on a highly cited publication from our lab. And through my presence as a URM female scientist, she gained more confidence about her career possibilities.

My role in championing DEI goes beyond that of representation and promoting an inclusive environment for my individual mentees. I am driven to contribute to and lead efforts that multiply DEI dividends. During my doctoral training, I sought out student representative positions on both the Graduate Admissions and Executive Faculty Committees. I used my platform to highlight the dearth of diverse candidate pools, applying that perspective to lead efforts to reinvigorate our recruitment strategies. As a result, my graduate program frequently participates in – and recruits exceptional URM candidates from – the BP-ENDURE Society for Neuroscience Graduate Fair, aimed at preparing undergraduates from diverse background to succeed in neuroscience PhD programs. Before graduating, I was honored to be one of only two students invited to serve on the inaugural Gale Memorial Lectureship Committee for Outstanding Women in Neuroscience in honor of the late Dr. Karen Gale, a dear mentor and a staunch advocate for women and URM in science. As I delivered my introductory remarks for renowned neuroscientist Dr. Karen Berman (NIMH), I placed particular emphasis on her prolific work both as a trailblazing female scientist and as a champion of women in science.

I continue to seek out podiums big and small to amplify the message that there is a path to success in science for historically underrepresented individuals. As a post-doc, I helped develop and implement NIDDK's pilot Elementary School Science Tour Day (2018-2019). This was a day-long event to increase awareness of what scientists do and who they are/what they look like, particularly for schools with high percentages of students receiving free/reduced lunch. I contributed as a standing member of the inaugural NIDDK Civility, Diversity & Inclusion Steering Committee, charged with advising leadership on DEI issues and initiatives. Most recently, I was invited by the NIDDK Scientific Director's Office to help develop and implement a trainee-led intramural scientific seminar series (Trainees Recognizing Excellence and Diversity in Science), for which I served as Chair for the first 3 years. The goal of TREaDS is to spotlight the science and DEI contributions of investigators with a demonstrated commitment to increasing diversity and equity in their respective fields. In 2021, TREaDS was awarded the NIDDK William G. Coleman Jr. Award for DEI. At the invitation of colleagues, (Dr. Shawn Bates, Chico State Brain Alliance; Dr. Robert Rivers, NIDDK STEP-UP), I have eagerly shared details of my own career path with a class of curious and impressionable URM undergraduates.

Gathering multiple perspectives to address the same scientific problem from different angles enhances likelihood of success by boosting innovation and minimizing blind-spots. As an IRP investigator, my objectives will be to create seats at the table for URM, provide them an equal voice in science at NIH, and foster longitudinal improvement by creating enduring programs. I will adapt strategies outlined in the NIH Scientific Workforce Diversity Toolkit to not only recruit staff and trainees from diverse backgrounds but support my team by cultivating an inclusive, hospitable lab environment where all ideas and feedback are welcome. As a mentor and sponsor, I will also encourage and provide guidance for trainees to apply for IRP-eligible, stage-appropriate competitive funding and awards so that they too are set up for success

in their scientific careers. The efforts highlighted above demonstrate my commitment not only to the *practice* of diversity but also of equity, and inclusion.

Ann Dean, PhD
Laboratory of Cellular and Developmental Biology

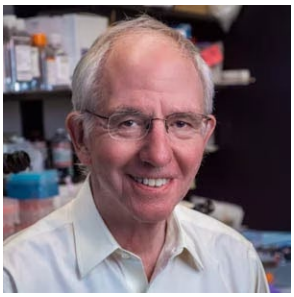
Keywords: transcription, chromatin structure, epigenetics, β-hemoglobinopathies

Project Description:
The LIM domain binding protein 1 (LDB1) protein complex mediates enhancer-promoter interaction by its dimerization or interaction with other transcription factor. While enhancer looping by LDB1 is critical for erythroid differentiation, transcription factors (TFs) responsible for coordinating enhancer-promoter interaction with LDB1 remain elusive. We found that chromatin looping between LDB1 bound enhancers and Specificity protein 1 and 3 (SP1/3) bound promoter activates its gene expression. LDB1 and both SP1/SP3 are required for enhancer-promoter interaction although Sp3 can compensate for Sp1 binding at some target genes.

We identified a substantial fraction of genes that are regulated by LDB1-SP1/3 in uninduced or induced murine erythroleukemia (MEL) cells, which correspond to an intermediate or terminal stage of erythroid differentiation, respectively. This project will further dissect the mechanisms underlying SP1/3 as a novel LDB1 binding partner and explore the critical role of SP1/3 in regulating erythroid gene expression through differentiation stage-specific enhancer looping.

Diversity Statement: Promoting diversity and inclusion in science has been a strong goal for me for decades. I served as the first Women Scientists Advisor (WSA) to the NIDDK Scientific Director when the position was first established. About half of my trainees (15/32) have been women and 16% (5/32) trainees have been underrepresented minorities. I am especially pleased to have mentored Luis Diaz, the first college graduate in his family, as a post-Baccalaureate fellow and seen him successfully gain admission to the MSTP MD/PhD program at Oregon Health and Science University for Fall 2019. I now serve on his Dissertation Advisory Committee. I have been interested in outreach to the community on behalf of science for many years, specifically as a means to increase the diversity of the scientific training pool and, thus eventually, research faculty members. My activities have included speaking at local high schools and judging science fairs at the invitation of science teachers, hosting science teachers for a day of hands-on work in my lab and hosting local high school students in summers and as part of school programs that support research rotations during the school year. In 2024, the two Distinguished Post-Bac Scholars in my lab, both

women and both members of underrepresented minorities, helped plan and carry out a day visit to NIDDK by fifth graders from a local elementary school with a large minority population. We hosted about twenty students in our lab and showed them live worms (a model organism) that glowed green because they had one of their proteins tagged with green fluorescent protein. I am so pleased that both these women post-bacs have just begun MSTP MD/PhD studies at the medical schools of the University of Rochester and University of Texas. I hope to see this outreach become a yearly event at NIDDK.



Jurrien Dean, MD
Laboratory of Cellular and Developmental Biology, NIDDK

Keywords: Women's health, Reproductive biology, Fertilization, Early development, Mouse genetics

Project Description

The focus of our investigations is on mouse gametogenesis, the maternal-zygotic transition of early development, and passage of the embryo through the female reproductive tract. Male germ cells maintain a permanent spermatogonial stem cell niche within the mouse testis throughout adult life. With ~35-day periodicity, cohorts are selected to multiply, differentiate, and undergo meiosis after which haploid spermatocytes transmogrify into mature spermatozoa. In contrast, female mice have a complete complement of germ cells at birth that are arrested at the prophase of the first meiotic division. Subsequent growth during folliculogenesis, asymmetrical meiotic cell divisions and sculpting of the maternal transcriptome ensure that ovulated eggs contain factors necessary for fertilization and early embryonic development. Perturbation of gametogenesis can decrease fecundity and cause infertility.

There is an interregnum of genomic transcription between mature eggs and 2-cell embryos that dictates a role for post-transcriptional mechanisms and maternal factors. Following fertilization in the ampulla of the oviduct, the embryo is transported through the female reproductive tract orchestrated by secreted fluid, unidirectional beating of epithelial cilia and smooth muscle contractions. Detailed understanding of gametogenesis and fertilization could have an immediate impact on human reproductive medicine, improving choices available to those wanting to conceive as well as to those who wish to limit procreation. Following fertilization, there is reprogramming of the terminally differentiated gametes into pluripotent embryonic stem cells, a process necessarily dependent on maternal factors that accumulate during oogenesis because of transcription quiescence. Ectopic pregnancy, the implantation of a fertilized ovum outside the endometrial cavity, occurs in approximately 3% of human pregnancies and is a major cause of maternal morbidity and mortality. Most ectopic pregnancies take place in the oviduct and embryonic transit through the female reproductive tract is critical for establishment of a viable fetus. The establishment of mouse lines lacking genes involved in gametogenesis, fertilization and early development can provide models of human disease and insight into failed fertility and early embryopathies. While most of our investigations are carried out in mice, conservation of structure and function often allow direct translation to human biology. Importantly, these research initiatives are concordant with recent increased national emphasis on issues of women's health.

We utilize a comprehensive spectrum of biochemical, cellular, and molecular biology approaches, each tailored to a specific research question. While much of our work begins with *in vitro* studies, we endeavor to confirm these results *in vivo* using transgenesis to establish mouse models with mutant proteins. As appropriate, we either seek out collaborations (cell-sorting, mass spectrometry, electron and high-resolution microscopy, bioinformatics) or develop the necessary technology within our research group (molecular biology, embryo manipulations, gene-editing, transgenesis, confocal

microscopy, next generation sequencing, and bioinformatics). Each Distinguished Postbaccalaureate Scholar initially speaks with me to gain an overall view of research projects and then with a senior fellow who will direct daily activities. A significant emphasis is placed on mentoring both individually and in a group setting to facilitate the success of the Scholar's lab and career prospects.

