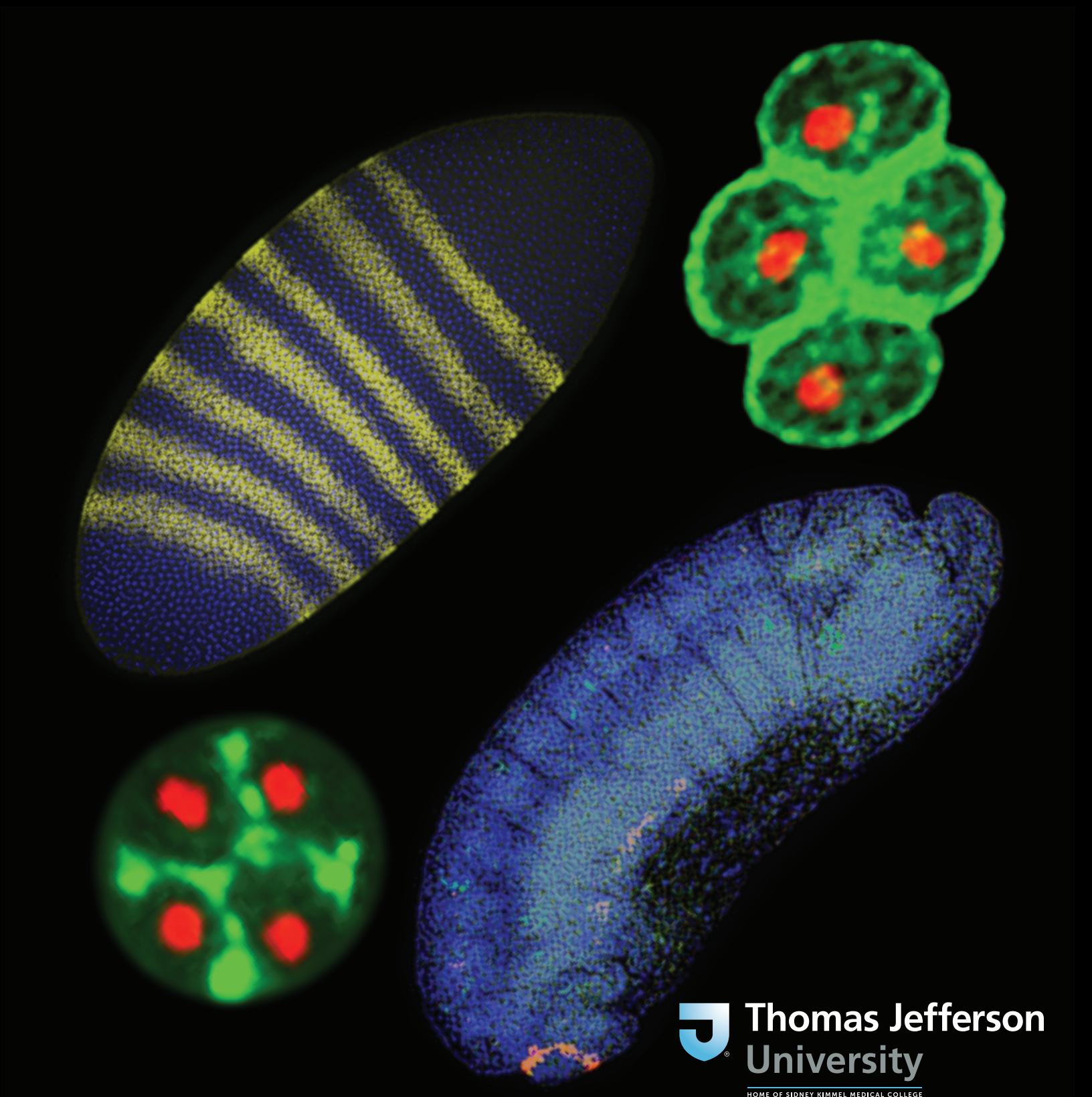
SIDNEY KIMMEL MEDICAL COLLEGE AT THOMAS JEFFERSON UNIVERSITY

IN THE LOOP

DEPARTMENT OF BIOCHEMISTRY & MOLECULAR BIOLOGY | FALL 2025



Thomas Jefferson University

HOME OF SIDNEY KIMMEL MEDICAL COLLEGE

From the Chair

As we share our Fall 2025 newsletter, our Department enters its third century. We began in 1824 when Jacob Green founded the Department of Chemistry, Mineralogy, and Pharmacy at George McClellan's new medical college. Recently, I have found it increasingly valuable to think about how the Department has achieved centuries of stability. Over the course of 18 different Chairs, and 200+ years, our Department has always found a pathway to success, despite whatever headwinds it faced at the time. While today's headwinds are objectively strong, our Department is thriving, primarily because of the resilience of my remarkable colleagues and their teams.

