THE CHRONOS CHRONICLE:
The Newsletter of the Aging Institute
Winter 2023

Message From the Director

As I write this, the cold reality of a typical Pittsburgh winter is evident. It was just a few short months ago that the trees were turning their usual brilliant autumnal colors. This process of leaf senescence is an annual ritual that teaches us that the biology of senescence and aging play out in many different biological contexts. In that spirit, the work of the Aging Institute is part of the larger ecosystem of aging research on campus.

Each year, our Institute is pleased to facilitate opportunities for us to come together as a community, to listen and learn from each other, and to celebrate all the various ongoing research activities. For the last several years, due to the COVID-19 pandemic, these in-person gatherings have not taken place. As such, it was really a special treat to gather this November for our Annual Research Day. We had an incredible turnout, including more than 60 poster presentations from trainees. These posters explored topics in basic science, work in the clinical and translational sphere, and efforts in population science.

Besides the spirited poster session, attendees heard a special lecture from Richard Hodes, MD, director of the National Institute on Aging. Dr. Hodes' talk was supplemented by a fantastic set of presentations from various University of Pittsburgh/UPMC faculty members. Details and photos of the festivities can be found inside this issue.

While the Annual Aging Institute Research Day represented a highlight for 2022, we are certainly not resting on our laurels. As you can see from what's inside this issue, we've been hard at work at the Aging Institute. In that regard, I hope you enjoy the profiles of some of our new faculty and trainees. We also go in-depth with some new research from the Institute, including the description of a novel pathway that we've named the PITT Pathway — which was published in the prestigious journal, *Nature*. Our faculty have also been incredibly successful in obtaining new research funding, including innovative proposals to generate new, more clinically relevant models for Alzheimer's disease.

I hope you enjoy this installment of our newsletter. It may be winter in Pittsburgh, the leaves may have fallen, and the bears might be hibernating, but as the following pages attest to — we've never been busier!

Toren Finkel, MD, PhD
Director, Aging Institute, University of Pittsburgh/UPMC
Professor of Medicine, Division of Cardiology
G. Nicholas Beckwith III and Dorothy B. Beckwith Chair in Translational Medicine

UPMC LIFE CHANGING MEDICINE
University of Pittsburgh
AGING INSTITUTE
University of Pittsburgh and UPMC

Faculty Spotlight: Shihui Liu, MD, PhD

by Zhihao Sun, PhD, Postdoctoral Associate in the Liu Lab

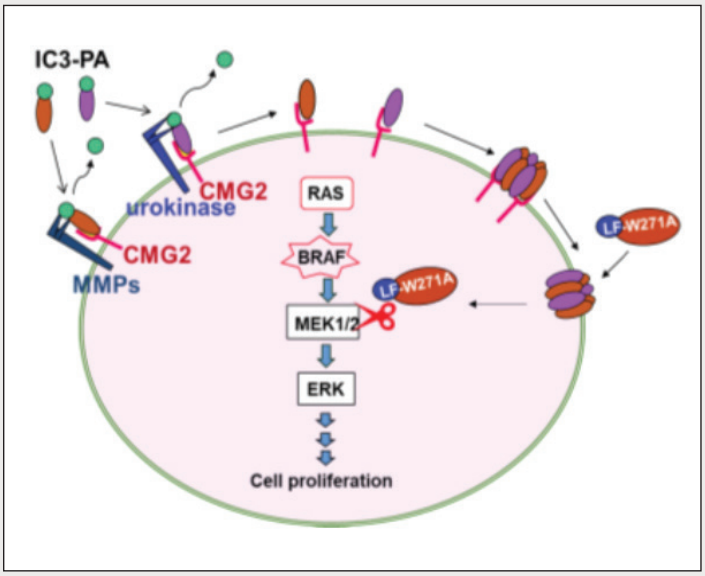
Shihui Liu, MD, PhD, is an associate professor of medicine in the Aging Institute of the University of Pittsburgh/UPMC, with an academic appointment in the Division of Infectious Diseases. His lab focuses on studying the roles of medically important bacterial virulence factors, including anthrax toxins, in bacterial pathogenesis. The Liu Lab investigates how these toxins initiate disease pathology by altering key signal transduction pathways — in particular the RAS and ERK pathways — and then leverages mechanistic insights to develop biological-based therapies for the diseases caused by these pathogens. Dr. Liu and his lab are also reengineering these protein toxins to develop novel anti-cancer drugs with high tumor specificity and to selectively eliminate senescent cells to address aging and diseases of aging.

What motivated you to pursue a career in science?

I have broad interest in all kinds of science — math and physics in particular — which I have had since I was a student in middle school. I even earned awards in math contests at municipal/province levels. At that time, it was my dream to be a mathematician. After taking a biology class, I was fascinated by the amazing biological processes, such as DNA replication, viral infections, and the human immune system and always wondered how it worked. With my increasing interest in biological and biomedical sciences, I decided to go to medical school where I could learn all those things and have the opportunity to practice medicine to improve the lives and health of other people. While in medical school, two of my professors, Dr. Weifeng Chen and Dr. Ji-Sheng Han, had a great impact on my career development. Under their instruction, I first took classes that covered both textbook material and the latest research, which completely expanded my horizon and brought my knowledge up to date. That innovative research addressed the long sought-after questions in the textbook, which inspired me to pursue a career in medical research. After completion of my residency, I continued to pursue my medical research career by obtaining my Master of Infection and Immunity and a PhD in Genetic Engineering.

What are your current research interests?

I have been working on bacterial protein toxins and their roles in pathogenesis for about 20 years, since I joined the National Institutes of Health (NIH). My entire science career has been dedicated to understanding anthrax toxin pathogenesis; my initial work focused on the mechanism of how anthrax lethal toxins gain entry to the cell. After a series of cell biology and biochemistry work, we unmasked the route by which anthrax lethal toxins enter the cell, providing key targets for anthrax toxin therapy. My research focus then shifted to another dimension when I started to investigate anthrax pathogenesis in animal models. By generating multiple genetically engineered mouse models, my group found the key tissue targets responsible for anthrax toxin-induced lethality. We are currently working to determine the molecular mechanisms underlying lethal toxin-induced lethality in animal models and to develop targeted therapeutics to treat patients beyond the late stage of anthrax toxin attack — the "point-of-no-return."



Mode of action of the reengineered anthrax toxin-based MEK inactivator. For detailed information, check our latest publications on PNAS and PNAS Nexus.

In my work on anthrax toxin and other bacterial protein toxins, I am amazed by the power and versatility of the anthrax protein delivery system. While the system is used by the bacterial pathogen, *Bacillus anthracis*, to cause disease, it can also be reengineered to have new features and specificity for good therapeutic purposes. For example, we are interested in modifying this protein delivery system to target KRAS with high specificity in cancer. The system may also be modifiable to deliver tumor neo-antigens to the cytosol of antigen presenting cells to elicit potent anti-tumor immune response.

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Faculty Spotlight: Shihui Liu, MD, PhD

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What challenges and rewards did you have during your transition from being a senior scientist at NIH to an independent principal investigator?

After an initial three years of postdoctoral training in Stephen Leppla's lab at NIH, I worked as an independent group leader in his lab and led my group in the discovery of anthrax toxin pathogenesis. I credit much of my career success to Dr. Leppla due to the great support and freedom he granted me and my group to explore whatever interested me. During this time, I mentored trainees, designed projects, and performed experiments similar to an assistant professor but without worrying about funding. This was a great experience from which I benefited a lot after being an independent PI.