Diversity Statement:
Promoting diversity and inclusion in science has been a strong personal goal over my years at the NIH. More than half of my fellows have been women, and many have become leaders in academe and philanthropy. The pool of under-represented minority applicants for fellowship positions remains small, but I have been able to recruit a Visiting Fellow (male) from Mexico and a Post-bac Fellow (female) who is Haitian-American. Two years ago, I hosted an outstanding NIDDK Distinguished Postbaccalaureate Scholar who is African American (female) and she has started a MSTP-funded MD-PhD program. These one-on-one interactions with fellows/scholars in the lab make a meaningful contribution to recruiting more women and under-represented minorities into the scientific pipeline. I also have served as a member or chair of the Developmental Biology Stadtman Investigator recruiting committee at the NIH. This is the mechanism for most appointments to the tenure track are made and has been an opportunity for me to make a difference in recommending a high number of qualified women and members of under-represented minorities.

My research group has participated with the Office of Intramural Training and Education in providing research opportunities to under-represented minorities through the Community College Summer Enrichment Program, the National Institutes of Health (NIH) Undergraduate Scholarship Program, and the High School Scientific Training and Enrichment Program (HiSTEP) which hosts under-represented minority students in the summer. In my research group, trainees and staff work together to support one another and form a productive balance of junior and senior scientists to provide opportunities for mentoring and training. My efforts in ensuring an environment of belonging and inclusion as I encourage discussion and feedback in the context of regularly scheduled one-on-one and group meetings. Going forward, these efforts will be strengthened by fostering outreach in recruitment of under-represented scientists and students to encourage participation in the NIH experience.

In recent years, there has been considerable determination on the part of the NIH to remediate groups that remain under-represented in scientific research. To that end, I have participated in multiple lectures/workshops including: NIDDK Inclusion, Diversity, Equity, Accessibility, and Civility (IDEA-C) Leadership Retreat, March 21-22, 2024; Beyond Safe Spaces Training with Whitman-Walker, January 25, 2024; 2nd Virtual Town Hall on Diversity, Equity, Inclusion, and Accessibility, May 18, 2023; NIDDK Speaker Series: Race, Racism, and Health: Advancing Health Equity, April 12, 2023; Conversations on Racial and Ethnic Equity, January 11, 2023; Women's Community DEIA Listening Session, November 9, 2022; The OIR/COSWD Diversity, Equity, Inclusion, and Accessibility Series (7 sessions), May 3, 2022 – June 21, 2022; National Academies of Sciences, Engineering, and Medicine (NASEM's) Committee on Addressing Diversity, Equity, Inclusion, and Anti-Racism in 21st Century STEMM Organizations, October 25, 2021; The Racial Equity Institute Groundwater Training, September 15, 2021; First Virtual Town Hall on Achieving Racial Equity at NIH, April 30, 2021; Picture a Scientist, March 22, 2021; NIDDK Town Hall, February 2, 2021; Conversations on Social Justice and Diversity, July 8, 2020; NIDDK Listening Circle – Societal Injustices, June 24, 2020.

I also serve on Advisory Committees for four tenure-track Stadtman Investigators (2, NICHD, 1 NHLBI, 1 NIDDK) and a K99/R00 Recipient (NICHD) which provide me with the ability to strengthen the commitment to diversity and inclusion across the NIH.

Douglas Forrest, PhD
Laboratory of Endocrinology and Receptor Biology

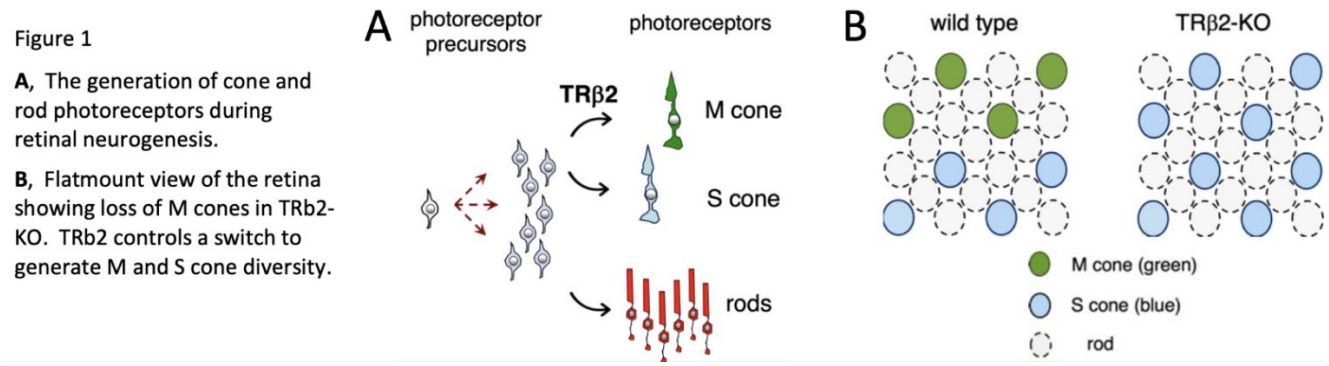
Key words: endocrine system, neurodevelopment, genetics and genomics

Project Description: ***"Endocrine and transcriptional control of sensory development"***
The senses are our interface with our habitat, community and wider world. From neonatal and even fetal stages, the sensory surfaces of the body detect information in the form of light, chemical and mechanical cues. In the retina, color vision is mediated by cone photoreceptors with sensitivity to different regions of the light spectrum, typically medium-long (M, "green") and short (S, "blue") wavelength regions in mammals. Elucidation of the controls for M and S cone diversity is key to understanding color vision and will also give insights into retinal diseases and loss of vision in retinal or macular degeneration.

We identified a rare thyroid hormone receptor (TRb2) that is unexpectedly critical for M cone development. In the absence of TRb2, all cones become S type indicating that TRb2 switches on the M cone identity. This link between the endocrine and sensory systems raises novel questions. How does a hormone control color vision? How is abnormal hormonal signaling involved in retinal degeneration? TRb2 is widely conserved, suggesting a fundamental role in human color vision and retinal function.

Thyroid hormone receptors act as ligand-regulated transcription factors and are thought to bind specific chromatin sites (enhancers) that regulate gene expression. We study how the hormone regulates cone differentiation. We have adapted genomic, single cell and physiological techniques to study cones. We also employ iPSC-derived organoids in culture as a human model system. Our research offers training in molecular biology, genetics, single cell and bioinformatic analyses.

https://irp.nih.gov/pi/douglas-forrest



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Diversity Statement:

Our research group has long been committed to diversity and inclusion regarding recruitment and also for supporting each person in our group. The more inclusive the endeavor, the greater the benefit for research and ultimately for society. My mentoring philosophy is to support each individual to achieve their training and career goals. Our research progress depends on cooperation. We aim to help each individual achieve their potential and their goals for a scientific career. All our trainees whether undergraduate, graduate, medical or postdoctoral fellows work with more experienced researchers to learn techniques and concepts while gaining experience and making their own contribution to our research program. Trainees are encouraged to take advantage of the wide range of career training workshops at NIDDK and to participate in other trainee opportunities at NIH.

At NIDDK, I have long supported the Diversity Summer Research Training Program, working with students from a wide variety of backgrounds. Trainees from our group have progressed to enter graduate school, medical school, or masters research programs. Several trainees have successfully sumbitted posters of their work and received travel awards to participate at national conferences including the Annual Biomedical Research Conference for Minoritized Students (ABRCMS) and the National Diversity in Stem Conference (SACNAS, Advancing Chicanos/Hispanics and Native Americans in Science). One dedicated student returned to our lab as postbaccalaureate trainee to advance her career in medicine with the long term goal of giving back to her community. We support diversity programs at NIH and have assisted in NIDDK outreach. Nationally, I have volunteered as a judge for scientific abstracts for SACNAS and ABRCMS. I have also served in career training and diversity activities in the American Thyroid Association. Our lab cultivates a supportive and stimulating environment for trainees at all stages of their career because it is people who make scientific discovery possible.

Ashley Frakes, PhD
Genetics and Biochemistry Branch

Keywords: neuroscience, glial cells, cellular communication, aging, metabolic disease

Project Description:
Glial cells are non-neuronal cells in the nervous system that play essential roles in regulating all aspects of brain function. Often glial cells are the first responders to any disruption in brain function long before patients or neurologists are aware of disease. Therefore, investigating the mechanisms by which glia sense and respond to stress (such as infection, injury, excess/insufficient nutrients, or disease-causing misfolded proteins) offers a unique opportunity to identify therapeutic targets and biomarkers for disease. Our lab leverages the use of multiple model systems including *C. elegans*, mice, and cell culture to identify the mechanisms glial cells employ to sense and respond to cellular stressors and coordinate homeostasis within the brain and whole organism.

Recently, we discovered that a small subset of astrocyte-like glial cells plays a central role in coordinating organismal stress resistance and longevity in *C. elegans* (Frakes AE. et. al. *Science*, 2020). Interestingly, other glial cell types do not seem to play a significant role in regulating longevity. This suggests that certain glial subtypes have unique mechanisms to sense and respond to cellular stress. This project will investigate how different glial cell types sense and respond to different cellular stressors such as diet, pathogen, or disease causing proteins and chemicals. We will use a combination of techniques including fluorescent microscopy, targeted genetic screening, and behavioral assays. Identifying these mechanisms will help us understand how the nervous system copes with cellular stress which could have implications for aging and age-onset diseases.

No prior *C. elegans* experience is required. We are excited to train you in all relevant techniques! *C. elegans* are a powerful model organism for neuroscience and aging research because they have a completely mapped neuronal connectome, defined glial cells, and exhibit many hallmarks of aging. The quick developmental timescale provides the unique opportunity for a fellow to learn the relevant techniques and be able to generate data that will make a significant contribution to publications from our lab.