As a scientist, I feel compelled to provide some data supporting these claims. My immediate predecessor as Chair, Jeffrey Benovic, PhD, took the Department from a ranking of #84 among comparable departments at the 148 allopathic medical colleges in the U.S., to #45, during his twelve-year tenure. Simultaneously, research funding in the Department rose from $1.4M to $3.9M under Jeff's leadership. Since I became Chair in 2017, our Departmental ranking has continued to rise, and we are now at #19 in the U.S., and for 2025, we will have $15.2M in research funding. For comparison, the Medical College itself has remained relatively stationary over this period, with research funding hovering at ~$68M from 2006-2025. Our current Departmental ranking of #19 among 148 biochemistry departments places us ahead of venerable institutions like Harvard, Stanford, University of Pennsylvania, Cornell, Dartmouth, Duke, UCLA, Ohio State University, and NYU. (The Blue Ridge Institute is the premier rating agency for academic departments in allopathic medical colleges, and the numbers I am providing are based largely on their analysis.)

Our explosive growth in research funding and ranking is a direct reflection of the science we do. What we are most proud of, and what gives us the best indication that we are making a substantive impact, is that scientists around the world cite our research nearly 10,000 times each year.

The 200-year history of our Department, coupled with the dramatic upward trajectory that we have sustained over the past two decades, gives me cause for optimism, despite the pressures facing the research community. I hope that you share this optimism as you read about the tremendous discoveries made by my colleagues, who have themselves been recognized with countless honors and awards. As always, there are many ways you can support our shared mission of generating the foundational knowledge critical for advancing human health.

Steven B. McMahon

Steven B. McMahon, PhD
Professor and Chair
Dept. of Biochemistry & Mol. Biology
Senior Associate Dean
Basic Science Research,
Sidney Kimmel Medical College
Senior Associate Provost
Thomas Jefferson University

Thomas Jefferson University Department of Biochemistry and Molecular Biology

Steven B. McMahon, PhD
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Senior Associate Provost
Thomas Jefferson University