In the transition to Pitt, securing funding for my lab was the first challenge I had. I still remember the anxiety I suffered worrying about funding and the exciting moment when my first and second R01 grants were approved. It was — and is — gratifying and inspiring when our grant applications and publications are recognized by peers. It can also be challenging to balance productivity in research with teaching and mentoring responsibilities. But, it is a highly rewarding and exciting experience to see the maturation and growth of your trainee under your mentorship. By training and supporting young trainees, we form a strong link in a long-running chain, ensuring that the next generation of scientists have all the tools and training they need to keep pushing the boundaries of knowledge.

What are your goals for the future?

It is always exciting to have new findings in science. I truly hope that new knowledge from our basic research can turn into something very useful for patients. Due to the rapid course of anthrax disease, patients usually seek medical assistance when the disease is already in the middle/late stages, making clinical management extremely challenging. Moreover, there is no therapy available to deal with the cellular/tissue damage caused by anthrax lethal toxin, resulting in a mortality rate from systemic anthrax as high as 50%. Recently, we found that disruption of the MEK-ERK pathway by anthrax toxin during anthrax infection can be reactivated by growth factors, such as EGF. One of our future goals is to apply these discoveries to develop an anthrax therapy for the patients who have reached the "point-of-no-return," which is often the case with inhalational anthrax.

We are also working on new therapeutic strategies for cancer. Pancreatic cancer is amongst the cancers with the worst prognoses. Greater than 95% of pancreatic cancers are caused by KRAS mutations, which are notoriously difficult to target therapeutically. We found a bacterial protein toxin (DUF5)

Group photo (left to right): Michael Ewing, MA; Zehua Zuo, MD, PhD; Jie Liu, MD, PhD; Shihui Liu, MD, PhD; and Zhihao Sun, PhD

that can be selectively delivered into tumors using our highly tumor-specific anthrax protein delivery system to inactivate oncogenic KRAS. We hope to develop an anthrax toxin-based tumor-selective KRAS inactivator for treatment of human cancer patients, which is the other future goal of my lab.

What advice do you have for early career scientists?

Early career scientists are important to scientific research. They bring new skills and bold leadership that drives innovative discoveries. To pursue scientific research as a career, you need to truly love science, because it is not possible to do it well without a persistent, long-term effort. As scientists, we need to follow the frontiers of our fields and related fields by reading literature and learning state-of-the-art technology and new approaches. Being a scientist essentially means being a professional question-asker. For scientists, getting answers is often much easier than asking novel, relevant, or appropriate questions. I would encourage early career scientists to spend more time asking critical scientific questions and designing projects to help answer those questions because asking big questions leads to big answers.

It is also important to attend relevant seminars/talks as much as possible to keep your knowledge up to date. Alternatively, there are many excellent related presentations available online, such as the NIH VideoCast. Watching and listening to these presentations is a fast way to learn new knowledge, as well as English for nonnative English speakers. Brains work better in healthy bodies. If you feel overwhelmed, you may find it helpful to sit in a garden and enjoy the views. Taking good care of yourself and maintaining good balance between research and life is the cornerstone for your science career. And finally, always remember, research is fun!

Trainee Spotlight: Nandini Doshi

Nandini Doshi is a trainee under the supervision of Matthew Steinhauser, MD, associate professor of cardiology and deputy director of human translation at the Aging Institute, and has worked in the Steinhauser Lab since May 2022. Doshi is a medical student in the University of Pittsburgh School of Medicine Physician Scientist Training Program (PSTP), a five-year training program for medical students who wish to become successful physician scientists. In the Steinhauser Lab, her research concentrates on elucidating novel immune signatures of resiliency in aging populations, with a focus on individuals undergoing cardiac surgery.

Despite improvements in overall outcomes after cardiac surgery, the proportion of patients who suffer from neurologic morbidity after cardiac surgery remains high. Inflammation has been implicated in causing neurologic complications post-surgery, but the exact molecular mechanisms of this phenomenon are still unknown. In order to interrogate the mechanisms involved, the Steinhauser Lab has created a novel whole blood assay that subjects patients' blood to various perturbations targeting specific aspects of molecular inflammatory and stress response. This *ex vivo* assay of fresh whole blood assesses intrinsic immune responsiveness. Their central hypothesis is that patients who do not experience neurologic morbidity after cardiac surgery — those who exhibit greater resiliency — will have an attenuated, intrinsic pro-inflammatory response to tissue stressors compared to patients who develop post-operative cognitive decline. In addition to this work, Doshi is analyzing electronic medical records of patients evaluated at UPMC to carefully phenotype and characterize patients who exhibit cardiac resilience.

Doshi is originally from the Los Angeles area and received her bachelor's degree from Emory University, where she studied Neuroscience and Behavioral Biology. At Emory, she conducted research pertaining to inter-generational influences of parental stress. Prior to matriculating into the PSTP, Doshi spent two years working at Biogen in Cambridge, Mass., where she supported the upstream process development of various early- and mid-stage biologic programs. She hopes to pursue a career as a physician-scientist. Outside of the lab, Doshi enjoys traveling, exploring Pittsburgh's food scene, and spending time with family and friends.

Join the Aging Institute – We are hiring!

- **Laboratory Research Specialist** - Gurkar Lab
- **Behavioral Research Specialist** – Positions available within the lab of Dr. Rizzo
- **Laboratory Manager** – Positions available within the labs of Drs. Finkel and Rizzo
- **Laboratory Research Specialist and Technician** – Positions available within the labs of Drs. Eisele, Finkel, Gurkar, Li, Parkhitko, Rizzo, and Tan
- **Postdoctoral Associate** – Positions available within the labs of Drs. Liu and Zhu
- **Research Scientist** – Position available within the lab of Dr. Rizzo
- **Senior Research Specialist** – Positions available within the labs of Drs. Eisele, Li, and Parkhitko

Faculty Update: Anne B. Newman, MD, MPH

Anne B. Newman, MD, MPH, clinical director of the Aging Institute, has received the UPMC Endowed Chair in Geroscience for the University of Pittsburgh School of Medicine. She previously served as the Kathryn Detre Chair in Population Science and the Chair of the Department of Epidemiology in the School of Public Health. A professor of epidemiology and medicine, Dr. Newman led a research and training program in the epidemiology of aging for more than 30 years while maintaining a clinical practice in geriatric medicine. As of July 2022, she has transitioned to full time research. Dr. Newman also has the distinction of completing her Bachelor of Science, Master of Public Health, Doctor of Medicine, and clinical training in internal medicine and geriatrics, all at the University of Pittsburgh.

Dr. Newman has conducted several long-term cohort studies of aging, as well as clinical trials designed to reduce disability and improve physical function. One of the cohort studies, the "Study of Health, Aging and Body Composition (Health ABC)," established the contributions of body composition, inflammatory markers, and muscle quality to disability. Disability in older adults can be explained in part by disease and inactivity, but functional decline with aging is apparent even in the healthiest and most active older adults. Muscle aging, with loss of endurance, speed, and strength, is a major contributor. Findings from this study are considered foundational in the field, are widely cited, and have led to new hypotheses about muscle aging and the role of aging biology in functional decline.