Diversity Statement:
The Frakes lab is committed to cultivating a work environment that is inclusive, equitable, collaborative, and supportive for all members regardless of race, religion, ethnicity, gender identity or expression, sexual orientation, disability status, socioeconomic status, age, citizenship or immigration status. We believe that science thrives when everyone has a voice, and that unique perspectives and life experiences are critical to advancing our scientific pursuit. The scientific community is facing some of the most challenging scientific questions of our time (infectious disease, climate change, aging populations

etc.) and we believe that tackling such daunting tasks will only be only possible in an inclusive, equitable and diverse space.

We acknowledge that the scientific community has largely failed certain members of our community including black, indigenous, persons of color, women, and LGBTQ+. We believe that we have a responsibility to continue to educate ourselves and acknowledge our role in addressing the disparities and barriers facing these excluded groups. While we embrace our different backgrounds, beliefs, and life experiences, we acknowledge that we can also do better. We are committed to fostering a culture of equity, mutual respect, and dignity.

As a group leader I am particularly passionate about removing systemic barriers of entry and supporting and fostering an interest and love of science in budding scientists. I believe that equity in science means that every trainee should have the opportunity to achieve the same level of success, regardless of their starting point. Therefore, I am especially passionate about training postbaccalaureate students in my lab. As a mentor, I will seek out ways to facilitate your training by providing opportunities for presentations, networking, and other aspects of your scientific development. I will provide advice and guidance on all aspects of your career and will be your steadfast advocate both during your time in my lab and once you move on. We hope that you will join us!

Nick Guydosh, PhD
Laboratory of Biochemistry and Genetics

Keywords: ribosome, gene expression, mRNA translation, viruses, immunity
Title: The role of ribosome recycling factor ABCE1 during viral replication

Project Description:
Our overall aim is to improve our understanding of how viruses work and why they can sometimes cause severe disease. We also hope to inform the development of antiviral therapeutics to improve human health. Viruses are obligate intracellular agents containing an RNA or DNA genome surrounded by a virus-encoded protein coat. However, viruses are unable to generate their own proteins and thus rely completely on the host cell's ribosomes for viral protein production[1]. Understanding how viruses gain control of the host's capacity to make proteins is therefore an important goal.

Protein synthesis is carried out by the ribosome during mRNA translation. The process of translation can be divided into four steps: initiation, elongation, termination, and ribosome recycling. Intriguingly, the last phase, ribosome recycling, appears to be particularly important for Human respiratory syncytial virus (hRSV), measles virus (MV), and mumps virus (MuV)[2]. These are highly contagious negative-sense single-stranded RNA viruses that produce monocistronic viral mRNAs that are indistinguishable from host transcripts. A genome-wide screen identified the gene encoding the protein translation factor ABCE1 as an important proviral factor. While ABCE1 depletion strongly decreased viral protein production, host protein production remained largely unaffected. ABCE1 is responsible for removing (recycling) ribosomes from mRNAs after they reach stop codons. Without ABCE1, ribosomes can read past the stop codon by reinitiating translation in the 3'-untranslated region (3'-UTR)[3]. An important determinant of stop-codon readthrough is the identity of the stop codon (UAG, UAA, or UGA) and the the sequence surrounding it[4]. Importantly, ribosomes that read through the stop codon and reach the end of the transcript can activate a mRNA degradation pathway that results in loss of the transcript[3]. Since viral transcripts contain short 3'-UTRs, we hypothesize that this makes the virus especially vulnerable to readthrough caused by ABCE1 depletion or suboptimal stop codon contexts. This project will examine the following questions:

(1) How do viral mRNAs differ from host mRNAs to cause this strong dependence on ABCE1?
(2) How do viruses utilize ABCE1 for efficient viral protein production?
(3) How does stop codon context in viral transcripts affect readthrough of stop codons?

We are generating stable, inducible ABCE1 knockdown cell lines to investigate the role of ABCE1 during viral infection. Molecular cloning techniques will be used to generate plasmid DNA containing different stop codon contexts to investigate the effect of optimal and suboptimal stop codon context during infection. These plasmids will be transiently transfected into cells using and readthrough will be measured by using fluorescent microscopy and bioluminescent readouts.

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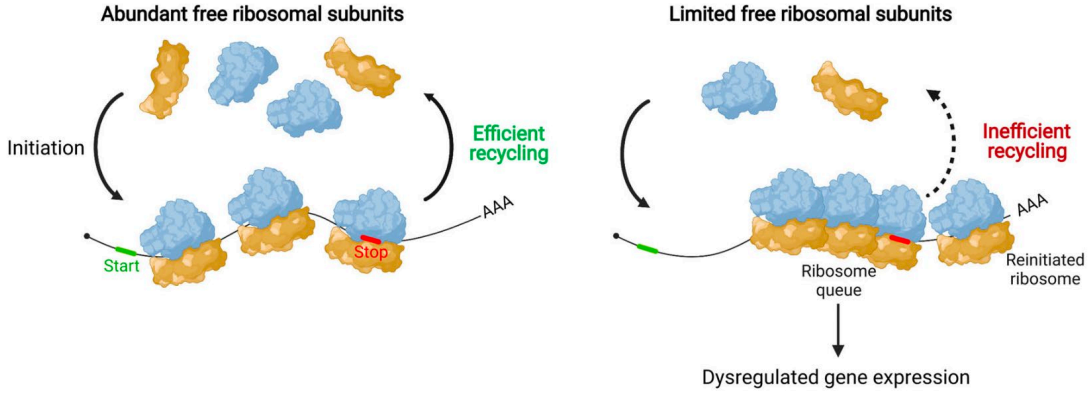
Figure. Illustration of the consequences of limited ribosome recycling (ref. 3).



Diversity Statement:

It is very important to me to create a welcoming and inclusive work environment in the lab. This helps ensure the everyone feels comfortable and productive, regardless of their race, ethnicity, gender identity, sexual orientation, ability, socioeconomic background, place of origin, religion, or other lived experiences. I have strived to ensure my laboratory staff is representative of the broader diversity in our community. Several former mentees have come from underrepresented backgrounds and/or programs aimed at ensuring greater equity in research (i.e. NIH HiStep 2.0). To promote a welcoming and cooperative workplace, my group has periodic discussions on topics such as diversity, values, shared expectations, and overall lab culture. It is important that everyone feel comfortable bringing their whole self to the workplace since that spurs creativity and better scientific research.

It has also been important to me to ensure equity in my work across the NIH and beyond. To this end, I participate in the NIDDK Race Ahead program, which is long-term program that aims to develop and maintain skills to promote discussion about diversity in race and ethnicity. I have attended conferences that aim to promote inclusion of historically excluded populations. For example, I participated in the SACNAS conference in 2023 to help make attendees become aware of opportunities at NIDDK, serve as a mentor-judge for posters, and learn about the diverse experiences of junior scientists. I have also served as a poster judge at ABRCMS. I have been part of working groups at NIDDK aimed at improving diversity in hiring. I have served on many commitees that evaluate applications to various programs including tenure-track positions, postdoc awards, conference speakers, and admissions to NIH graduate partnership programs. In these capacities, I make a point to be aware of unconscious bias that can influence outcomes. I encourage my group to attend seminars sponsored by the NIH on topics of diversity as well as speaker series, such as NIDDK TREaDs, which brings in top-tier scientific speakers who share about their personal journeys in science and efforts to promote diversity.

In the interest of equity in opportunities, I ensure all the trainees in my lab receive strong mentoring support. I hold regular meetings with trainees to discuss their scientific work and semi-annual meetings to go over career goals, ensure awareness of opportunities, and disc

Kevin D. Hall, PhD
Integrative Physiology Section
Laboratory of Biological Modeling

Keywords: Obesity, Nutrition, Metabolism, Clinical Research

Project Description:
The Distinguished Postbaccalaureate Scholar in my laboratory join our clinical research team in the conduct of ongoing studies in the field of human nutrition and metabolism science. In this role, the Distinguished Postbaccalaureate Scholar will learn how to perform a variety of different procedures, including indirect calorimetry and body composition analysis, and gain valuable experience at the NIH Clinical Center, a hospital setting where they will be working with physicians, nurses, dietitians, pharmacists, and scientists as part of multidisciplinary clinical research teams actively conducting three clinical studies.

The first study is a 4-week inpatient investigation of the mechanisms by which diets high in ultra-processed foods cause excess calorie intake. The second study involves a pair of 2-week inpatient periods to investigate the effects of ketogenic diets along with nicotinamide riboside supplementation on liver metabolism and sleeping energy expenditure in patients with overweight and obesity. The third study is a 2-month outpatient diet intervention to investigate whether body fat changes depend on whether patients receive a ketogenic diet followed by a low-fat diet for 1 month each as compared to the reverse order. All three studies have the potential to have a major impact on human nutrition and metabolism science.

Our laboratory has had success mentoring several Postbaccalaureate IRTAs on related projects over the years and many have found the experience to be particularly helpful preparation for the next phases of their careers, including gaining acceptance to prestigious medical schools such as Yale, Duke, NYU, and Georgetown.