Yohei Kirino, PhD
Professor, Vice Chair for Research

Diane E. Merry, PhD
Professor, Vice Chair for Faculty Development and Engagement

Charles P. Scott, PhD
Associate Professor, Vice Chair for Education

Emad Alnemri, PhD
Thomas Eakins Professor

Teresa Fernandes-Alnemri, PhD
Research Assistant Professor

Jeffrey L. Benovic, PhD
Thomas Eakins Professor

Erik W. Debler, PhD
Associate Professor

Guru Chandramouly, PhD
Research Instructor

Maria Elena Cicardi, PhD
Research Instructor

Miki Fujioka, PhD
Research Assistant Professor

Howard Gamper Jr, PhD
Research Assistant Professor

Lin Guo, PhD
Associate Professor

Megumi Hamasaki, PhD
Research Instructor

Hideharu Hashimoto, PhD
Research Instructor

Ya-Ming Hou, PhD
Professor

Fadia Ibrahim, PhD
Assistant Professor

Konstantin Komolov, PhD
Research Instructor

Qiaoli Li, PhD
Research Professor

Isao Masuda, PhD
Research Instructor

Alexander M. Mazo, PhD
Professor

Svetlana Petruk, PhD
Research Assistant Professor

Anna Pluciennik, PhD
Associate Professor

Richard Pomerantz, PhD
Professor

Michael Root, MD, PhD
Professor

Zheng Ruan, PhD
Assistant Professor

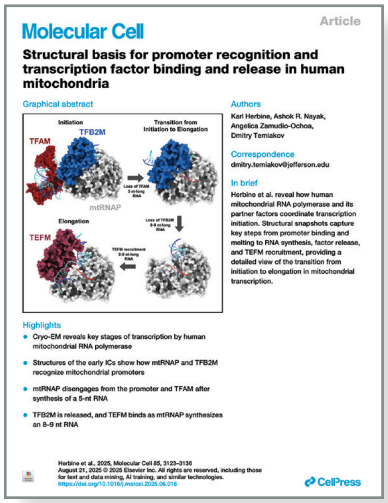
Michael Soniat, PhD
Assistant Professor

Dmitry Temiakov, PhD
Professor

Philip B. Wedegaertner, PhD
Professor

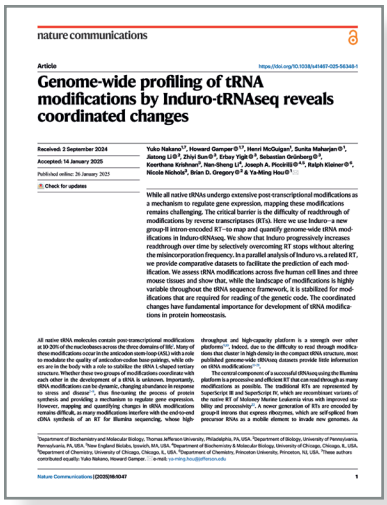
Edward Winter, PhD
Professor

Notable Contributions to Biochemistry and Molecular Biology: High Impact Publications



Herbine K, Nayak AR, Zamudio-Ochoa A, **Temiakov D.** Structural basis for promoter recognition and transcription factor binding and release in human mitochondria. *Mol Cell.* 2025 Jul 22:S1097-2765(25)00545-3. doi: 10.1016/j.molcel.2025.06.016. **https://pubmed.ncbi.nlm.nih.gov/40712587/**

Transcription in human mitochondria is driven by a core apparatus consisting of a Pol A family RNA polymerase, the initiation factors TFAM and TFB2M, and the elongation factor TEFM. While earlier structures of initiation and elongation complexes provided valuable snapshots, they represent isolated stages of a highly dynamic and multistep process. Critical aspects of mitochondrial transcription such as DNA recognition and melting, promoter escape, and the release of initiation factors-remain poorly understood. This presents a series of cryoelectron microscopy (cryo-EM) structures that capture the transcription complex as it transitions from the initial open promoter complex to the processive elongation complex through intermediate stages. Dr. Temiakov lab's research reveals new, previously unidentified determinants of promoter specificity: the sequential disengagement of mtRNAP from TFAM and the promoter, the release of TFB2M, and the recruitment of TEFM. Together, these findings provide a detailed molecular mechanism underlying transcription in human mitochondria.



Nakano Y, **Gamper H**, McGuigan H, Maharjan S, Li J, Sun Z, Yigit E, Grünberg S, Krishnan K, Li NS, Piccirilli JA, Kleiner R, Nichols N, Gregory BD, **Hou YM**. Genome-wide profiling of tRNA modifications by Induro-tRNAseq reveals coordinated changes. *Nat Commun* 16, 1047 (2025). **https://pubmed.ncbi.nlm.nih.gov/39865096/**

As the bridge for information transfer from DNA to RNA to protein, tRNA molecules acquire extensive post-transcriptional modifications as they transmit the genetic code. These modifications are critical for the quality of protein synthesis, which is essential for cellular functions, including differentiation and proliferation. However, genome-wide mapping and quantification of these tRNA modifications has remained challenging because they are not visible in standard tRNA sequencing analyses. Dr. Hou and her team used a recently developed "RT enzyme" for reverse transcription of each tRNA into a full-length cDNA. By optimizing the RT reaction for complete end-to-end cDNA synthesis, they were able to identify unique signatures for many of the challenging modifications. As such, they were able to discover changes in tRNA modification patterns across 5 human cell lines and 3 different mouse tissues, demonstrating coordinated changes important for protein homeostasis.

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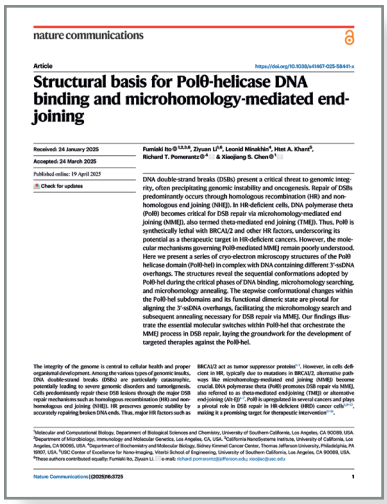
nature communications

Article

https://doi.org/10.1038/s41467-025-58441-x

Structural basis for Polθ-helicase DNA binding and microhomology-mediated end-joining

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Check for updates

Fumiaki Ito[1,2,3,9], Ziyuan Li[1,9], Leonid Minakhin[4], Htet A. Khant[5], Richard T. Pomerantz[6] ✉ & Xiaojiang S. Chen[1] ✉