Dr. Newman continues to address such questions in one of her current observational cohort studies, "Study of Muscle, Mobility and Aging" (SOMMA). SOMMA is a national, multi-PI R-01 designed to evaluate muscle tissue from biopsy to determine which features predict loss of mobility. It is the first population study of aging to both collect muscle tissue in a large group of older adults and to follow these adults over time to track clinical outcomes. SOMMA's recruitment and examination of 879 men and women over age 70 was successfully completed in January 2022, despite several delays related to the COVID-19 pandemic. In addition to respirometry in fresh muscle biopsies, novel measures include D3 creatine dilution to assess muscle mass, NMR 31P spectroscopy of phosphocreatine recovery after exercise (reflecting adenosine triphosphate regeneration), whole-body MR of body composition, and peak oxygen consumption during a treadmill test. Preliminary analyses of the baseline exam show strong associations of maximal oxidative phosphorylation in muscle with endurance and muscle power. Fiber typing is ongoing. In addition, bulk RNA sequencing is underway, and new assays of single nuclei RNA sequencing and DNA damage are planned to determine the roles of DNA damage and senescence in muscle aging. Repeat biopsies have been proposed in a renewal grant. The study participants are asked to return each year to assess their muscle power, walking speed and endurance, allowing the detection of early changes in performance before the onset of more severe disability and linking aging biology in muscle to clinical outcomes. These findings can be used in the future to plan intervention studies targeting muscle aging.

In 2023, Dr. Newman will launch a new study, "Reducing Inflammation for Greater Health Trial (RIGHT)."

With the support of the UPMC Chair in Geroscience, Dr. Newman plans to develop new clinical trials that address the fundamental biology of aging. In 2023, she will launch a new study, "Reducing Inflammation for Greater Health Trial (RIGHT)," which will test a novel IL-6 antibody, clazakizumab, to block chronic inflammation in older adults. This trial will include clinical outcomes of aging linked to excess IL-6, such as walking speed, fatigability, strength, and cognition. In addition, the trial will bank cells, serum, and plasma to assess potential mechanisms.

In addition to her research, Dr. Newman mentors trainees in epidemiology and medicine. She is currently serving on the National Institute on Aging (NIA) Board of Scientific Counselors, the NIA Clinical Trials Advisory Panel, and the National Scientific Advisory Panel of the American Federation of Aging Research. She completed a four-year term as editor-in-chief of the *Journal of Gerontology: Medical Sciences* in 2020 and remains an associate editor.

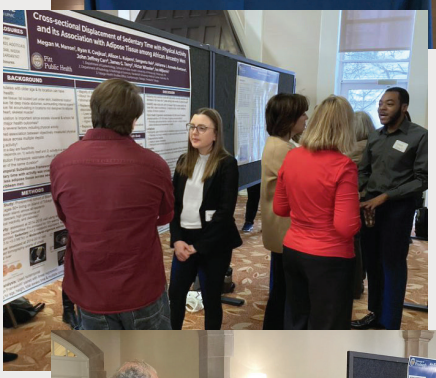
Celebrating Research in Aging

by Toren Finkel, MD, PhD, and Matt Steinhauser, MD

The National Institute on Aging (NIA) is the federal agency that directs the nation's effort on aging research. With an annual budget of more than $4 billion, the NIA funds research that spans work at the level of a single molecule or gene to studies involving aging assessments in large human populations. As such, when you are presented with an opportunity to hear from the Director of the NIA, it's always informative.

As part of the annual Aging Institute Research Day in November, we were given the special opportunity to hear a lecture from Dr. Richard Hodes, the NIA's current director. Dr. Hodes laid out present and future opportunities for innovation, as well as challenges, to the field. He reviewed exciting work taking place across a number of areas in aging research, including senescent cell biology, genetics and biomarkers of aging, the latest results from candidate anti-aging interventions and clinical trials, and his view of areas ripe for future investigation. His talk also highlighted work the NIA is currently undertaking to increase and prioritize diversity and inclusion in aging research.

From the lively question and answer session that followed, it was evident how much the presentation and discussion by Dr. Hodes resonated with the faculty, trainees, students, and staff. Unquestionably, the talk captured the excitement in the field and the growing sense that understanding how and why we age will undoubtably facilitate new treatment strategies to combat a host of age-related diseases.



In addition to Dr. Hodes, we had several distinguished speakers from the University of Pittsburgh:

Babak Razani, MD
Professor of Medicine
Director, Center for Immunometabolism, University of Pittsburgh/UPMC
Chief of Cardiology, Pittsburgh VA Medical Center
"From arsonist to firefighter: Reprogramming macrophages in atherosclerosis and obesity"

Matthew Steinhauser, MD
Associate Professor
UPMC Division of Cardiology, Aging Institute
"Fat, Fasting and the Search for Metabolic Health and Longevity"

J. Timothy Greenamyre, MD, PhD
Love Family Professor and Vice-Chair of Neurology
Director, Pittsburgh Institute for Neurodegenerative Diseases
"Environmental Triggers of Parkinson's Disease"

Karl Herrup, PhD
Professor
Department of Neurobiology
"Alzheimer's Disease 2022: Data and Diatribes"

Caterina Rosano, MD, MPH
Professor, Epidemiology
Vice Chair for Research, Epidemiology
Associate Director for Clinical Translation, Aging Institute
"Brain and Mobility Resilience to Aging: A Story of Music and High Heels"

David Nace, MD, MPH
Chief Medical Officer, UPMC Senior Communities
Chief; Associate Professor of Medicine, Division of Geriatric Medicine
Director, Long Term Care and Flu Programs
University of Pittsburgh School of Medicine
"Shaping the Future of Long Term Care through Pandemic-Driven Innovation"

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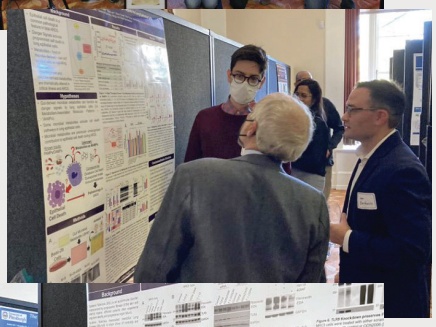
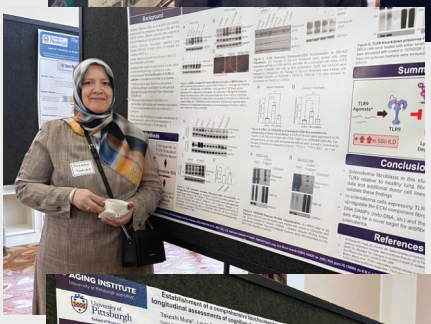
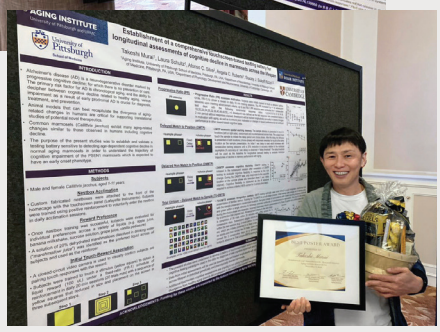
Aging Institute Annual Research Day

More than 150 people attended our Aging Institute Research Day!

