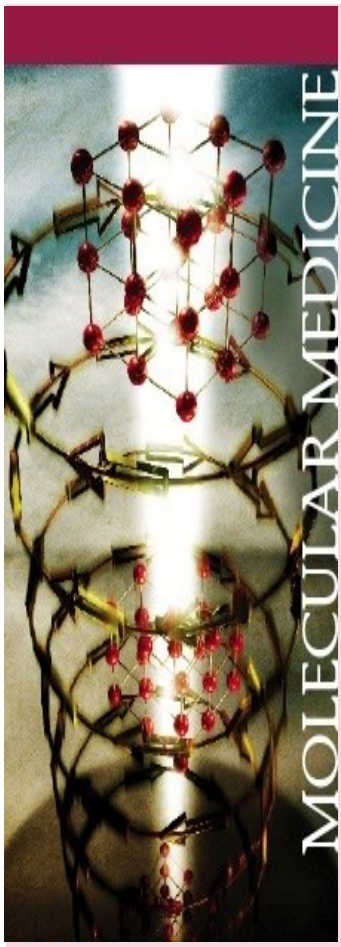

CENTER FOR
MOLECULAR MEDICINE AND GENETICS
Fall 2024

Inside this issue:

Faculty Spotlight — Audrey Fu, PhD

Dr. Audrey Fu Brings Expertise in Statistical Genetics

Audrey Fu, PhD

Dr. Audrey Fu, Associate Professor of Family Medicine and Public Health Sciences and of Molecular Medicine and Genetics, our newest faculty addition, is a statistician who aims to connect statistical methods with real-world biomedical challenges.

A graduate of the University of Washington, she received a PhD in statistics with a concentration in statistical genetics. Dr. Fu comes from the University of Idaho, where she most recently was an Associate Professor of Statistics and of Bioinformatics and Computational Biology in the Department of Mathematics and Statistical Science.

One factor that really stuck out to Dr. Fu about Wayne State's School of Medicine was that it offers a dynamic environment for interdisciplinary collaboration.

"I am excited to be at Wayne State and was really looking forward to working in a place where I could have close collaborators," Dr. Fu said. "At some places, research can often feel like a solo endeavor, especially in math and

Fu article continued on page 3

Faculty Spotlight — Adi Tarca, PhD

Data Challenge Seeks to Advance Research on Placenta Aging

Dr. Adi Tarca, Professor of Molecular Medicine and Genetics and of Obstetrics and Gynecology, recently kicked off a research project called the Placental Clock DREAM (Dialogue on Reverse Engineering and Assessment Methods) Challenge. In this initiative, machine learning experts from around the world were tasked with creating models to predict the biological age of placentas using epigenetic data.

"The DREAM Challenge is all about bringing together the best minds to solve complex problems in biomedical research," said Dr. Tarca, who was recently appointed to the board of directors of the DREAM Challenge. "We provide participants with epigenetic data from placentas and challenge them to create models that accurately predict the age of these tissues. Gaining insights into how placentas age can help

Adi Tarca, PhD

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Data Challenge cont.

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us better understand obstetrical syndromes."

More than 70 participants from around the world joined the DREAM Challenge, with data generated by the Perinatology Research Branch (NICHD) previously at Wayne State University / Detroit Medical Center being used to test the accuracy of their models. The top models were presented at the annual RECOMB/ISCB Conference on Regulatory & Systems Genomics with DREAM Challenges in October.

A key goal of the research is to explore the link between accelerated placental aging and pregnancy issues like preeclampsia and pre-term birth.

"We aim to see how the predicted age from the epigenetic profile relates to the actual age," Dr. Tarca said. "By identifying any discrepancies, we can better understand the role of placental aging in these diseases."

In addition to the DREAM Challenge, Dr. Tarca's lab is collaborating with Dr. Nardhy Gomez-Lopez's lab at Washington University in St. Louis as well as Wayne State's Dr. Roger Pique-Regi, Professor of Molecular Medicine and Genetics and of Obstetrics and Gynecology, on a project funded by the Burroughs Wellcome Fund to find biomarkers of obstetrical diseases in blood samples using single-cell placenta data. Dr. Gomez-Lopez is a former Center faculty member. The group plans to create machine learning models of pre-term birth by using blood omics data guided by single-cell biology of the placenta.

Single-cell placental data refers to a technique that allows researchers to study gene expression within individual cells in the placenta. This provides more insight into how each type of cell contributes to the overall health of the placenta and helps identify which cells are associated with certain pregnancy complications such as pre-term birth.

"By focusing on biomarkers identified through placenta data, we hope to refine our search and create more reliable models that can be validated across different cohorts," Dr. Tarca said. His studies also include grant proposals that focus on proteomics and machine learning to improve maternal-fetal medicine and omics data analysis. In collaboration with Dr. Kevin Theis, Associate Professor of Biochemistry, Microbiology and Immunology at Wayne State, and Dr. Gomez-Lopez, Dr. Tarca published a paper in *eLife* that highlighted how the vaginal immune proteome could help predict pre-term birth.