DNA double-strand breaks (DSBs) present a critical threat to genomic integrity, often precipitating genomic instability and oncogenesis. Repair of DSBs predominantly occurs through homologous recombination (HR) and non-homologous end joining (NHEJ). In HR-deficient cells, DNA polymerase theta (Polθ) becomes critical for DSB repair via microhomology-mediated end joining (MMEJ), also termed theta-mediated end joining (TMEJ). Thus, Polθ is synthetically lethal with BRCA1/2 and other HR factors, underscoring its potential as a therapeutic target in HR-deficient cancers. However, the molecular mechanisms governing Polθ-mediated MMEJ remain poorly understood. Here we present a series of cryo-electron microscopy structures of the Polθ helicase domain (Polθ-hel) in complex with DNA containing different 3′-ssDNA overhangs. The structures reveal the sequential conformations adopted by Polθ-hel during the critical phases of DNA binding, microhomology searching, and microhomology annealing. The stepwise conformational changes within the Polθ-hel subdomains and its functional dimeric state are pivotal for aligning the 3′-ssDNA overhangs, facilitating the microhomology search and subsequent annealing necessary for DSB repair via MMEJ. Our findings illustrate the essential molecular switches within Polθ-hel that orchestrate the MMEJ process in DSB repair, laying the groundwork for the development of targeted therapies against the Polθ-hel.

The integrity of the genome is central to cellular health and proper organismal development. Among the various types of genomic insults, DNA double-strand breaks (DSBs) are particularly catastrophic, potentially leading to severe genomic disorders and tumorigenesis. Cells predominantly repair these DSB lesions through the major DSB repair mechanisms such as homologous recombination (HR) and non-homologous end joining (NHEJ). HR preserves genomic stability by accurately repairing broken DNA ends. Thus, major HR factors such as BRCA1/2 act as tumor suppressor proteins[1–3]. However, in cells deficient in HR, typically due to mutations in BRCA1/2, alternative pathways like microhomology-mediated end joining (MMEJ) become crucial. DNA polymerase theta (Polθ) promotes DSB repair via MMEJ, also referred to as theta-mediated end-joining (TMEJ) or alternative end-joining (alt-EJ)[4–6]. Polθ is upregulated in several cancers and plays a pivotal role in DSB repair in HR-deficient (HRD) cancer cells[7–11], making it a promising target for therapeutic intervention[12–14].

[1]Molecular and Computational Biology, Department of Biological Sciences and Chemistry, University of Southern California, Los Angeles, CA 90089, USA. [2]Department of Microbiology, Immunology and Molecular Genetics, Los Angeles, CA, USA. [3]California NanoSystems Institute, University of California, Los Angeles, CA 90095, USA. [4]Department of Biochemistry and Molecular Biology, Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA 19107, USA. [5]USC Center of Excellence for Nano-Imaging, Viterbi School of Engineering, University of Southern California, Los Angeles, CA 90089, USA. [9]These authors contributed equally: Fumiaki Ito, Ziyuan Li. ✉e-mail: richard.pomerantz@jefferson.edu; xiaojian@usc.edu

Nature Communications | (2025)16:3725 1

Ito F, Li Z, Minakhin L, Khant HA, **Pomerantz RT,** Chen XS. Structural basis for Polθ-helicase DNA binding and microhomology-mediated end-joining. *Nat Commun.* 2025 Apr 19;16(1):3725. doi: 10.1038/s41467-025-58441-x.PMID: 40253368. **https://www.nature.com/articles/s41467-025-58441-x**

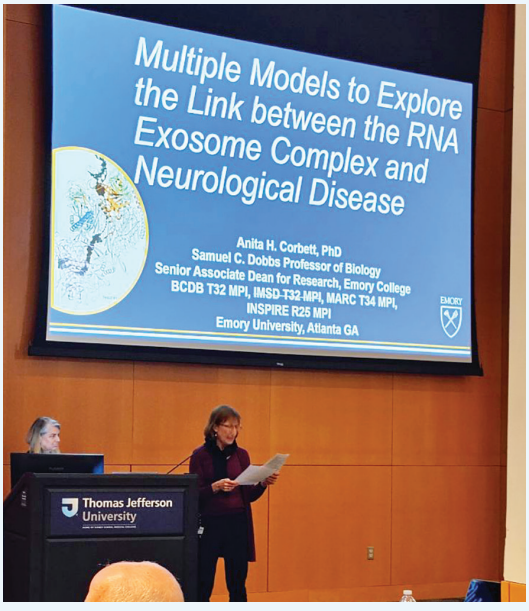
Over the past 10-20 years, proteins that repair DNA chromosomes have become increasingly important as cancer drug targets. This is because certain types of cancers, such as breast and ovarian cancers with heritable mutations in BRCA1 or BRCA2 tumor suppressors, become hyper-dependent on so-called back-up DNA repair proteins. One such back-up DNA repair protein called DNA polymerase Theta is important for the growth and survival of BRCA1/2 mutated cancer cells but is dispensable for normal healthy cells. DNA polymerase Theta also promotes resistance to many types of cancer therapies that damage DNA, including radiation, topoisomerase inhibitors and PARP inhibitors. The Pomerantz lab and collaborators recently discovered how the helicase domain of DNA polymerase Theta binds to DNA and initiates the repair of DNA breaks. Using cryo-electron microscopy and biochemistry methods, the helicase domain was unexpectedly found to form a head-to-head dimer and undergo a major conformational change that is necessary for it to bind DNA and join DNA breaks during the initiation of DNA repair. With this discovery of how DNA polymerase Theta initiates the DNA end-joining repair process, new drugs can be developed to suppress this mechanism of DNA repair which promotes resistance to cancer therapies and facilitates the growth and survival of BRCA1/2 mutant cancers.