There were 66 posters presented and 14 winners:







Basic Science

Faculty: Emily Rocha, PhD
A Lysosomal-based Strategy to Improve Brain Health and Prevent Neurodegeneration in a Rat Model of Parkinson's Disease

Postdoctoral: Zhihao Sun, PhD
Two Classes of Novel Proteins Facilitate Efficient NLRP1b-mediated Pyroptosis

Predoctoral: Thais Rafael Gimaraes, BS
Development of an Age-relevant Patient-derived Neuronal Model to Study Tau Aggregation

Undergraduate: Elise Thyrum
Repurposed Drugs Regulate Abundance of Suppressor of Cytokine Signaling 3 (SOCS3) in Lung Epithelial Cells: Implications for Cellular Senescence and Aging

Staff: Austin Sims, BS
Development of a Nanoparticle Tool to Map Senescent Cells

Clinical and Translational

Faculty: Aditi Gurkar, PhD
Molecular Fingerprinting of Biological Age

Postdoctoral: Emma Baillargeon, PhD, DPT
Dual-Task Changes in Prefrontal Activation and Gait Quality in Older Adults

Predoctoral: Qianjiang Hu, MS
Chronic WNT/ß-catenin Signaling Impairs Mitochondrial Function in Lung Epithelial Cells

Research Scientist: Takeshi Murai, PhD
Establishment of a Comprehensive Touchscreen-based Testing Battery for Longitudinal Assessments of Cognitive Decline in Marmosets Across the Lifespan

Population Research

Faculty: Samaneh Farsijani, PhD
The Relationship Between Protein Intake and Gut Microbiota in Community-dwelling Older Men From the MrOS Study

Postdoctoral: Benjamin Schumacher, PhD
The Association Between Frailty and Perceived Fatigability: The Long Life Family Study

Predoctoral: Sarah Royse, MPH
Unhealthy White Matter Connectivity in African American and Non-Hispanic White Older Adults

Research Scientist: Janelle Christensen, PhD
Older Adult Community Engagement Studios: A Service to Improve Outreach & Recruitment of Older Adults in Your Research

Undergraduate: Emma Gay, BS
Energy Metabolism Related Candidate Gene Association Study of Perceived Physical Fatigability

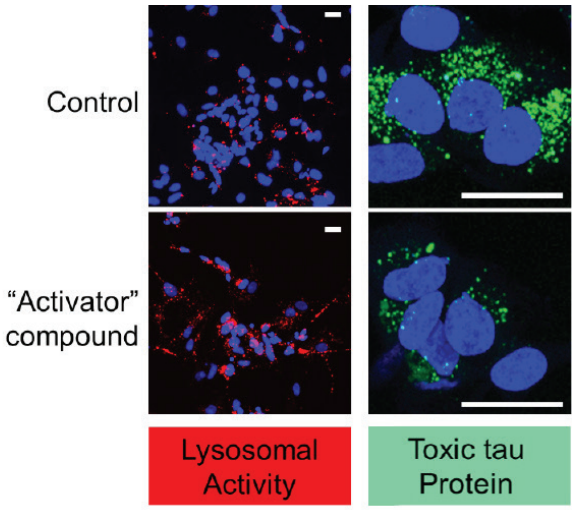
Trainees Receive Research Awards

Travis Lear, PhD, has received a K99 Pathway to Independence Award from the National Institutes of Health (NIH), National Institute on Aging (NIA) to investigate a new pathway that regulates the disposal of protein aggregates associated with neurodegeneration.

Travis Lear, PhD, a postdoctoral researcher at the Aging Institute in the Chen Lab, recently received a K99 career development award from the NIA to study a new mechanism regulating nutrient sensing, which controls the activity of a key cellular component — the lysosome — and may ultimately aid in clearing toxic proteins associated with neurodegenerative diseases.

A common thread among several neurodegenerative diseases is the accumulation of protein in insoluble bundles, known as aggregates. In Alzheimer's disease (AD) and other dementias, the buildup of aggregates of the protein tau results in toxicity to brain cells and plays a direct role in the progression of the disease. Cells naturally have a means to recycle these pathogenic protein aggregates, particularly through the process of autophagy and the cellular organelle, the lysosome.

Autophagy is the process by which the cell identifies and 'eats' damaged proteins or other materials, a process that culminates at the lysosome. The lysosome is a 'recycling bin' of the cell, providing an acidic, enzyme-filled environment that breaks down cellular components, including protein aggregates. Intriguingly, the lysosome itself has been noted to be dysfunctional in many neurodegenerative diseases, such as Parkinson's, Huntington's, and AD, attenuating lysosomal activity and potentially reducing the recycling of protein aggregates. As such, restoration of lysosomal function may be helpful in clearing toxic protein aggregates.



One way that lysosomal activity is controlled is through the ability of a cell to 'sense' the amount and availability of nutrients, such as amino acids. When faced with low nutrient status, the cell up-regulates pathways to augment lysosomal function as part of a recycling effort; whereas, higher nutrient sensing leads to a dampening of autophagy.

An essential cog in this 'sensing' process is the protein mTOR, which integrates nutrient sensing signals from across the cell and serves as a key 'switch' in regulating lysosomal activity. Interestingly, Alzheimer's patients show unusual mTOR activity in their brains, leading to the question of whether aberrant mTOR activity is responsible for dysfunctional lysosomes. There has been much effort toward finding approaches to inhibit mTOR activity, however direct inhibition causes many side effects and can have unintended consequences in other parts of the body. Instead of direct inhibition, Dr. Lear sees potential in inhibiting mTOR by manipulating one of its protein regulators that naturally exist in the cell.

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As the basis for this grant proposal, Dr. Lear investigated a family of inhibitory mTOR regulator proteins to measure if their protein stability was short-lived. Proteins naturally have a 'lifespan' in the cell — which ends with their recycling into component amino acid pieces — and the length of these lifespans varies greatly among different proteins. Short-lived proteins exist for only hours, thus prolonging their period of activity by preventing their destruction, can have immediate effects. Dr. Lear and colleagues discovered an mTOR inhibitor protein that is short-lived and potently inhibits mTOR activity. Further, the expression of this mTOR inhibitor protein decreased tau protein in neuronal cell culture. By using the high-throughput screening technology at the Small Molecule Therapeutic Center of the Aging Institute, the team uncovered novel small molecule 'activators' of the mTOR inhibitor protein; these agents prolong the lifespan of mTOR, decrease aggregate protein levels, and enhance lysosomal activity in neuronal cells. In addition, Dr. Lear and his colleagues uncovered the destruction mechanism by which the mTOR inhibitor protein is destroyed and found that by targeting the key destroyer protein, they could extend the lifespan of the mTOR inhibitor protein.

Collectively, this grant will build on Dr. Lear's preliminary work and investigate both genetic and pharmacological approaches to inhibiting mTOR activity as a strategy to augment lysosomal activity in models of Alzheimer's disease. Investigation of this regulatory pathway will provide new understanding of how nutrient sensing regulation affects recycling of protein aggregates and may provide new targets for drug development for dementias.

William Dion, MS, third-year PhD candidate in Integrative Systems Biology at the University of Pittsburgh School of Medicine and member of Dr. Bokai Zhu's Laboratory at the Aging Institute, was recently awarded the Diana Jacobs Kalman/AFAR Scholarship for Research in the Biology of Aging from the American Federation for Aging Research (AFAR) to pursue his research project, "Nuclear speckle liquid-liquid phase separation dynamics in senescence and aging."

Dion is currently mentored by Bokai Zhu, PhD, assistant professor in the Division of Endocrinology & Metabolism at the University of Pittsburgh School of Medicine and the Aging Institute. Dr. Zhu and his lab are interested in chronobiology — the study of biological clocks and rhythms — with a particular focus on the 12-hour biological clock, which plays a central role in managing protein homeostasis, also called proteostasis. The Zhu Lab hypothesizes that this clock deteriorates over the course of aging and can lead to age-related diseases.

Dion hopes to further investigate this hypothesis with his AFAR research project award and anticipates that this research project will exhibit the importance of ultradian biological rhythms and help to uncover how the 12-hour clock is altered as we age. In particular, Dion will concentrate on one specific piece of this 12-hour clock, the nuclear speckle.

As part of his work in the Zhu Lab, Dion previously helped to unveil the rhythms of nuclear speckle shape as essential to proteostasis and now studies how these rhythms change during cellular senescence, or the arrest of the cell cycle. The accumulation of senescent cells is associated with aging and age-related diseases. Dr. Zhu and his lab hypothesize that cellular senescence and associated age-related diseases are a result of disrupted 12-hour rhythms.