Diversity Statement:

As someone whose research has often crossed scientific disciplines, I recognize the value of different perspectives and viewpoints that can come from unique experiences and backgrounds. I have sought to include people in my laboratory from diverse races, ethnicities, genders, and sexual orientations and worked to create an inclusive and welcoming environment to support work-life balance. I have regularly mentored trainees from underrepresented groups in the biomedical sciences and worked diligently to promote their careers. For example, I have had six postdoctoral fellows in my career and two have been underrepresented minority women whose pursuit to become Principal Investigators was facilitated by my mentorship. The first, Dr. Carla Prado, is now a Full Professor at the University of Alberta and the second, Dr. Valerie Darcey, received a NIH Pathway to Independence Award (K99/R00) and recently

accepted a tenure-track Investigator position at NIDDK in the Diabetes, Endocrinology and Obesity Branch. While in my lab, Dr. Darcey has shown boundless passion and energy for diversity and inclusion initiatives at the NIH and beyond. While I can obviously take no credit for Dr. Darcey's substantial accomplishments in this area, she has had my full support in these efforts!

I also recently participated as a faculty member in an NSF-sponsored Introductory Colloquium and Undergraduate Research Experience in Mathematical Biology for students of Historic Black Colleges and Universities with the goal of generating interest and enthusiasm for STEM careers and increase diversity in the sciences and mathematics.

Andrew Lutas, PhD
Neuromodulation and Motivation Section; Diabetes, Endocrinology, Obesity Branch

Keywords: Appetite; Food addiction; Fluorescent biosensor imaging; Neuromodulation; Behavioral neuroscience

Project Description:

Dopamine signaling in central amygdala and cue-induced feeding.

Almost 50% of American adults are obese, an alarming number considering the associated risks, which include heart disease and diabetes. External cues (e.g. food advertisements) and contexts (e.g. social gatherings) play an important role in motivating us to eat and together with the easy access to high-calorie palatable foods contributes to the obesity epidemic. **Our ability to willfully override these cue-triggered food cravings is limited and necessitates therapeutic assistance.** The brain contains neuromodulatory circuits that regulating both the learning and expression of cue-associated food seeking behaviors in humans and model organisms. Targeting these neuromodulatory circuits with pharmacological treatments is a promising avenue for suppressing unwanted food seeking. However, our mechanistic understanding of these neuromodulatory systems during cue-evoked food seeking is limited.

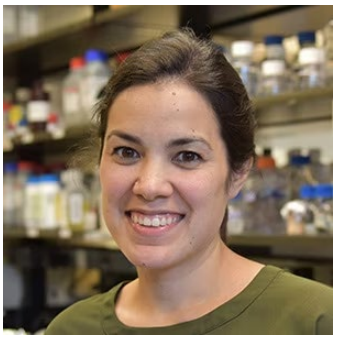
The **central amygdala** is a critical brain area necessary for our ability to learn about the salience and value of cues and contexts. In addition, the amygdala and its interconnected brain areas is important for regulating on-going motivated behaviors, which can often be conflicting such as the drive to replenish energy while also avoiding predators. Animals learn and use external stimuli to make decisions about when to prioritize one motivated behavior over another. Neuromodulators such as **dopamine**, serotonin, enkephalin, as well as other hormones and neuropeptides can instruct the learning of these cues and their state-dependent salience.

Our goal in this project is to develop an understanding of how dopamine signaling in the central amygdala controls the state-dependent learning and expression of food associated cues. We aim to achieve this goal by using fluorescent biosensors that report on either the presence of dopamine or the postsynaptic biochemical and molecular signaling (cAMP and protein kinase A activity). In addition, by using customized mouse behavior equipment and two-photon microscopes we can continuously track these fluorescence biosensors with subcellular resolution and high temporal precision across weeks. This allows us to watch neuromodulatory signaling as mice learn about food-associated cues, as motivation shifts to prioritize different goals, and as animals physiologically change (e.g. become obese). Finally, we can employ both optogenetic activators and inhibitors of neural and biochemical signals to causally investigate the role of neuromodulation in the amygdala.

Diversity Statement:

As a child of immigrant parents who fled a communist dictatorship, I am directly aware of how familial circumstances and societal inequalities can influence one's upbringing. Despite these challenges, being a white male has afforded me many privileges and shielded me from most forms of discrimination. I strive to be a mentor that can contextualize my identities and use my agency to help others achieve success. Recruiting underrepresented minority scientists, passing on my research knowledge in a safe lab environment, and supporting career advancement of minority scientists are the most direct ways that I can make a significant contribution to DEIA issues in academia.

I have been fortunate enough to have mentored several incredible students that come from diverse backgrounds in the past two years. All but one identified as women and over half identified as underrepresented minorities in STEM. Remembering my early days in science, I have helped each student build self-confidence and battle imposter syndrome, all while maintaining a high standard of scientific excellence. As part of my mentoring philosophy, I entrust my students with important scientific studies—often resulting in co-authorship on publications—and provide opportunities for experiential learning to develop the independence to achieve their goals and the resilience to overcome their challenges. I emphasize that science is about developing exciting, yet rigorous, scientific goals and learning from failure. Having these insightful experiences early on is critical in the retention of scientists. I can always do more, which is why I will devote my time to personally training future scientists from all backgrounds while supporting an open and affirming lab culture.



Katherine McJunkin, PhD or MD
Laboratory of Cellular and Developmental Biology

Keywords: **miRNAs, non-coding RNA, RNA decay**

Project Description:

MicroRNAs (miRNAs) are endogenously-encoded small non-coding RNAs that regulate the expression of complementary mRNAs. Because of their roles in normal gene regulation, miRNAs are essential to most developmental processes, and their mis-regulation can contribute to diverse human diseases. Our lab is interested in how miRNAs are regulated post-transcriptionally. One aspect of regulation we are interested in is how miRNAs and their protein co-factor Argonaute are targeted for decay. We hypothesize that decay is a crucial point of regulation since the precise spatio-temporal expression of a miRNA in a specific stage and tissue is often crucial to its biological role. The post-bac project would be to investigate mechanisms of miRNA decay using techniques that include CRISPR/Cas9-mediated genome engineering, forward genetic screens, and next-generation sequencing.

Diversity Statement:

I believe that problems are best solved by a group with diverse perspectives, which we are currently largely lacking in the scientific community. My primary contribution to increasing the diversity of the scientific workforce is my mentorship of a very diverse group of trainees. We regularly discuss diversity and inclusion as a group informally. As part of our Individual Development Plan annual review, trainees are also provided with a built-in opportunity to raise concerns about lab culture and inclusivity. Outside of my lab, I have volunteered as a mentor in two mentoring initiatives: the secondary mentor program in NIDDK which provides trainees with a second advocate/advisor beyond their own PI, and the Worm Board paired mentoring initiative which aims to support trainees and faculty from minoritized backgrounds. Beyond NIDDK, I serve as a member of the Stadtman Developmental Biology faculty search committee and the Johns Hopkins-NIH Graduate Partnership Ph.D. program admissions; in these capacities, I judge applicants with an acute awareness of implicit bias against minoritized groups (aided by annual NIH anti-bias training). Finally, as a woman in science, I serve as a positive role model for female trainees through publishing good science, providing supportive mentorship, and being a visible member of the scientific community.

Priyanka Narayan, PhD
Genetics and Biochemistry Branch

Keywords:
Neurodegeneration, Alzheimer's disease, APOE, metabolism, iPSC-derived glia, cell biology, genetics

Project Description:

Harnessing cellular lipid metabolism to modulate Alzheimer's disease risk

Diet has long been known to change brain function. Neuroinflammation is a characteristic of metabolic diseases. Metabolic alterations are increasingly being appreciated as a component of many neurological diseases. In fact, many Alzheimer's disease risk factors impact lipid metabolism.

Our lab's goals include understanding the cellular dysregulation of metabolism in Alzheimer's disease and learning how we can reverse this dysregulation. We use human induced pluripotent stem cells to generate human brain immune cells called microglia (see Figure). We then use these microglia to characterize how metabolism interacts with neuroinflammation in the context of healthy cells and those harboring risk mutations for Alzheimer's disease.

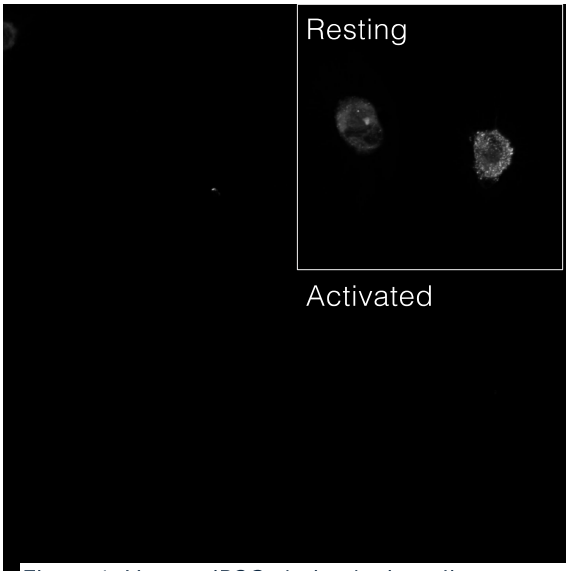


Figure 1. Human iPSC-derived microglia can mount a response to immune activation by changing their morphology (left) and accumulating lipids (right, white stain).

In our early work (https://www.biorxiv.org/content/10.1101/2024.04.11.589145v1), we uncovered that neuroinflammation in microglia was controllable by controlling biosynthesis and catabolism of triglycerides, an energy storage lipid in the cell. We also found that the strongest genetic risk factor for Alzheimer's disease, called *APOE4,* accumulates triglycerides resulting in chronic inflammation. Putting these findings together, we targeted triglyceride biosynthesis and catabolism to decrease disease-associated inflammation in *APOE4* microglia.