For additional publications from the Department, please see pages 16-17.

Cellular, Biochemical, and Molecular Sciences T32 Training Program Update

The Department of Biochemistry and Molecular Biology recently hosted the annual Cellular, Biochemical, and Molecular Sciences (CBMS) T32 Training Program retreat, an event designed to foster interaction and discussion between CBMS trainees and their mentors, with the long-term goal of developing future scientific leaders. This half-day event featured research of CBMS trainees from five PhD programs, their faculty mentors from six academic departments at Sidney Kimmel Medical College, and a keynote lecture by Dr. Anita Corbett from Emory University. Dr. Corbett's lecture was entitled "Exploiting multiple models to explore the link between the RNA exosome complex and neurological disease." Dr. Corbett is also a member of the CBMS T32 External Advisory Committee, with whom she met during her visit.

Another highlight of the retreat was the array of high-quality platform and poster research presentations delivered by 18 predoctoral trainees, ranging from advanced research in protein structure to innovative investigations into disease pathogenesis.



DR. DIANE MERRY INTRODUCES KEYNOTE SPEAKER DR. ANITA CORBETT

Sidney Kimmel Medical College Dean's Awards for Faculty Achievement

On June 19th, The Sidney Kimmel Medical College held a ceremony at the Downtown Club to celebrate the 2025 winners of the Dean's Awards for Faculty Achievement. The Dean of Sidney Kimmel Medical College, Said Ibrahim, MD, MBA, MPH, presented the awards. Faculty of the Department of Biochemistry and Molecular Biology were well-represented among the recipients.

FACULTY TEAM ACHIEVEMENT AWARD: BASIC SCIENCE RESEARCH TEAM

This award recognizes the collaborative work of faculty teams leading to innovations or other achievements in clinical care, education, or research.

RECIPIENTS:

Jeffrey Benovic, PhD, Professor
Department of Biochemistry and Molecular Biology

Charles Scott, PhD, Associate Professor
Department of Biochemistry and Molecular Biology

In collaboration with:

Raymond Penn, PhD, Professor
Department of Medicine

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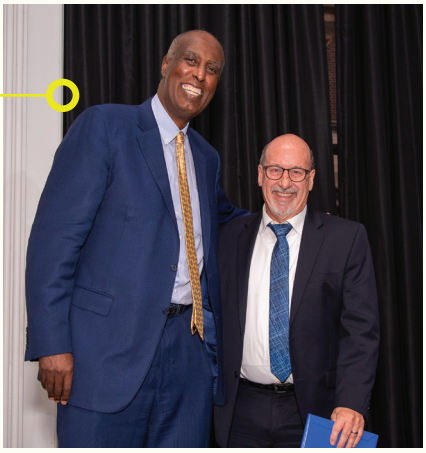
DEAN SAID IBRAHIM, MD, CHARLES SCOTT, PHD AND JEFFREY BENOVIC, PHD

LEFT TO RIGHT: CHIKA INOUE, DR. CHARLES P. SCOTT, JANE FRIES, DR. PHILIP B. WEDEGAERTNER, DR. ANNA PLUCIENNIK, DR. JAMES B. JAYNES, DR. STEVEN B. MCMAHON, DR. MIKI FUJIOKA, LORIE BENOVIC, AND DR. JEFFREY L. BENOVIC

SKMC DEAN'S AWARD FOR FACULTY MENTORING

The 2025 SKMC Dean's Award for Faculty Mentoring is presented to faculty members who demonstrate a tangible and sustained impact on the professional development and careers of their colleagues through effective mentoring relationships.