In addition to his work in the Zhu Lab, Dion is currently supported by a T32 through the Center for Sleep and Circadian Science at the University of Pittsburgh School of Medicine. He received a Bachelor of Science from Michigan State University and a Master of Science from Michigan Technological University.

UPMC Hillman Cancer Center Academy

Hillman Academy

Over the summer of 2022, the Aging Institute had the pleasure of hosting three students from UPMC Hillman Cancer Center Academy, an award-winning immersive and experiential learning program for high school and undergraduate students. Faculty members Beibei (Bill) Chen, PhD; Yuan Liu, PhD; Matthew Steinhauser, MD; and Xiaojun (Jay) Tan, PhD, and their labs spent the summer mentoring these high school students as they completed research projects in the laboratories at the Aging Institute, developed their scientific and technical skills, and learned about educational and career opportunities in STEM fields. In addition to providing students with a unique opportunity, this program is also an opportunity for trainees and faculty to gain experience in teaching, mentorship, and science communication. You can find more information about the Hillman Academy and Aging Institute training for high school and undergraduate students on our website. Below, a few of the Hillman Academy mentors from the Aging Institute share their experiences in mentoring from the summer and what it takes to get the most from a mentor/mentee relationship.

Pictured, left to right: Yuan Liu, PhD; Hillman Academy students: Elise Chu, Franco Alvarez, Tomi Olaore; Travis Lear, PhD; Áine Boudreau, BS; Qing Cao, MMed

Tânia Amorim, PhD — *Postdoctoral Associate, Steinhauser Lab*

During the summer, the Steinhauser Lab hosted Franco Alvarez, a high school student interested in pursuing higher education in research and medicine. Franco joined our lab for an eight-week program to expand his knowledge on research and laboratory skills. The TDX program complements our lab vision to support mentorship, enhance science literacy, and disseminate our work to a broader audience.

Franco learned about research methods through hands-on activities. With our guidance, he learned how to read scientific papers, create a hypothesis, and design experiments. He also implemented his own research project and performed experiments to investigate the effects of bioactive metabolites on osteoblast differentiation. In addition, Franco attended our group meetings and was involved in our weekly scientific discussions.

At the end of the program, Franco presented his project to researchers from the Aging Institute and UPMC Hillman Cancer Center. We believe that his summer in our lab helped him gain a better understanding of how research labs operate, and we hope this experience fosters an interest in pursuing a career in science.

Áine Boudreau, BS — *Laboratory Research Technician, Chen Lab*

I was excited to participate in the Hillman Academy program as a mentor because I volunteered in a UPMC/Pitt lab one summer during college. Both the PI and the tech with whom I worked were super nice and I learned a lot. I enjoyed seeing my mentee's enthusiasm when learning new techniques and putting those new skills to use. I also enjoyed the challenge of condensing the necessary information for our project into something [hopefully] comprehensible for a high school student.

Patience, listening, asking for clarification, and enthusiasm on the part of both the mentor and mentee are essential to a good mentoring experience. Also, for the mentor, it's important to remember what your level of understanding was like when you were in your mentee's position, so you can provide explanations at their level. Also, if while volunteering or interning in a lab, you find yourself with some free time, ask if there's anything else you can do or help with. It's a good way to learn more techniques and gain experience.

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UPMC Hillman Cancer Center Academy *(continued)*

Travis Lear, PhD — *Postdoctoral Associate, Chen Lab*

This year was my first time with the Hillman Academy program. I believe mentoring roles are excellent opportunities for teaching, learning, and growth that ultimately benefits both the mentee and the mentor. One benefit of these summer programs is that trainees in high school or undergraduate programs have the free time to really focus in on a research project and improve their skills. Also, it gives the mentors a chance to focus and improve their own mentoring while making research progress. The added help in the lab is a great benefit!

Seeing our mentee's (Elise Chu) growth and skill over the summer was one of the most rewarding experiences. When Elise started in the lab, she had limited experience with wet-lab biomedical research, but by the end, she was confidently collecting and processing cells to run protein gels, conducting cell experiments, and organizing her data in notebooks and digitally. By the end of the program, she was a part of the lab and project, and we were sad she had to go!

Some of the best experiences for me in mentoring Elise were those moments when things 'clicked' and an experiment or concept suddenly made sense. Those leaps helped give her ownership over the project, and it was a delight to see her suggest next steps forward. Looking at the summer as a whole, I think one of the most impactful experiences for Elise was when she presented her project to the whole group. She even had one of her high school teachers watching on the Zoom feed, able to ask questions. That moment of putting it all together and sharing a tangible result with your colleagues and mentors is a great experience.

Also, I was fortunate to have a co-mentor for Elise in my lab-mate, Áine Boudreau. Áine is a talented research technician in our lab, and I have been fortunate to serve as a bit of a mentor for her in our research projects. So, I had the added bonus of seeing Áine's mentoring skills in action as well, hopefully continuing the cycle of mentee to mentor.

Clear communication and encouragement are important factors for effective mentor/mentee experiences, especially in biomedical research. One of the benefits of academic research is being on the cutting-edge of knowledge, but because of that, the learning curve can be very steep and intimidating. I think by focusing on clear and specific communication, one can circumvent a lot of these challenges. Additionally, I try to provide encouragement and perspective to mentees. Another challenging aspect of biomedical research is that it is very easy for experiments to not work out. But a mentor can help avoid this by providing encouragement and trying to untangle the reason why something didn't work as planned. Dr. Bill Chen, my mentor, always helped me and others learn something from our "failed" experiments and encouraged us to keep going, and when things finally worked out, his enthusiasm made you feel like you hit a home run. Together I think these traits of communication and encouragement are necessities for biomedical mentors.

I think other key skills for future scientists are organization, networking, and perseverance. Without a way to organize, it is easy to get swallowed by your ideas, data, and results. Science is a team sport! Networking leads to some great personal and scientific connections that can give you ideas and viewpoints you would never have considered. And finally, perseverance—as science is a marathon not a sprint. There are a lot of bumps along the way, and it can be tough. Hang in there, and research will fall into place.

This is a great program that allows some truly talented students to get hands-on research experience, and I'm happy to participate in it!

Xiaojun (Jay) Tan, PhD — *Assistant Professor, Cell Biology & Aging Institute*

Mentoring is an important aspect of my career. Helping students achieve their goals is a great pleasure to me. I have had two Hillman Academy students in the past three years. Both were very successful in their summer projects, which I believe helped them when they moved to the next steps of their careers. One went to the University of Pennsylvania for college, and the other graduated early from high school to start college.

In general, laboratory research is challenging for high school students. It requires students to actively learn completely new skills, to solve completely new problems they have never encountered in their lives, and to do so in a completely new environment. The entire summer program is only two months. One of my previous students spent the first month struggling with the first experiment. She was very stressed, but she persisted and kept trying her best. Finally, the problem was solved. She then quickly finished all the follow-up experiments of that project. Her final oral presentation was wonderful, and she received one of the very few awards out of 75 students. She also presented her work to other local scientific communities where it was recognized with multiple additional awards.

There are several elements to a good mentor and mentee relationship. The student's motivation is the most important. It is also important to communicate, including through daily informal communications and weekly formal meetings, and to make sure students clearly understand tasks and expectations. Research is about problem solving. Think independently, analyze carefully, try your best, and be persistent. Failure is the daily routine for scientists. Mentoring and teaching are important for STEM careers. The Hillman Academy program provides a mentoring opportunity not only for junior faculty members but for our trainees as well.