He is also working with Wayne State's Office of Women's Health on several clinical studies, which have led to new publications with researchers across Michigan.

Dr. Tarca's work showcases the Center's role in Wayne State's commitment to advancing medical science and improving patient care through data-driven research. His studies address some of the most pressing challenges in obstetrics and contribute to broader fields of medical research.

Faculty Spotlight—Dr. Maik Hüttemann

Adding Precision to Spinal Cord Treatment

Dr. Maik Hüttemann, Professor of Molecular Medicine and Genetics and of Biochemistry, Microbiology, and Immunology, is leading a collaborative effort that could transform how spinal cord injuries are most effectively treated. His team is exploring the ability of innovative, non-invasive technology based on near-infrared light to target the mitochondria – the cell's energy centers but also the main producers of toxic "free radicals," especially under conditions of stress – in the injured spinal cord.

The team's research is driven by a discovery that challenges conventional thinking. Previously, scientists believed that near infrared light activates mitochondrial function, helping cells generate energy. However, Dr. Hüttemann's team found specific wavelengths, particularly at 750 and 950 nanometers, that actually slow down the key mitochondrial enzyme cytochrome c oxidase in mitochondria. This counterintuitive approach might be a game-changer in treating spinal cord injuries.

"The idea with our therapy is that we want to get the patient treated as quickly as we can because, when someone suffers a spinal cord injury, the mitochondria go into overdrive, creating harmful free radicals that cause cells to die," said Dr. Hüttemann. "Our goal is to use infrared light to calm those mitochondria down and prevent further damage."

The non-invasive nature of Dr. Hüttemann's method could be a key advantage for the more than 300,000 people estimated to live with a spinal cord injury in the United States. The light can be applied directly to the site of injury through a special device and deliver immediate results. Unlike traditional drugs that need time to circulate through the bloodstream, this method works on the spot, offering a potentially faster and more targeted response.

Maik Hüttemann, PhD

"Picture a first responder arriving at the scene of a car accident, using this light therapy to treat a spinal cord injury right away," Dr. Hüttemann said. "The sooner we can apply the treatment, the better the chances of minimizing damage."

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Fu Spotlight

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statistics. But here at Wayne State, I have the chance to work alongside experts in family medicine, genetics, and biomedical sciences, which makes my work more impactful and relevant."

At Wayne State, Dr. Fu's research will focus on causal inference and deep learning, two fields that are changing how researchers deal with complex biomedical data.

In causal inference, Dr. Fu is creating new methods to find causal relationships between genes without using traditional experiments, which can be expensive and take a long time. Her work with Mendelian randomization, which uses genetic data to mimic experimental conditions, could give key insights into the genetic causes of diseases like high blood pressure, providing a new way to look at complex biological interactions.

In deep learning, Dr. Fu is building algorithms specifically for genomic data, aiming to map gene regulatory networks as hierarchies of multiple levels. Her method uses graph neural networks to examine these networks at different levels with an increasing resolution, from broad big-picture views down to single genes. She uses the analogy of zooming in on a map from a country's borders to the streets of a city.

Dr. Fu's move to Wayne State also highlights a growing trend in biomedical research: collaboration. Unlike in theoretical mathematics or statistics, where assumptions can be made without real-world data, biomedical research needs people in different fields to work together to ensure that models and algorithms are correct.

"Collaboration is essential in biomedical sciences because the problems are very real and complex," Dr. Fu said. "What seems crucial from a statistical standpoint might not matter as much in a biomedical context, and vice versa. That's why it's so important to work closely with researchers from different disciplines."

Please welcome our incoming Fall 2024 Graduate Students!

MS Genetic Counseling Students

- Chad Adkins (University of Toledo)
- Nikki Coleman-Glasser (Ohio State University)
- Susanna Hagan (University of Michigan)
- Zahra Jaffar (University of Western Ontario)
- Lucy Jennings (Clemson University)
- Jaclyn Melasi (Michigan State University)
- Erica Schafer (Michigan State University)
- Aleksandra Srbovska (University of Guelph)

PhD Molecular Genetics and Genomics Students

- Nevil Khurana, MS (Georgetown University)
- Celestina Klaye, MS (Virginia Commonwealth University)
- Carson Moen (Saginaw Valley State University)
- Kristen Tran (Michigan State University)

MS Molecular Genetics and Genomics Students

- Christina Diez (Lawrence Technical University)
- Courtney Fillmore (Wayne State University)
- Sebastian Morales-Bermudez Espinel (Universidad Peruana Cayetano Heredia)
- Sydney Rudolph (Wayne State University)
- Eboni Sawyer (University of Michigan)

Faculty and Student Honors

Erin Carmany, MS, CGC was awarded the Wayne State University President's Award for Excellence in Teaching.