RECIPIENT:
Jeffrey Benovic, PhD, Professor
Department of Biochemistry and Molecular Biology



DEAN SAID IBRAHIM, MD AND
JEFFREY BENOVIC, PHD

DEAN SAID IBRAHIM, MD AND
JAMES JAYNES, PHD

SKMC DEAN'S AWARD FOR EXCELLENCE IN EDUCATION

The 2025 SKMC Dean's Award for Excellence in Education honors faculty who exhibit superior effectiveness as educators over a sustained period or make major contributions to an educational course, clerkship, or training program.

RECIPIENTS:
James Jaynes, PhD, Professor
Department of Biochemistry and Molecular Biology

Anna Pluciennik, PhD, Associate Professor
Department of Biochemistry and Molecular Biology

Philip Wedegaertner, PhD, Professor
Department of Biochemistry and Molecular Biology

DEAN SAID IBRAHIM, MD AND
PHILIP WEDEGAERTNER, PHD

DEAN SAID IBRAHIM, MD AND
ANNA PLUCIENNIK, PHD

Structural and Molecular Basis of PCNA-Activated FAN1 Nuclease Function in DNA Repair

A Key Protein Sheds Light on Huntington's Disease

Huntington's disease is a genetic disorder that kills nerve cells in the brain, causing people to lose their cognitive and motor abilities. New research led by Thomas Jefferson University Associate Professor, **Anna Pluciennik, PhD,** is revealing the molecular pathways behind the disease. Along with graduate researcher Fenglin Li, MS, research associate Ashutosh Phadte, PhD and postdoctoral research fellow Mayuri Bhatia, PhD, she and the rest of her team found a protein complex that fixes abnormal DNA and could be a potential target for Huntington's disease.

Huntington's is characterized by an abnormal repeating sequence in the DNA. As people with Huntington's age, this sequence gets longer, causing the strands of DNA to misalign, like a shirt with its buttons in the wrong holes. This misalignment creates extra loops in the DNA that make the DNA longer and longer. This in turn leads to the production of a toxic protein which eventually kills nerve cells.

Prior research showed small mutations in a protein called FAN1 could hasten or delay the onset of Huntington's disease. Dr. Pluciennik believed FAN1 may play an important role in removing these extra loops of DNA, so the research team set out to test the theory.

Using an electron microscope to generate "pictures" of FAN1 interacting with DNA, the team found that the protein acted like a pair of scissors, snipping off extra loops of abnormal DNA. To do this, FAN1 teamed up with another protein, called PCNA, forming a stable complex. Dr. Pluciennik found the same mutations that were associated with earlier disease onset also impacted the stability of the FAN1-PCNA complex, making it less effective at removing extra pieces of DNA, like scissors with dull blades.

"Based on our research, if you made the FAN1-PCNA complex more stable, or made more of the FAN1 protein, it could be protective and delay disease onset," says Dr. Pluciennik, a member of the Sidney Kimmel Medical College.

In addition to helping researchers understand the molecular basis of Huntington's, this research positions the FAN1-PCNA complex as a promising therapeutic target.

Li F, Phadte AS, Bhatia M, Barndt S, Monte Carlo III AR, Hou CD, Yang R, Strock S, **Pluciennik A**. Structural and molecular basis of PCNA-activated FAN1 nuclease function in DNA repair. *Nat Commun.* 2025 May 14;16(1):4411. doi: 10.1038/s41467-025-59323-y. PMID: 40368897; PMCID: PMC12078661. **https://pubmed.ncbi.nlm.nih.gov/40368897/**

Recent Honors and Awards

The Department of Biochemistry and Molecular Biology faculty members garnered multiple awards in recognition of their research and educational accomplishments during the 2023-2025 academic year.

DIANE E. MERRY, PHD RECEIVES JAVITS NEUROSCIENCE INVESTIGATOR AWARD

Diane E. Merry, PhD, Professor of Biochemistry and Molecular Biology and Chair of the Scientific Advisory Board of the Vickie and Jack Farber Institute for Neuroscience at Jefferson, received the prestigious Javits Neuroscience Investigator Award from the National Institute of Neurological Disorders and Stroke, part of the National Institutes of Health (NIH). Established by an act of Congress in 1983, this award is bestowed on leading scientists who have demonstrated superior competence and outstanding productivity.

For 2024, Dr. Merry was one of only six Javits awardees nationwide, and the first Thomas Jefferson University recipient since the award was established. She will receive nearly $4.5 million to support her research program, which focuses on defining new therapeutic targets in the neurodegenerative disease spinal and bulbar muscular atrophy.