University of Pittsburgh and UPMC

AGING INSTITUTE RESEARCH SEMINAR SERIES

Visiting Speakers, 2022 - 2023

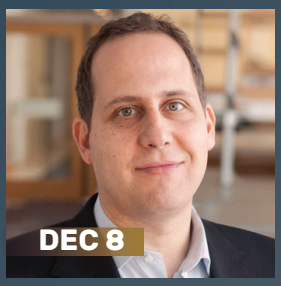
2nd Thursday of the Month | 4:00 pm - 5:00 pm

Bridgeside Point 1 | 100 Technology Drive | 5th Floor Conference Room

Zoom link: https://pitt.zoom.us/j/99688230409

Yousin Suh, PhD

Charles and Marie Robertson
Professor of Reproductive Sciences in Obstetrics and Gynecology
Professor of Genetics and Development
Director, Reproductive Aging
Columbia University



Paul Cohen, MD, PhD

Albert Resnick, MD, Associate Professor
Senior Attending Physician
Rockefeller University

Li Gan, PhD

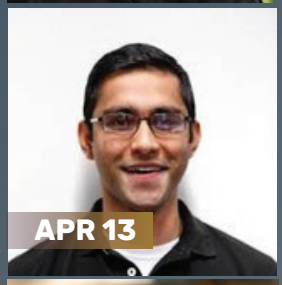
Director of the Helen and Robert Appel Alzheimer's Disease Research Institute and the Burton P. and Judith B. Resnick Distinguished Professor in Neurodegenerative Diseases
Cornell University

Richard Youle, PhD

Senior Investigator in Biochemistry
National Institute of Neurological Disorders and Stroke (NINDS)

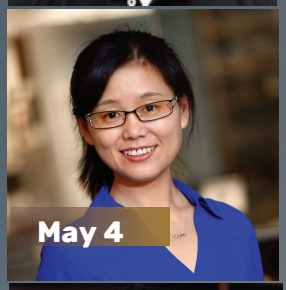
Matt Kaeberlein, PhD

Professor| Director, Healthy Aging and Longevity Research Institute
Director, Biological Mechanisms of Health Aging Training Program
Co-Director, Dog Aging Program
University of Washington



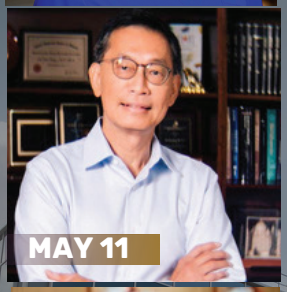
Vivek Philip, PhD

Director, Biostatistics and Technologies, Computational Sciences
The Jackson Laboratory



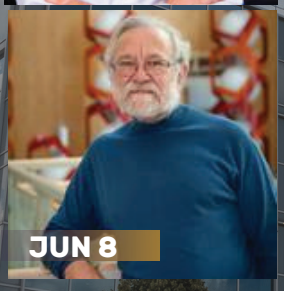
Special Seminar
Meng Wang, PhD

Janelia Senior Group Leader
Howard Hughes Medical Institute



Chi Van Dang, MD, PhD

Professor, Molecular & Cellular Oncogenesis Program, Ellen and Ronald Caplan Cancer Center
Scientific Director of the Ludwig Institute for Cancer Research
Strategic Advisor to the President
The Wistar Institute
Location: To Be Announced



Peter Walter, PhD

Distinguished Professor Emeritus
Biochemistry and Biophysics
Howard Hughes Investigator
Director, Bay Area Institute of Science
Altos Lab
University California, San Francisco
Location to be Announced

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University of Pittsburgh | Department of Medicine School of Medicine | UPMC LIFE CHANGING MEDICINE

A Chance to Change Lives

by Aditi Gurkar, PhD

The Chance to Change Lives Foundation (CCL-US) is a non-profit organization based in Pittsburgh with a "pay-it-forward" vision to mentor and support the next generation of leaders and knowledge creators in Science, Technology, Engineering, and Mathematics (STEM) fields. The organization was founded with a mission to support high impact experiential learning experiences for students, especially from underrepresented groups, to prepare them for 21st century research and development careers in STEM disciplines.

The demands of 21st century jobs will be multi-disciplinary, multi-modal, and multi-dimensional, and a diverse workforce is vital to meet those demands. According to a 2021 report by the American Institute of Physics on "*Building America's Workforce*," the development of an inclusive and diverse workforce in STEM fields is cited as not only important to "boost the innovation and productivity of science and technology" but is crucial to maintain America's global influence in these fields. We strongly believe that diversity is the strength of this nation, and our vision is to empower researchers committed to providing invaluable training and learning experiences for students to become future leaders in STEM fields.

Empowering Future STEM Leaders

Within the first six months of its operations, CCL-US launched its inaugural call for proposals from faculty members supporting undergraduate research in STEM disciplines. These grants are designed to provide support and mentorship for undergraduate students or recent graduates working on innovative research projects in STEM fields. Dr. Rama Bala, president and CEO of the CCL-US Foundation, recognizes the positive impact such undergraduate research can have in not only training the next generation of the workforce in the cutting-edge fields of science, technology, and medicine, but also in promoting an inclusive and diverse community of researchers.

"We are thrilled to support the work of faculty members like Dr. Aditi Gurkar of Pitt's Aging Institute because of the valuable and enriching experiences that students and recent graduates receive through one-on-one interaction with Dr. Gurkar and her team," explains Dr. Bala.

Currently, the partnership between CCL-US and the Gurkar Lab at the Aging Institute supports Austin Sims. Sims recently graduated from the University of Pittsburgh with a Bachelor of Science in Biomedical Engineering. Unfortunately, due to the pandemic, his initial research experience in the Gurkar Lab was cut short and left him unsure of whether he wanted to stay in science. With support from CCL-US, Sims is now back in the lab and reinvigorated about his future in STEM.

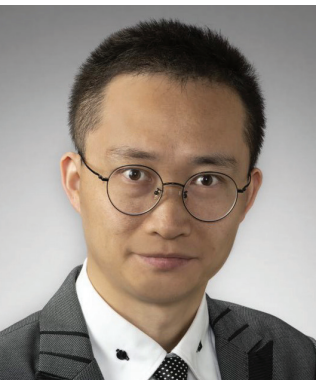
Rama Bala, PhD, and Austin Sims, BS

"It's refreshing to work in person again, and I feel encouraged to continue my career in science. Thank you to the CCL organization for the opportunity. Contributing to aging research has always been my ambition, and I'm happy to be a part of the Aging Institute," says Sims. He hopes to continue his passion and go to graduate school to get his PhD in the biology of aging.

Dr. Bala is a physicist, professor, scholar, author, educator, and mentor. Inspired by her own journey from humble beginnings, Dr. Bala's vision is to make research and education accessible to all. In particular, she has dedicated herself to making that vision a reality, especially for underrepresented groups in STEM fields. She has more than 20 years of working in academia — most recently as a full professor of physics at Roanoke College — and has taught physics and nanotechnology courses at Harvard University, Stanford University, Georgetown University, and James Madison University. Dr. Bala uses a variety of pedagogical methods and active learning tools to promote student engagement in her classes. Her areas of specialization are quantum physics and nanoscience, including the study of magnetic properties of nanocrystalline oxides, 2D materials and nanotubes, and spectroscopy of minerals on Mars. She is also active in empowering female and underrepresented minority students to pursue and thrive in physics and other STEM fields. Dr. Bala is regularly invited to give presentations on nanotechnology and STEM education at community events in order to make science publicly accessible and to promote public engagement and enthusiasm in science. Her passions for empowering underrepresented minorities and for quantum physics and its connection to other STEM fields are equaled by her passion for Indian classical music.