We're excited for a postbaccalaureate scholar to join the team to work two possible projects. The first is to understand how microglia that harbor protective mutations against Alzheimer's disease regulate their lipid metabolism to confer protection against disease-associated neuroinflammation. The second is to understand whether we can treat healthy or Alzheimer's disease risk microglia with dietary lipids to

modulate their immune responses. These projects could involve techniques like human stem cell culture and derivations into brain cell types, biochemistry (western blotting, qPCR), microscopy, transcriptomics, metabolomics, and proteomics among other techniques.

These projects will help us understand how cellular lipid metabolism can be used to mitigate risk and even confer resilience to Alzheimer's disease.

Diversity Statement:

Traditional structures within academia have historically excluded women, racial and sexual minorities, individuals with visible and less visible disabilities. This is reflected in the composition of our scientific communities where those in positions of power and leadership tend to be white and male. These traditional structures reflect systemic discrimination present in broader society. DEIA-focused initiatives in academia present an opportunity to adjust the traditional structures to include and support individuals from underrepresented backgrounds in the academic enterprise. These initiatives are crucial for building and growing an academic community that better reflects the diversity of our country.

My approach to promoting DEIA in STEM fields occurs at four levels: 1) Building awareness of systemic discrimination within my own research group and within the larger institution, 2) Participating and designing DEIA-focused initiatives within my research group and larger institution, 3) Recruiting a diverse research team, and 4) Incorporating an awareness of diversity within my own research. To build awareness for myself and my team members, I've participated in initiatives like the Groundwater training and design data-driven journal clubs within my own lab to explore problems with systemic discrimination and innovative efforts to address these problems in academia. As a former member of the Assembly of Scientists, I advocated for more inclusive practices as a part of the Stadtman Recruitment Process. I also participated in summer research initiatives to introduce trainees from different backgrounds to the research at NIH. I've recruited a team from a variety of personal and professional backgrounds and helped build internal lab mechanisms to establish support and trust. Through societies like SACNAS and Leading Edge, I've been fortunate to be able to share my work, support different levels of trainees, and recruit from diverse applicant pools.

I would like to discuss how I incorporate DEIA within my own research in depth. My group studies the biology behind Alzheimer's disease risk and resilience. One of the genetic mutations we study, APOE4, increases risk for Alzheimer's disease up to 12-fold in populations with Northern European ancestry—it is commonly known as the strongest genetic risk factor for sporadic Alzheimer's disease. In populations of African ancestry, however, the effect of the *APOE4* mutation is far less potent with barely detectable association with Alzheimer's disease, while in East Asian populations Alzheimer's disease risk with *APOE4* is even greater than for those with European ancestry. For many years, genetics research has been performed predominantly in populations with European ancestry and these genomic intricacies have been largely overlooked. Even the research we do to understand how these genes impact cell biology has been largely conducted in stem cell lines from donors with Northern European ancestry. I want to change the Alzheimer's disease research community addresses racial diversity. Through the NIH Center for Alzheimer's and Related Dementias (CARD), I am spearheading an effort called the iDA project (**i**PSCs for **D**iversity in **A**lzheimer's). We are generating 200 new iPSC lines from an assortment of patent donors. This repository will be far more diverse than any existing biobank. We are also generating foundational data on these lines to provide to the community a resource for studying genetic risk factors in diverse ancestral backgrounds.

Lynnette Nieman, MD
Diabetes, Endocrinology and Obesity Branch

Keywords: social determinants of health, Cushing syndrome, cardiometabolic disorders, cortisol

Project Description: This is a two-part project that explores aspects of social determinants of health (SDOH)

A. *Does African racial ancestry vs European ancestry affect the time to the diagnosis of Cushing syndrome?*

This is a retrospective analysis of NIH patients with an established diagnosis of Cushing syndrome and its etiology. By reviewing health records, we can estimate the approximate data of initial symptoms, the number of non-NIH physicians involved, and calculate the time to the NIH surgical procedure that established the cause. An early snapshot of the data suggests that Black patients have a delay of more than a year vs Whites. We hope to expand this evaluation to patients who identify as Hispanic.

Feasibility of this project

The data are available in the medical and research records. Our research nurse (Raven McGlotten), senior clinical fellow (Dr. Elenius) and PI (Dr. Nieman) are experienced in providing this education, coaching, and review of progress.

B. Development of U-RHYTHM microdialysis for measurement of hormone levels in subjects with adverse SDOH and in patients with adrenal disorders

This is a prospective study with multiple aims, as listed above. The Distinguished Postbaccalaureate Scholar would be primarily involved in the substudy that investigates whether cortisol mediates the cardiometabolic disorders that are prevalent in individuals with adverse SDOH. This study aims to recruit non-Hispanic reproductive-age women of European or African ancestry with high or low socio-economic status, as evidenced by educational level, neighborhood, income and occupation. We will obtain interstitial tissue fluid through use of the U-RHYTHM device worn for 27 hours as an outpatient. U-RHYTHM couples an external pump to a microdialysis catheter inserted into the abdominal subcutaneous tissue, with a collection device that spools the fluid-filled tubing. An air bubble can be inserted into the fluid every 20 minutes so that timing of the samples is known; hormone levels will be measured by tandem mass spectrometry. We also plan to study these women using measurements of cardiovascular health (family history, smoking status, BMI, blood pressure, body composition, fasting insulin and glucose, HgbA1c, lipids, interstitial glucose (via continuous glucose monitor), and MRI for atherosclerosis and hepatic elasticity (a correlate for steatosis caused by metabolic syndrome)), measurements of inflammation (TNFa, TGFb, fibrinogen, hs-CRP, IL-6), and validated questionnaires related to social environment (i.e. perceived neighborhood physical environment, social

cohesion, safety), psychosocial factors (perceptions of racism/discrimination), resilience, sleep, perceived levels of stress and anxiety, and overall allostatic load.

Feasibility of this project: the study is funded by a bench-to-bedside award; collaborations for labwork and outreach are in place; another Post-Baccalaureate trainee also will participate; equipment is ordered and IRB approval is anticipated in October.

C. Educational value and techniques for these projects: Learn how to be a clinical investigator

- In-depth learning about factors that influence social determinants of health and Cushing syndrome.
- Recruitment: Learn to interact with potential subjects and explain the protocol
- Application of this knowledge to develop databases to includes all relevant information
- Completion of case report forms and review of the electronic medical records to extract relevant data; data entry and review of database quality, completeness and need for additional information
- Analysis of the data and preparation of an abstract for a national meeting, presentation of data at national meeting and writing initial draft of manuscript.
- Mentoring from expert clinical investigator endocrinologists and research nurse.

Diversity Statement:

I am absolutely committed to increasing diversity and inclusion in Endocrinology. Of the direct hires I have had since 2010, three have been African American women, one white man, two white women and one South Asian woman. Over the years, about half of the trainees (non-direct hires) working with me have been women and 18% have been under-represented minorities (URM).

As president of the Endocrine Society (2017-18), I championed training of our Council (16 leaders of the Society) on unconscious bias. The president appoints members to task forces, committees and working groups. I substantially increased the number of younger members and URM members in these groups. \

I believe that statements of interest in diversity, equity and inclusion must be extended to one's philosophy of mentorship. My goal as a mentor is to enable all colleagues to grow into their potential, to find the best career fit and to achieve a work-life balance that supports these goals. This philosophy grew out of 30 years experience in NIH administrative leadership positions, as well as my roles as a research team leader and teacher. The scope of interactions with my trainees is broad: I have always had an open door (during COVID, an open-zoom) policy for trainees and faculty, which they use as needed. Hence the agenda often is set primarily by the person seeking advice. I meet with the research team weekly, as needed to review patients, data and progress and every 4 – 6 weeks one-on-one to review progress and evolving goals.

The principles that work for me are: engaged listening (seek first to understand); be authentic, honest and humble; admit when I don't know something; give specific and constructive advice; be optimistic and enthusiastic about the person's ability to solve a problem or achieve a goal; don't gossip or betray confidences; have compassion; be data-driven; state opinions as options and respect trainees and learn from them -- it should be a two-way street.

I talk to the trainees about having a "toolkit for success" that includes: 1. Insight about their own personalities and preferences about mentor-mentee relationships, 2. Communication skills (written and oral), 3. Administrative skills (QA/QI projects, scheduling, serving on committees), 4. Learning skills (how to master endocrine competencies, keeping up with the literature, reading primary sources and not just UpToDate, lifelong commitment), 5. Professionalism (getting along with peers and patients, use of

social media, handling conflict). I hope that this is helpful in deciding whether to work in our group will be a good fit.

Florencia Pratto, PhD
Genetics and Biochemistry Branch

Keywords:
Meiosis, genomic diversity, genomic instability, replication, recombination

Project Description:
Meiosis is the specialized cell division that allows diploid organisms to generate haploid gametes (sperm and eggs) for sexual reproduction. If meiosis fails to execute properly, it can lead to aneuploidy (having the incorrect number of chromosomes). In humans, it is estimated that approximately 5% of sperm and a staggering 60% of oocytes may harbor an incorrect chromosome complement. Consequently, errors in meiosis represent a leading cause of mental disabilities, miscarriages, and infertility. The main focus of research in the lab is to peel back the multiple layers that shape the meiotic recombination landscape over size scales ranging from single nucleotides to whole chromosomes in the human and mouse germlines. To achieve this goal we use a combination of genetics, multi-omics analysis and microscopy.