2023 BENOVIC SYMPOSIUM

In the fall of 2023, the Department of Biochemistry & Molecular Biology held the Jeffrey L. Benovic Award and Lectureship ceremony. The award recipient and honoree was **Richard Cerione, PhD,** the Goldwin Smith Professor of Pharmacology and Chemical Biology, in the Department of Molecular Medicine at Cornell University College of Veterinary Medicine.

The next Benovic Symposium is scheduled for Wednesday, January 7, 2026, featuring Keynote speaker Mark Von Zastrow, MD, PhD, Professor, UCSF.

DR. JEFFREY L. BENOVIC: 2024 ASPET FELLOW HONORING A LEGACY OF GPCR DISCOVERY & MENTORSHIP

Dr. Jeffrey L. Benovic, the Thomas Eakins Professor of Biochemistry and Molecular Biology, has been named a Fellow of The American Society for Pharmacology and Experimental Therapeutics (ASPET).

ASPET created its Fellows program in 2019 to recognize sustained impact in the field of pharmacology, service to ASPET, and demonstrated excellence in mentorship and education. The ASPET Council recognized Dr. Benovic for his exceptional contributions to the advancement of pharmacology, for his decades of service as a member of the editorial board of its flagship journal Molecular Pharmacology, and for his outstanding commitment to mentorship and education. He was previously recognized by ASPET in 2014 with its Julius Axelrod award, which is presented for significant contributions to understanding the biochemical mechanisms underlying the pharmacological actions of drugs and for contributions to mentoring trainees in the pharmacological sciences. In 2023, Dr. Benovic was recognized with the George Koelle award, which is the highest award bestowed by his home ASPET chapter, the Mid-Atlantic Pharmacology Society.

DIANE E. MERRY, PHD RECEIVES THOMAS JEFFERSON UNIVERSITY PRESIDENT'S AWARD FOR EXCELLENCE IN RESEARCH INTEGRITY

Diane E. Merry, PhD, Professor and Vice-Chair in the Department of Biochemistry and Molecular Biology, has received the Thomas Jefferson University President's Award for Excellence in Research Integrity. This award recognizes individuals who exemplify an ongoing dedication to advancing research integrity, conduct, and compliance within the academic research community.

Dr. Merry's contributions to the field of molecular neuroscience and, specifically, to understanding molecular mechanisms of neurodegeneration are widely acknowledged; she currently chairs the Scientific Advisory Board of the Vickie and Jack Farber Institute for Neuroscience and serves as Vice Chair of the Department of Biochemistry and Molecular Biology. Her exceptional research endeavors have garnered her the prestigious Javits Neuroscience Investigator Award in 2024, underscoring her significant impact on the discipline.

DR. MERRY RECEIVES THE THOMAS JEFFERSON UNIVERSITY PRESIDENT'S AWARD FOR EXCELLENCE IN RESEARCH INTEGRITY FROM THOMAS JEFFERSON UNIVERSITY PRESIDENT DR. SUSAN ALDRIDGE

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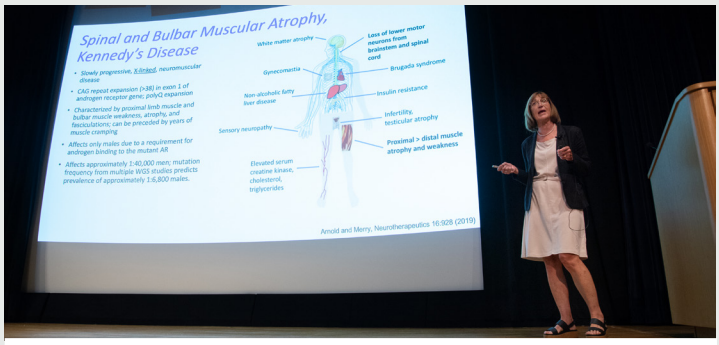
Department of Biochemistry and Molecular Biology Annual Retreat

The Department of Biochemistry and Molecular Biology held its annual retreat on September 22, 2025, at the Academy of Natural Sciences. Following opening remarks by Dr. Steven McMahon, graduate students, postdocs, and faculty delivered ten oral presentations describing their latest discoveries. During the afternoon poster session, students and fellows presented on a broad array of research topics. Keynote speaker Dr. Diane E. Merry, Professor and Vice Chair for Faculty Development and Engagement in the Department, presented her lecture "The impact of polyglutamine expansion on androgen receptor metabolism – identifying pathogenic mechanisms in spinal and bulbar muscular atrophy". Dr. Merry's research focuses on the molecular pathogenesis of Spinal and Bulbar Muscular Atrophy, a neurodegenerative disease caused by a polyglutamine expansion in the Androgen Receptor (AR). Her work seeks to understand how the mutant AR misfolds and aggregates to cause motor neuron toxicity, and to use this knowledge to develop novel therapeutic strategies. Her work has resulted in numerous high-impact publications, dozens of invited lectures, and has been recognized with numerous awards, including the Javits Neuroscience Investigator Award (R37), received in 2024 from the National Institute of Neurological Disorders and Stroke. With over 100 attendees, the retreat provided an ideal forum for learning about the work of our peers.