Highlighted Manuscripts at the Aging Institute

Xiaojun (Jay) Tan, PhD, and **Toren Finkel, MD, PhD** – Published Manuscript in *Nature*



Xiaojun (Jay) Tan, PhD, assistant professor of cell biology at the Aging Institute, recently published a study, "A Phosphoinositide Signaling Pathway Mediates Rapid Lysosomal Repair," in *Nature*, in collaboration with Toren Finkel, MD, PhD, distinguished professor of medicine and director of the Aging Institute. In this study, Drs. Tan and Finkel discovered an essential mechanism for rapid lysosomal repair, which they named the "PITT" pathway for **p**hosphoinositide-**i**nitiated membrane **t**ethering and lipid **t**ransport.

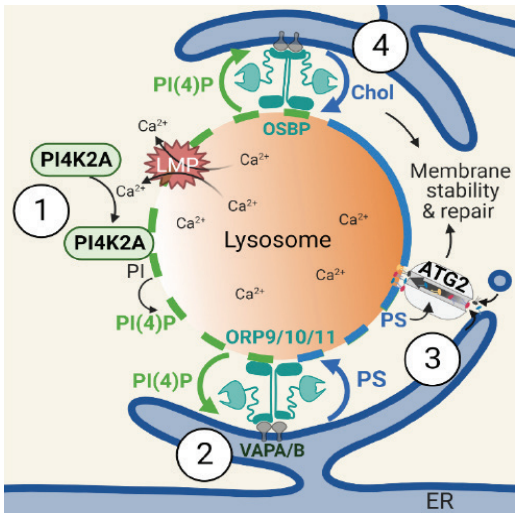
As an important hydrolysis system in animal cells, lysosomes are essential for the timely removal of damaged proteins and organelles, as well as endocytosed pathogens — in addition to routine macromolecule degradation, nutrient sensing, and growth signaling. There is growing evidence that lysosomal damage is involved in aging and the development of age-related diseases, while many long-lived animal models show increased lysosomal activity. Thus, maintaining lysosomal quality and activity is essential for health and longevity. Despite these discoveries, the search for cellular mechanisms for lysosomal quality control only began recently, and essential mechanisms of rapid lysosomal repair are still unknown.

To search for such mechanisms, Dr. Tan designed a proteomic approach to identify proteins selectively recruited to damaged lysosomes. He anchored a biotin ligase TurboID to the lysosomal surface to rapidly label and purify lysosomal surface proteins. Through mass spectrometry analysis, Drs. Tan and Finkel found that multiple proteins associated with Phosphatidylinositol 4-phosphate (PI4P) lipid signaling were enriched on the surface of damaged lysosomes, suggesting initiation of a new PI4P signaling pathway on damaged lysosomes.

The authors found that damaged lysosomes rapidly recruit an enzyme called PI4K2A that generates PI4P as a lipid messenger on the lysosomal surface. PI4P further recruits another family of proteins called ORPs that simultaneously bind to lysosomal PI4P and the endoplasmic reticulum (ER) membrane, driving extensive membrane tethering between the ER.

At membrane contact sites, the ORP proteins mediate robust lipid exchange between the ER and damaged lysosomes, which converts lysosomal PI4P into cholesterol and phosphatidylserine (PS). Cholesterol can, by itself, improve the stability and rigidity of lysosomal membrane. However, in the absence of cholesterol, enrichment of PS on lysosomal membranes promotes lysosomal repair.

Additional screening led to the discovery that the large-scale lipid transporter ATG2 can be activated by PS on lysosomes and plays a key role in lysosomal repair. ATG2 acts as a bridge connecting two organelles and transports large amounts of lipids to damaged lysosomes through its hydrophobic tunnel, which patches lysosomal pores. ATG2 has an established role in autophagosome membrane expansion through lipid delivery. This new function for ATG2 in rapid lysosomal repair resembles its previously known role in autophagy, however, the two functions are independent of one another.



The PITT pathway: phosphoinositide-initiated membrane tethering and lipid transport. Damaged lysosomes are rapidly repaired by a new lipid signaling pathway that drives extensive endoplasmic reticulum-lysosome membrane tethering and subsequent lysosomal lipid transport.

The PITT pathway appears to be a major pathway for rapid lysosome repair in pathophysiological conditions. It can be activated by a diverse set of disease-related lysosomal damaging conditions, suggesting that it is a general mechanism for lysosomal quality control. For example, loss of the PITT pathway can exacerbate the spread of tau fibers, a critical step in the progression of Alzheimer's disease. Lack of the PITT pathway also increases cellular accumulation of lipofuscin, a pathological feature of senescent lysosomes and a known hallmark of aging. In mouse models and human patients, the deletion of PI4K2A, the first key enzyme of the PITT pathway, leads to severe neurodegeneration and premature aging.

The discovery of the PITT pathway is an important step toward better understanding of human aging and diseases associated with lysosomal dysfunction. Dr. Tan is currently searching for small molecule activators of the PITT pathway and developing mouse models to explore the impact of the PITT pathway *in vivo*.

Tan JX, Finkel T. A phosphoinositide signalling pathway mediates rapid lysosomal repair. *Nature*. 2022 Sep; 609(7928): 815-821. doi: 10.1038/s41586-022-05164-4. Epub 2022 Sep 7. PMID: 36071159; PMCID: AI5291805.

Highlighted Grants at the Aging Institute

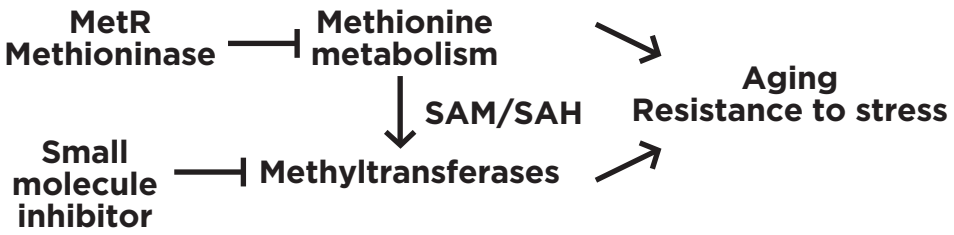
Andrey Parkhitko, PhD, was awarded an R35 MIRA grant to investigate crosstalk between methionine metabolism and methyltransferases in healthy and disease states.

Dr. Parkhitko hypothesizes that methyltransferases provide resistance to stress and, as a result, are responsible for the mechanisms by which methionine metabolism regulates essential cellular processes.

Andrey Parkhitko, PhD, assistant professor of endocrinology and metabolism at the Aging Institute, received a new five-year, R35 Maximizing Investigators' Research Award (MIRA) for Early Stage Investigators from the National Institute of General Medical Sciences to investigate crosstalk — when biological outputs are affected by the integration of cellular signals from multiple pathways — between methionine metabolism and methyltransferases in healthy and disease states.

Methionine metabolism is a central regulator of protein synthesis, mitochondrial function, antioxidant defense, autophagy, and other critical cellular processes. Tightly regulated flux via the methionine metabolism pathway is essential for healthy cellular function. Not surprisingly, an imbalance in this fundamental metabolic pathway has been attributed to numerous diseases, including cancer, obesity, neurodegeneration, and aging. Yet, the molecular link between alterations in methionine availability and dysregulation of downstream cellular processes remains obscure.