DNA double-stranded breaks are introduced on purpose as cells enter meiosis to initiate recombination. In turn, recombination is necessary to ensure proper chromosome segregation and to introduce genetic diversity in a population. Double strand breaks occur soon after the genome is replicated and in yeast, replication and recombination are mechanistically linked. A major challenge is that mammalian meiosis must be studied *in vivo*, in the context of a complex tissue such as testis. This has hindered the ability to interrogate meiotic DNA replication at the molecular level. We have recently established that meiotic replication is distinct in mammals and that it influences the location and repair of meiotic double-strand breaks that initiate meiotic recombination but have not demonstrated a mechanistic link.

The projects in the lab are now geared towards answering this question. We will begin by asking how changes in the DNA replication program affect recombination initiation. Genetic perturbations of the replication program are challenging; therefore we will use meiosis-specific conditional knockout mouse models. RIF1, a key genome-wide regulator of replication timing, is a prime candidate for this approach. The loss of RIF1 in mitotic cells causes major changes in the RT program by increasing heterogeneity between individual cells rather than causing discrete RT shifts in all cells. Initial experiments will consist of mapping origins of replication, generating replication timing profiles (bulk and single-cell derived), and mapping DSB hotspots in these mice. Single-cell analysis of replication timing will allow us to explore cell-to-cell heterogeneity. This would inform us whether changes in the replication program are coupled with altered recombination dynamics. If necessary, chemical inhibition of DNA replication (such as hydroxyurea treatment) can be considered.

Diversity Statement:

My personal and professional decisions are guided by a commitment to positively impact both my immediate surroundings and society at large. My lab started in January and I strive to promote an inclusive, diverse environment. During my time as a postdoctoral fellow and a staff scientist at NIH, I mentored students from underrepresented groups and these initiatives greatly enriched the lab from a human and scientific perspective and set the tone for how I would approach mentoring in my lab. I was recruited as part of a program that aims to build a more inclusive community within the NIH Intramural Research Program. I am dedicated to paying forward the support I've received by actively fostering the career advancement of individuals from underrepresented backgrounds in my field. Through mentorship, creating opportunities, and sharing resources, I aim to build a cycle of support that empowers the next generation of diverse professionals to succeed and, in turn, uplift others.

Barbara Rehermann, MD
Immunology Section, Liver Diseases Branch, NIDDK

Keywords: microbiome, liver disease, immunology

Project Description:

The Immunology Section performs translational and basic studies to understand the regulation of hepatic and systemic inflammation. We study immunological factors that contribute to inflammatory diseases such as viral hepatitis, investigate how immune responses and chronic inflammation are regulated by the microbiome and devise strategies that modulate the progression of chronic liver disease and/or induce protective immune responses. This is done in (1) translational immunological studies with biospecimens (blood and liver biopsies) of patients with hepatitis virus infection, and (2) basic immunological studies in preclinical models.

1. Our current translational studies focus on hepatitis B virus (HBV) infection. Although there is a vaccine that prevents new infections, there is no cure for those who have been chronically infected at birth (currently more than 254 million people worldwide). Studying immune responses is key to understanding disease progression in chronic viral hepatitis and to assessing immune-modulatory therapies. In previous studies we have identified innate immune cell populations in liver and blood that contribute to the therapeutic effect of pegylated interferon and mechanisms that can interfere with such response (Nishio et al, Sci. Transl. Med. 2021: 13, eaba6322). In new studies that are about to start, we will assess the effect of immunomodulatory treatments on immune responses in the liver and blood of chronic HBV patients.

2. As preclinical models we have established mouse colonies with natural, wild-derived microbiota and have shown that these better model human diseases than conventional laboratory (please see video here: https://www.youtube.com/watch?v=SbFM7NC8yUg). The wild-derived microbiota are the natural microbiota from wild mice – they are important for all aspects of host physiology, have co-evolved with their hosts over eons of years in a symbiotic relationship, but are missing in conventional laboratory mice. As a result, mice with wild-derived microbiota have immune responses that resemble those of adult humans whereas conventional laboratory mice have immune responses similar to those of neonatal humans. We have found that natural microbiota confer health benefits, including protection upon colorectal carcinoma and other cancer and protection against diet-induced obesity, that are not seen in conventional laboratory mice and now study the mechanisms (Rosshart et al., Cell 2017, 171: 1015-1028; Science 2019, 365(6452), Hild et al., Nature Metabolism 2021, 3: 1042-1057).

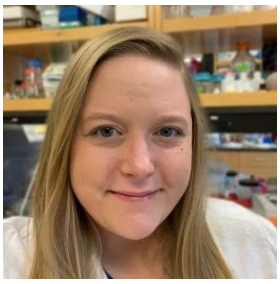
Each member of my group has his or her own research project, but the group works very closely together as a team, so you would learn immunologic as well as molecular techniques from other fellows in the group. You would conduct a research project from start (study design, set up of experimental assays and controls) to finish (data acquisition, data analysis, trouble shooting, scientific presentation and preparation of posters and manuscript), participate in weekly branch meetings, in which research

projects of the whole branch are discussed and in biweekly immunology meetings, where my group discusses in detail our own research projects. I also meet individually with all trainees once a week.

Diversity Statement:

I am strongly promoting gender, racial, and ethnic diversity within the Immunology Section, NIDDK, and NIH. Many of the diseases that we study are highly prevalent in other parts of the world, in particular viral hepatitis in Asia and Africa, and autoimmune diseases in Northern Europe. Many of the international postdoctoral trainees have worked as hepatologists and/or gastroenterologists in their home countries prior to joining the NIH for research and thus, bring unique clinical experiences and insights.

My former trainees include an almost equal number of men and women (27 (49%) women; 29 (52%) men) and diverse races (Caucasian, African-American/Black, Asian) and ethnicities (including Hispanics). Trainees are recruited not only from the US (23/56, 41%) but also internationally (Germany, Greece, India, Israel, Italy, Japan, South Korea, Spain). The diverse ethnic, culture and geographic backgrounds brings an open-mindedness to the laboratory that is conducive to developing novel research ideas. Many trainees confirm that this diversity was a unique and valuable experience during their postdoctoral or postbac IRTA fellowship. More than one third (34%) of these trainees have reached academic positions (as assistant, associate or full professor), one third (36%) are still in training (medical or graduate school or postgraduate training) and one third (29%) are in non-academic positions in the biomedical field (56% research, 44% clinical). I was awarded the 2015 Norman P. Salzman Memorial Mentor Award in Virology and the 2010 and 2024 Nancy Nossal Scientific Mentorship Award for exemplary contribution to the mentoring mission of NIDDK.



Margaret Rodgers, PhD
Laboratory of Biochemistry and Genetics

Keywords: RNA, Gene Expression, Bacteria, Stress Response, Microscopy

Project Description:

My lab studies how ribonucleic acids (RNAs) are employed by bacteria to rapidly alter gene expression during stress adaptation. Bacteria are bombarded with stress in the wild – and in our bodies – and adaptation is essential to their survival. We would like to understand the mechanisms bacteria use to turn on or off specific genes involved in adaptation. This is highly important for understanding bacterial pathogenicity as well as interactions within microbial communities such as in the human gut.

RNAs are versatile, dynamic biomolecules that are major players in gene expression. To fulfill their cellular function, RNAs must fold into complex three-dimensional structures and are often complexed with protein co-factors. Virtually all RNAs interact with RNA-binding proteins which help RNAs fold, direct modification, carry out processing, and protect RNAs from degradation. RNA-binding proteins can interact with RNAs for short periods of time or they can form a complex called a ribonucleoprotein particle (RNP). In this project, we aim to understand how RNAs and RNA-binding proteins work together to help a bacteria adapt to stress and how RNAs could be harnessed for antibacterial treatment.

In this project, we will examine assembly of a bacterial RNP that regulates gene expression in response to many different environmental stresses. To regulate a specific mRNA, bacteria overexpress a small RNA (sRNA) that contains a sequence complementary to that specific mRNA (Fig. 1), similar to eukaryotic microRNAs. The sRNA and a protein partner, Hfq, seek out and bind to the target mRNA. Formation of a Hfq-sRNA-mRNA RNP changes the structure of the mRNA and somehow changes how that mRNA is transcribed and translated (Fig. 1). We will examine in detail how the sRNA and Hfq find the complementary region in the target mRNA. In this project, you will learn a number of techniques including bacterial expression and genetic manipulation, molecular biology, *in vitro* biochemistry, and microscopy techniques.

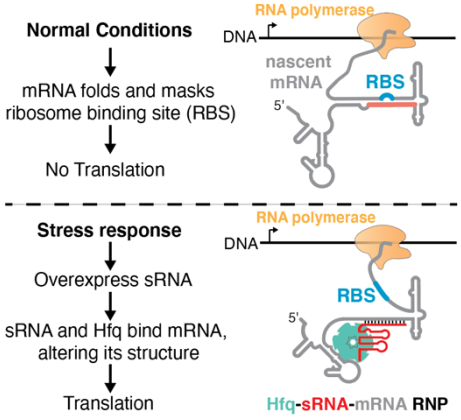


Fig. 1. The Hfq-sRNA-mRNA RNP regulates mRNA expression during transcription.