Ren Zhang, PhD was awarded the 2024 School of Medicine Teaching Award.

Allison Jay, MD was promoted to Adjunct Clinical Professor in March 2024. Dr. Jay is the Director of Cancer Genetics at the Van Elslander Cancer Center in Grosse Pointe.

Maik Hüttemann, PhD was awarded the 2024 Wayne State University Board of Governors Award.

Claire McCarthy-Leo, PhD successfully defended her PhD on June 6, 2024. Dr. McCarthy-Leo was mentored by Dr. Michael Tainsky.

Have an accomplishment to share?

Please contact us at

info@genetics.wayne.edu

Spinal Cord Treatment Innovation cont.

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Collaboration is also a big part of this project, described as a co-principal investigator grant application and currently supported by a $2.76 million grant from the National Institutes of Health. Leading the grant with Dr. Hüttemann is Dr. Moh Malek of Wayne State, and they are also joined by WSU colleagues Dr. Dragana Komnenov and Dr. Dennis Goebel. Outside of Detroit, the Wayne State team is also collaborating with experts from the University of Michigan and the University of Texas.

The team's ambitions aren't limited to spinal cord injuries, either. They're also developing medical devices for brain injuries, targeting conditions like strokes and cardiac arrest, where brain cells are starved of oxygen. Through the startup company Mitovation that Dr. Hüttemann co-founded, they hope to translate their lab work into real-world treatments that could benefit patients.

"We're thrilled to start this next phase. It's been a long journey, but we believe this technology has the potential to make a real difference," Dr. Hüttemann said.

As the research progresses, there's a growing sense of anticipation about how this new approach could transform the way spinal cord injuries and other medical conditions are treated.

Congratulations to

Warlley Cunha, a Molecular Genetics and Genomics PhD student in Dr. Espinosa-Diez's lab, was recently awarded a Histochemical Society 2024 Cornerstone Grant that will support his project, "*Investigating the Role of CASC15 in Vascular Health and CKD Progression.*" This project has the potential to uncover critical insights into the mechanisms driving microvascular remodeling and senescence in CKD and to identify novel therapeutic targets for preventing or mitigating the vascular damage associated with this disease.

Faculty Spotlight—Alexander Gow, PhD

A New Approach to Multiple Sclerosis Research

Dr. Alexander Gow, Professor of Molecular Medicine and Genetics, and of Pediatrics, and of Neurology, believes that the early onset of MS may begin in patients years, or potentially decades, before the symptoms become noticeable.

"We know of disease processes in oligodendrocytes from MS patients that are not directly linked to autoimmunity," Dr. Gow said. "Could these processes contribute to the disease? That is our question."

Dr. Gow is studying the disease's effects on oligodendrocytes, a type of neuroglia that play an important role in the central nervous system by providing support and insulation to axons. By studying oligodendrocyte metabolism and the stress it causes, Dr. Gow aims to provide new insight on the origins and development of MS within patients.

A promising aspect of Dr. Gow's research has been the identification of a protein in oligodendrocytes called Trb3, which might be a potential target for new drug treatments. Dr. Gow's team will test whether Trb3 can reduce disease in oligodendrocytes and will characterize two other proteins that interact with Trb3, known to control metabolism in cells.

"We have identified a protein in oligodendrocytes, called Trb3, that might be a good drug target for this," said Dr. Gow. "In this project, we will test whether Trb3 can reduce disease in oligodendrocytes. We will also characterize two other proteins that interact with Trb3 because they are known to control metabolism in cells."

Dr. Gow will focus on processes involved with oligodendrocyte metabolism and how it may cause a type of damaging stress in the cells. This stress can also be associated indirectly to the activation of inflammatory cells in the brain and, by looking at MS from this new perspective, Dr. Gow and his team may develop a better understanding of how MS begins and advances as well as improved treatments for the disease, thereby improving the lives of people affected by this chronic condition.

Dr. Gow's work is being funded by an award from the National Multiple Sclerosis (MS) Society – part of his ongoing commitment to transforming the medical community's understanding of neurological diseases. The three-year, $644,827 grant, supports Dr. Gow's study on metabolic stress and oligodendrocyte pathophysiology. Dr. Gow, who has been studying genetic diseases since 1990, views this grant as a significant step forward in uncovering the early roots of MS.

Alexander Gow, PhD

Faculty Spotlight—James Granneman, PhD

Collaborative Approach Seeking Breakthroughs in Fat Metabolism

James Granneman, PhD

James Granneman, Professor of Molecular Medicine and Genetics and of Internal Medicine, is leading a group of researchers across multiple Wayne State University departments, to make significant strides in understanding fat metabolism, with potential therapeutic applications for major health issues such as diabetes, obesity, and cancer. He and the other team members are part of the Barber Integrative Metabolic Research Program that is leading innovative projects aimed at harnessing the power of fat tissue for better health outcomes.