Methionine and Adenosine triphosphate are the sole precursors for production of the methyl donor S-adenosylmethionine, the principal and rate-limiting methyl donor for methyltransferases, which catalyze a variety of methylation reactions via the transfer of methyl groups onto different substrates. Although alterations of methionine metabolism have been observed with aging or different diseases, it is not known which downstream methyltransferases link methionine metabolism to the development of these pathological conditions and what mediates the specificity of this interaction.



To answer this question and to explore crosstalk between methionine metabolism, methyltransferases, and their downstream molecular processes, the Parkhitko Laboratory uses *Drosophila* as a model system. Resistance to stress is one of the conserved characzstics of methionine restriction across different species. In preliminary work, the lab identified several arginine-specific methyltransferases catalyzing the methylation of arginine residues within proteins, which extended survival by more than 100% in flies undergoing starvation, an effect similar in magnitude to that of methionine restriction. In the R35 MIRA grant proposal, Dr. Parkhitko hypothesizes that methyltransferases provide resistance to stress and, as a result, are responsible for the mechanisms by which methionine metabolism regulates essential cellular processes. An important corollary of this hypothesis is that targeting these methyltransferases is an attractive therapeutic strategy for different pathological conditions.

During the next several years, the Parkhitko Laboratory will explore mechanisms of crosstalk between methyltransferases and methionine metabolism in different organs, identify prospective downstream targets of key methyltransferases, and test how these methyltransferases affect functional responses to stresses, such as aging. This project holds promise to identify *druggable* targets — targets which are viable for modulation in the drug discovery process — relevant to multiple human pathologies associated with dysregulated methionine metabolism, including cancer, obesity, neurodegeneration, and aging.

Highlighted Grants at the Aging Institute

Stacey J. Sukoff Rizzo, PhD, received an award from the National Institute on Aging to investigate primate-specific mechanisms that contribute to the pathogenesis of Alzheimer's disease.

Stacey J. Sukoff Rizzo, PhD, associate professor of neurobiology at the Aging Institute, received a new five-year, $32.5 million U19 award from the National Institute on Aging to investigate primate-specific mechanisms that contribute to the pathogenesis of Alzheimer's disease. Dr. Rizzo will serve as principal investigator in collaboration with co-principal investigators Drs. Afonso Silva, PhD, of the University of Pittsburgh Brain Institute, and Gregory Carter, PhD, of The Jackson Laboratory. The award consists of three integrated research projects which will study genetic mutations that lead to early onset Alzheimer's disease, as well as the more common form of sporadic, late onset Alzheimer's disease.

Alzheimer's disease (AD) is a devastating neurodegenerative disorder affecting nearly 30 million individuals worldwide. The prevalence of AD is expected to increase exponentially over the next decades, and there is currently no way to stop, cure, or prevent the disease.

In order to better understand AD, model systems that can recapitulate the human disease are critical. Features of AD include amyloid plaques and tau tangles in the brain, as well as neurodegeneration, a shrinking of key brain areas related to memory loss and dementia. Non-human primate models, such as the marmoset, exhibit similar changes as they age.

While rodent models can be genetically engineered to mirror facets of AD and have provided critical insights into the disease process, several gaps between rodent and human remain, which is critical for cognitive function. As the prefrontal cortex is a major focus of these studies, marmosets, which are non-human primates with a prefrontal cortex, provide an ideal alternative to rodent models and will be used in this study. This new award will provide funds to develop, characterize, and validate marmoset models of AD with similar genetics to human patients.

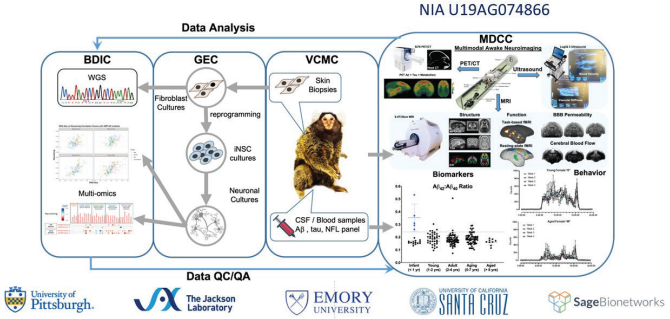
The marmosets will be studied using the same assessments used to diagnose AD in human patients, including non-invasive blood biomarkers, MRI and PET neuroimaging, and comprehensive cognitive assessments for learning and memory, using touchscreen devices. In addition, the marmosets will be tracked from birth and throughout their lifespan, which will allow close monitoring for the earliest changes that may indicate AD.

These models will enable the investigation of the underlying cellular and molecular root causes of the pathogenesis and progression of AD and will support future translational studies. Importantly, the simultaneous assessment of genetic, molecular, functional, behavioral, and pathological phenotypes in marmosets will provide translatable knowledge of the origins and progression of AD in human populations.

These projects will be supported by five research cores focused on project administration, bioinformatics, genetic engineering, multimodal disease characterization, and veterinary and colony management. These cores will integrate marmoset and human genomic signatures and disseminate data and resources to the greater research community in line with a commitment to open science. As marmosets have many similar biological processes to humans, this award presents an important opportunity to better understand the primate-specific mechanisms that contribute to Alzheimer's disease and to evaluate next steps in how to stop, cure, and fully prevent the disease.

U19 – Development, Characterization, and Validation of Marmoset Models of Alzheimer's Disease: MARMO-AD

NIA U19AG074866



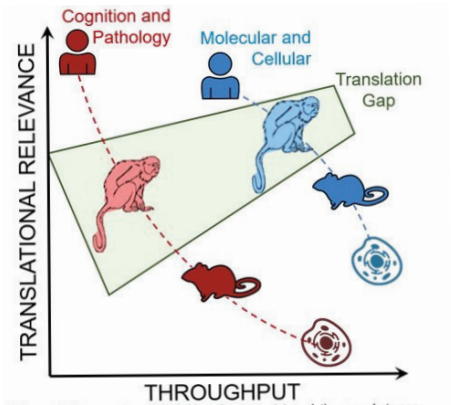


Figure 1. Marmoset models bridge the current translation gap between human studies and cell and rodent models of AD. Establishment of marmoset models of aging and AD will enable robust and reliable mapping of cognitive and molecular outcomes across species.

Additional **New Grants** at the Aging Institute

Principal Investigator	Grant Title	Grant Type	Sponsor
Finkel, Toren, Chen, Beibei (Bill), and Liu, Yuan	Identifying novel molecular degraders and stabilizers		Generian Pharmaceuticals, Inc.
Finkel, Toren, Chen, Beibei (Bill), and Liu, Yuan	Small molecules that act as degraders of membrane surface proteins		Generian Pharmaceuticals, Inc.
Ghosh-Choudhary, Shohini	*In vitro* and *in vivo* biology of telomere stress induced senescence	F30	National Institutes of Health
Gurkar, Aditi	Nanoscale diagnostic tool to detect senescence		National Academy of Sciences
Zhu, Bokai	Ultradian to circadian transcriptome reprogramming underlies liver aging	R21	National Institutes of Health

Co-Investigator	Grant Title	Grant Type	Sponsor
Chen, Beibei (Bill)	Clinical-translational studies in skin, lung, and vascular complications in systemic sclerosis	P50	National Institutes of Health
Finkel, Toren and Steinhauser, Matthew	An endothelial-fibroblast axis connecting senescence to amino acid metabolism for control of vascular stiffness in PA	R01	National Institutes of Health/ Baylor College of Medicine
Zhu, Bokai	Metabolic impacts of Type II interferon signals in obesity	R01	National Institutes of Health/ Baylor College of Medicine

Thank You from the Aging Institute Team

Contact the Aging Institute

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