The major questions we will address are:

1. How do mutations in the mRNA-sRNA complementary region influence the timing of Hfq-sRNA-mRNA RNP assembly?
2. How do mutations in the mRNA-sRNA complementary region alter mRNA regulation *in vivo*?

Using single-molecule fluorescence microscopy, we will examine how mutations within the complementary region affect recruitment of the Hfq and sRNA to the mRNA as it is transcribed. To do this,

we will employ a new method called single-molecule co-localization co-transcriptional assembly which enables monitoring of both transcription of the mRNA and binding of Hfq and sRNAs in real time (1). Using this method, we will examine the timing of binding of Hfq and sRNAs relative to when the complementary region in the mRNA has been transcribed and compare the change in recruitment between different mRNA mutants. We will examine the effect of these mutations *in vivo* using gene reporter assays (2) to measure changes in regulation and determine if RNP assembly during transcription hastens regulation.

References: 1. Rodgers,M.L. and Woodson,S.A. (2019) *Cell*, 179, 1370-1381. 2. Peng,Y., Soper,T.J. and Woodson,S.A. (2014) *J Mol Biol*, 426, 275–285.

Diversity Statement:

My lab is dedicated to increasing diversity in science. I believe that everyone regardless of their race, age, gender, socioeconomic status, sexual orientation, or ability should have the same opportunities to succeed and I am dedicated to work towards achieving this goal.

I believe that success in science is predicated on enthusiasm and creativity and I am focused on fostering an environment that celebrates these values. Creativity thrives in a diverse setting with people from different backgrounds, both personal and scientific, who can share their experiences to grow as individuals and as a team. I intend to increase diversity in my lab by utilizing recruitment resources that target underrepresented groups, like the Distinguished Postbac Scholars Program, as well as actively work towards eliminating unconscious bias in hiring at any level.

In addition to creating a diverse workforce, my lab values inclusivity. I believe one of the best ways to establish an inclusive environment as a mentor is to ensure that all ideas are shared and honesty about mistakes is encouraged. This attitude towards the act of science is something that inspired me to be more creative and allowed me to flourish as an independent scientist. As the PI, I will continually evaluate how well the lab grows and changes to ensure that the lab environment aligns with these core values. Specifically, I will evaluate the lab environment with check-ins like anonymous lab surveys to better understand feelings about lab climate and propose possible changes.

Increasing diversity in the workforce also necessitates that mentorship styles are adapted to effectively reach all students equally. Mentoring style is an adaptive skill that needs to be developed on individual basis and altered throughout the course of the student's career. I have been trained on developing the mentor/mentee relationship through the Delta program, an extension of the Center for the Integration of Research, Teaching and Learning (CIRTL). I have used several strategies from this course when I mentored students from different backgrounds. These experiences have helped me not only develop as a mentor but also increased my awareness of the challenges underrepresented groups face.

As my lab grows, I will continue advocating for underrepresented groups in my own lab and the broader scientific community. I am committed to advocating for underrepresented groups of different races, genders, ages, sexual orientations, ability/disability, or socioeconomic backgrounds. I strongly believe that building an inclusive, diverse research group will promote creativity, engender enthusiasm, and therefore will be a catalyst in achieving our short and long-term scientific goals.

Anne E. Sumner, MD
Senior Investigator
Chief, Section of Ethnicity and Health
Director, NIH-Rwandan Health Program

Keywords: Diabetes, health disparities, social justice, African Americans, African immigrants

Distinguished Postbac Research Plan

The goal of the Section of Ethnicity and Health is to recruit trainees who want to become physicians and health disparity researchers with the knowledge and skills to design new protocols which lead to improved health care for underserved populations. The program is directed towards recent college graduates who are planning to apply for an MD or an MD-PhD in the social, nutritional or physiologic sciences. The training goal for postbac fellows in the Section of Ethnicity and Health is that in a 2-year period they will become Clinical Investigators with the skills and tools to set up and run a clinical investigation where none previously existed. The Postbac will gain experience with recruitment, screening, enrollment, scheduling, informed consent documents, patient interaction (often called bedside manner), administering psychosocial questionnaires, collecting blood samples at the bedside, aliquoting them and transporting them to the proper laboratory for analyses and storage. Additionally, they will learn how to organize, enter and analyze data, as well as write abstracts and manuscripts for publications. In short, with this training they will have the tools, confidence, and experience to design new research protocols and successfully compete for funding nationally and internationally.

The Section of Ethnicity and Health is specifically focused on determining ways to improve detection and prevention of diabetes in African descent populations. Currently, we are working with both African American and African immigrants and through collaborations, with Africans living in Sub-Saharan Africa. Our research questions address key metabolic, social, and genetic issues. In the metabolic arena, we are focused on screening for diabetes and designing protocols which could lead to diabetes remission. In the social arena, we are examining the social determinants of health including behavior, stress, sleep, resilience, the experience of discrimination and spirituality. Our genetic research is done in collaboration with NHGRI. Within these metabolic, social and genetic arenas, Postbacs choose a specific focus area.

While our Postbacs will work in the field of diabetes screening, the experience will give them the skills to work with diverse populations across a broad range of health conditions. In short, the skills gained working with the Section on Ethnicity and Health are designed to be foundational for a career in medicine, social justice, and health disparities research.

Diversity Statement

The Diversity focus of the Section on Ethnicity and Health is divided into three spheres:

1) Research goals are directed towards eliminating health disparities relative to diabetes risk and complications in African descent populations with a specific focus on African Americans, African immigrants and Africans living on the African continent.
2) Goal of the training program are to develop a diverse workforce able to conduct health disparities research, to formulate key clinical questions and set up and run new clinical studies where none previously existed.
3) Ensuring trainees develop a sensitivity and inclusiveness for colleagues and trainees with disabilities.

For Sphere 1, I have personally enrolled over 1000 individuals of African descent into Section on Ethnicity and Health protocols. This kind of enrollment demonstrates engagement, trust, and communication between communities of African descent and the Section on Ethnicity and Health. Our success is this arena can be demonstrated by the fact that previous participant referral has become our leading recruitment method.

For Sphere 2, as our protocols are of direct and immediate relevance to people of African descent, trainees of African descent often seek us out for training. In addition, because of our program's emphasis on clinical training relative to health disparities, we welcome and attract trainees from many different backgrounds.

In the last 23 years the Section has had 69 trainees (72% women). The race/ethnicity of the trainees in the Section of Ethnicity and Health are provided in the table.

Diversity of Section on Ethnicity and Health Trainees 1999 to 2023

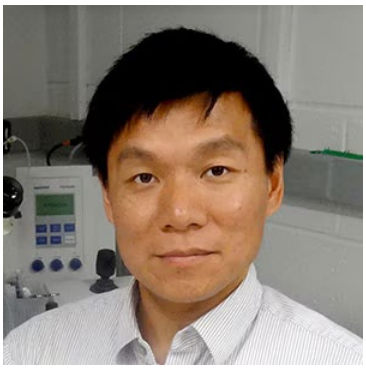
Race/Ethnicity	Number	Percent
African descent	37	54%
White	12	16%
Native American	8	12%
Hispanic	6	9%
Asian	6	9%

For Sphere 3, as a person with a mobility impairment, I walk with 2 forearm crutches and 2 leg braces and use a manual wheelchair and scooter to do my work as a physician investigator. Therefore, I seek out opportunities and inclusive policies across the NIH campus for people with disabilities. The trainees in the Section become familiar to working with people with disabilities.

Due to the Section of Ethnicity and Health's commitment to Diversity, I have received 8 NIH Awards for improving diversity and inclusion on the NIH campus and 2 Awards for mentoring, including the Nancy Nossal Award from NIDDK and the Ruth Kirschstein Award from the OD.

In addition**,** I have been awarded adjunct faculty positions at Howard University and two African universities, specifically the University of Global Health Equity in Rwanda and the NorthWest University in South Africa.

In short, for the Section on Ethnicity and Health training a diverse and committed workforce is our highest value.



Yihong Ye, Ph.D.
Laboratory of Molecular Biolology

Keywords: neurodegenerative disease, protein aggregation, organelle homeostasis, CRISPR gene editing, iPSC-derived neuron

Project Description:

Mammalian cells employ a diverse array of protein quality control (PQC) mechanisms to maintain the delicate balance of protein and organelle homeostasis. When these processes fail, they can lead to age-related neurodegenerative diseases such as Alzheimer's and Parkinson's. My lab focuses on unraveling the molecular mechanisms behind protein translocation-associated quality control at the endoplasmic reticulum (ER), the unconventional secretion of misfolded proteins, and the cell-to-cell transmission of misfolded alpha-synuclein and tau aggregates.

The new postbaccalaureate researcher will be exploring how the ubiquitin-proteasome system contributes to the repair of damaged lysosomes, a key organelle that plays an essential role in protein quality control and nutrient sensing. We have recently discovered that a neurodegenerative disease-associated mutant protein, CLN4, forms aggregates on the surface of lysosomes, leading to lysosomal damage. Through genetic screening, we identified a ubiquitin ligase that promotes endosomal microautophagy, a process that aids in the clearance of CLN4 protein aggregates. Remarkably, overexpression of this ubiquitin ligase rescues CLN4 mutation-induced cell death in iPSC-derived neurons and a Drosophila model of CLN4 disease.