The Barber Program, established in December 2023, brings together a diverse team of around 30 PIs, postdocs, and students from multiple institutions. A key feature of these projects is their transdisciplinary nature. "It's university-wide, not just the School of Medicine. I think it's somewhat of a rare beast at Wayne State that we actually have a truly organic collaboration that spans the School of Medicine and College of Liberal Arts and Sciences at Wayne State, and Henry Ford Health System," said Dr. Granneman.

Supported by a philanthropic donation from the late Richard Barber, the program includes cell biologists, physicists, computational biologists, and cancer researchers. Dr. Christopher Kelly, Associate Professor, and Dr. Mindy Huang, Assistant Profesor, from the Department of Physics study the membrane biophysics and molecular dynamics of ABHD5, while Dr. Hyeong-Reh Kim, Professor, and Dr. Jian Wang, Associate Professor, from the Department of Pathology explore its cancer therapy implications. Additionally, Dr. Emilio Mottillo, Associate Scientist of Henry Ford Health and Associate Professor of Physiology at Wayne State University investigates fat metabolism in the liver, with potential applications for treating fatty liver disease.

Currently, the Granneman lab is focused on two NIH-funded projects related to lipid metabolism. The first project investigates the biology of adipose tissue and addresses how new fat cells are formed. Contrary to popular belief, fat tissue plays a crucial role in protecting the body from diabetes by safely storing excess energy. However, when this storage capacity is exceeded, as occurs in obesity, additional fat spills into other tissues, which triggers insulin resistance and diabetes. The importance of fat tissue in metabolic health is highlighted by the fact that individuals who lack fat tissue for genetic reasons cannot store fat energy and are highly prone to developing diabetes.

The Granneman lab aims to identify and understand the different cell types within adipose tissue, especially progenitor cells that can transform into fat cells. These progenitor cells constantly monitor the body for metabolic imbalances and are poised to become new fat cells when needed. Using cutting-edge techniques like single-cell RNA sequencing, genetic tracing, and 3D histochemical analysis, Dr. Granneman's team can study the microscopic signaling processes within fat tissue. This research provides valuable insights into how new fat cells form and function.

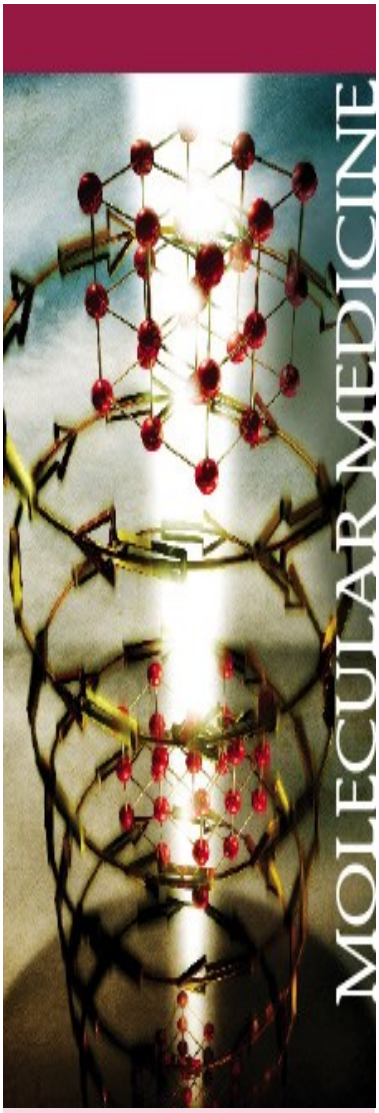
The second project focuses on characterizing lipolysis, the process by which cells break down stored fat to release energy. The team discovered that the protein ABHD5 is a master regulator of lipolysis. Interestingly, ABHD5 lost its enzymatic activity around 500 million years ago but retained its ability to bind lipids, evolving into a receptor that regulates other enzymes.

By conducting chemical screening and computational analyses, the team developed synthetic activators and inhibitors of ABHD5. These compounds can regulate lipolysis in fat tissue as well as other tissues, offering potential therapeutic applications. One exciting element of this research is targeting cancer cell survival pathways, suggesting that these ligands might have anti-cancer properties. Additionally, these synthetic ligands show promise for treating various metabolic disorders.

As Dr. Granneman's collaborative team continues to unravel the complexities of fat metabolism, their work shows great potential for developing new treatments beyond diabetes and obesity, for instance extending to cancer and liver disease, while demonstrating the power of collaborative research.

Come join us for one of the Center's 2024-2025 seminars.

The schedule can be found at *https://genetics.wayne.edu/news-events*



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