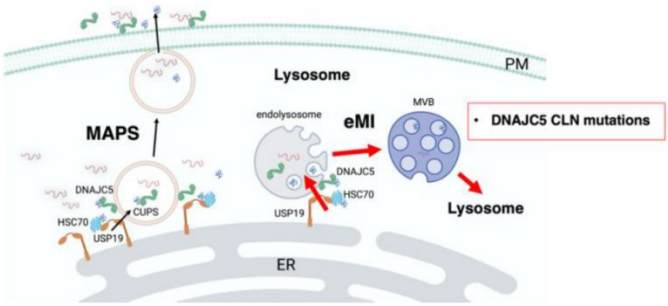


Figure 2 Misfolding-associated protein secretion (MAPS) and endosomal microautophagy are coupled protein quality control (PQC) mechanisms collectively maintaining lysosome and cell homeostasis. CLN4 disease mutants (DNAJC5) have diminished MAPS-stimulating activity but increase substrate flow to eMI, causing lysosome dysfunction and neurodegeneration. By enhancing the degradation of CLN4 mutant, we can improve lysosome homeostasis and rescue CLN4 mutatipon-associated

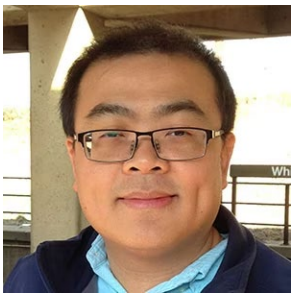
The goal of the current project is to investigate whether enhancing endosomal microautophagy could serve as a general therapeutic strategy for lysosomal storage diseases caused by other damaging proteins. Our initial focus will be on CLN diseases due to their phenotypic similarities. We will use CRISPR-mediated gene editing to introduce disease-associated mutations in iPSC cells, differentiate these cells into neurons, and subsequently analyze lysosome morphology and the resulting cell death phenotype. We will then assess whether the overexpression of

the identified ubiquitin ligase can reverse the cellular abnormalities associated with these disease mutations.

The postbaccalaureate researcher will gain hands-on experience with a variety of cutting-edge molecular biology, cell biology, and genetic techniques. These include modeling human diseases through gene editing in iPSCs, super-resolution microscopy, live-cell confocal fluorescence microscopy, organelle-based proteomic analysis, and other multi-omics approaches.

Diversity Statement:

I believe that science should be blind to race and gender. It is my ultimate goal to establish a democratic, fair, and transparent environment that will be equally beneficial for everyone with different backgrounds. Since the inception of my research group at NIH, I have been working tirelessly to building a diverse research group. I am certainly aware that being a Chinese descent, I might be more attractive to new Ph.D. graduates from countries in Asia. Thus, I constantly remind me of being more open-minded. I tried every opportunity to recruit qualified postdoctoral candidates with different backgrounds. Over the years, we have managed to attract staffs (including fellows and students) from China, Iran, US, India, and Korea. These trainees also come from diverse religious backgrounds including Christianity, Islam, or Atheism, etc. What makes me particularly proud of is that among the four trainees who went on to establish their own independent research groups, three are women scientists.

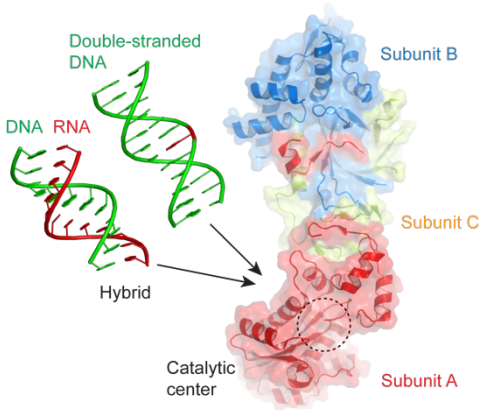


Jinwei Zhang, Ph.D
Laboratory of Molecular Biology

Keywords: Aicardi-Goutières Syndrome (AGS), RNA structure, RNase H2, RNA-protein interactions, Immunity.

Project Description:
Aicardi-Goutières Syndrome (AGS) is a severe neurological and developmental disorder that primarily affect newborn infants. Among the four human genes strongly associated with AGS, three map to the three subunits of the human Ribonuclease H2 (RNase H2) enzyme. RNase H2 is the principal nuclear enzyme responsible for the degradation of DNA-RNA hybrids generated during genome replication and transcription, and the removal of ribonucleotides (RNA) mis-incorporated into genomic DNA.

Although the crystal structures of human RNase H2 were previously reported, it remains unclear how this important enzyme achieves dual substrate specificity towards both the DNA-RNA hybrid ("A"-form geometry) and double-stranded DNA carrying RNA nucleotides ("B"-form geometry), a property unique to eukaryotic RNases H2. This gap in our knowledge is due to the unavailability of human RNase H2 complex structures bound to its substrates.



Human RNase H2

Therefore, this project aims to characterize the interactions between human RNase H2 and its two type of nucleic acid substrates using a collection of biophysical analyses. To this end we will employ rational RNA design and engineering, X-ray crystallography, single-particle cryo-electron microscopy, fluorescence-based RNase H catalytic and binding assays, etc. Once the structures are determined, extensive functional validation will be performed using site-directed mutagenesis and fluorescence-based in vitro assays. The incoming scholar will work closely with Dr. Zhang and postdoctoral fellows in the group in designing, planning, executing, evaluating, and documenting portions of the work, with the goal of publishing the research findings. Besides working chiefly with the Zhang lab in NIDDK, the incoming scholar will also collaborate with Dr. Robert Crouch's lab in NICHD on the project, to validate structural and biophysical findings using in vivo techniques including yeast genetics, cell culture, and possibly mouse models. A second project objective is to design mutations based on the complex structures, to uncouple and disentangle the catalytic activity on the DNA-RNA hybrids from that on the double-stranded DNA with mis-incorporated RNA nucleotides. A third project aim is to use structural analyses and computer modeling to map known AGS-causing mutations onto the human RNase H2-substrate complex structures, to understand the molecular mechanisms of AGS pathogenesis. Overall, the project aims to uncover novel mechanistic insights into how human RNase H2

enzyme recognizes its nucleic acid substrates, and to expose the incoming scholar to basic science research in biochemistry, biophysics, structural biology, RNA biology, and auto-immune diseases.

Diversity Statement:
We as a research team are firmly committed to promoting diversity, equity, inclusion, and accessibility (DEIA) for all individuals in our shared workplace at NIDDK and NIH. We believe that an inclusive team that is diverse in gender, race, ethnicity, culture, religious beliefs, sexual orientation, and physical and mental abilities is inherently advantageous and conducive towards producing science and other work of the highest quality. Such diversity naturally creates an open, collegial, fair, and respectful environment that spurs and fosters creativity, innovation, and collaboration. This environment further welcomes and empowers people from a broad spectrum of geographical and cultural backgrounds and with distinct lived experiences to share, exchange and amalgamate a wide range of ideas, opinions, and perspectives.

Promoting and maximizing diversity and inclusion in our workgroup has been a significant consideration in making recruiting decisions. These efforts have produced and maintained a diverse group of trainees. Among the trainees at all levels we have had the pleasure to work with so far, more than 50% of them are women scientists and they originally come from 8 different countries. One minority summer student joined us as part of the Amgen Scholar at NIH Program on Health Disparities, and presented her research work here at the 2017 Annual Biomedical Research Conference for Minority Students (ABRCMS). Career development of the diverse trainees in our group has been a top priority. Anticipating the significant challenges that they face on the job market, we help prepare them by organizing regular group-based and one-on-one discussions about job searches, preparation of applications, and interview and negotiating strategies.

Inspired and encouraged by the strong NIH and NIDDK commitment to DEIA, we have proactively sought to further our education in understanding the origins and histories of structural and institutional racism in the U.S. and in the world, key characteristics of contemporary racial inequity in society and in the biomedical research enterprise, and in identifying solutions and actionable items to the problem. Among these learning experiences, we have particularly benefited from five days of in-depth, sobering “Groundwater” and “Phase I” training programs provided by the Racial Equity Institute (REI). We learned a great deal from the screening and group discussions of the “Picture a Scientist” documentary sponsored by NIH Office of Equity, Diversity, and Inclusion (EDI), and excellent presentations in the NIDDK Trainees Recognizing Excellence and Diversity in Science (TREaDS) Seminar series. Whenever possible, we try to attend the trainee-led TREaDS seminars and interact with the diverse speakers, even when the topics are distinct from our own research. I have completed the inaugural NIDDK “Race Ahead” Program, an intensive months-long program designed to promote diversity and equity at NIDDK. This highly effective program combines multimedia, didactic teaching with frequent small-group activities, role playing, and sharing of personal reflections with the group. Participants are further grouped in 4-person learning and action teams through which we support each other in regular meetings after the initial 5-day launch workshop. Since 2023, I have served as a mentor for the American Society for Microbiology (ASM) MOSAIC (Maximizing Opportunities for Scientific and Academic Independent Careers) K99 program and regularly attended the annual ABRCMS conferences.

To further advance and share our learning and contribute to the DEIA efforts at NIDDK, I have served as a member of NIDDK Inclusion, Diversity, Equity, Accessibility and Civility (IDEA-C) Steering Committee, and NIDDK Racial and Ethnic Equity in the Workforce (REEWork) Working Group (WG). These committees have helped design, launch, and support several highly effective DEIA initiatives including

the creation of a LGBTQ+ community support working group and the aforementioned Race Ahead program.

In the future, we plan to continue, expand, and deepen our efforts, education, and services to further promote DEIA in NIDDK and NIH Intramural Research Program.