DR. MERRY (SECOND FROM LEFT) IS PRESENTED WITH A PLAQUE COMMEMORATING HER KEYNOTE LECTURE BY DR. MCMAHON (LEFT), AND RETREAT ORGANIZERS DR. FADIA IBRAHIM (THIRD FROM LEFT), AND DR. MICHAEL SONIAT (RIGHT)



Collaborative Success Stories

The Kirino and Deshpande Laboratories Jointly Focus on the Role of Non-Coding RNA in Asthma

Dr. Kirino's laboratory in the Department of Biochemistry and Molecular Biology began a collaboration with **Dr. Deepak Deshpande'**s laboratory in the Department of Medicine at SKMC more than 10 years ago. The partnership began with a small NIH grant shared between the two groups and has now led to a large portfolio of federal funding and impactful collaborative publications. Dr. Deshpande's expertise in airway physiology has provided an ideal complement to Dr. Kirino's long track record of discovering novel, non-coding RNA species that regulate various disease processes. The collaboration has recently expanded to examine the possibility that these unusual RNA molecules might also serve as biomarkers and even therapeutic targets in patients with either chronic obstructive pulmonary disease, or acute lung injury.

Immunoactive signatures of circulating tRNA- and rRNA-derived RNAs in chronic obstructive pulmonary disease. ***Shigematsu M****, Kawamura T,* ***Deshpande DA****,* ***Kirino Y****,* Molecular Therapy Nucleic Acids*. 2024, 35(3):102285.*

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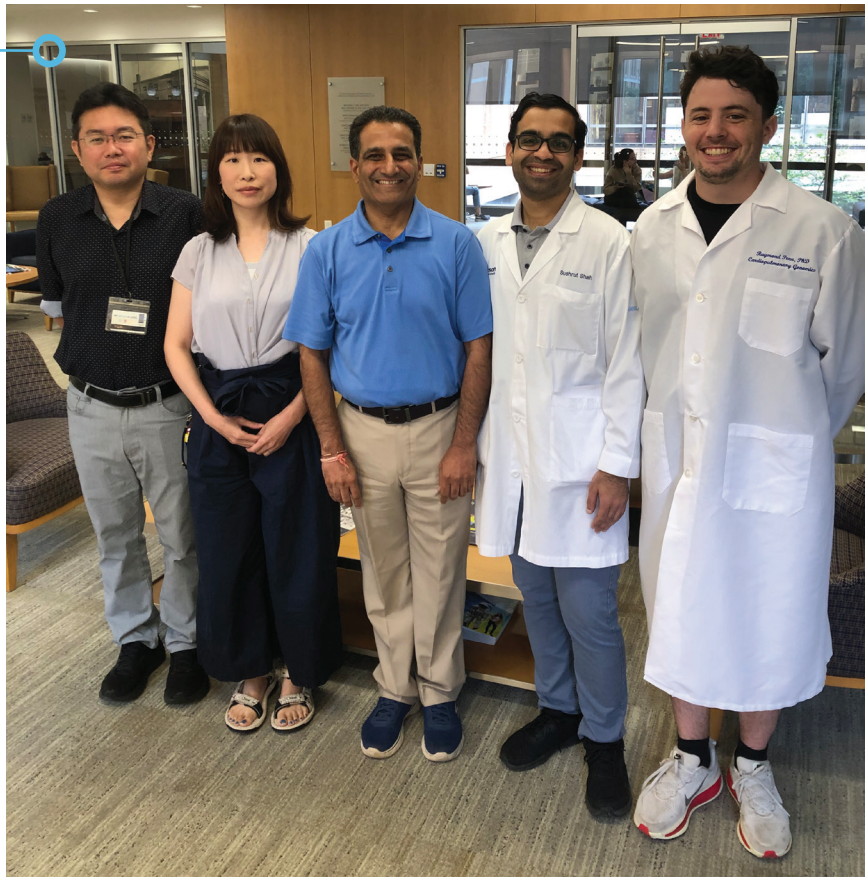
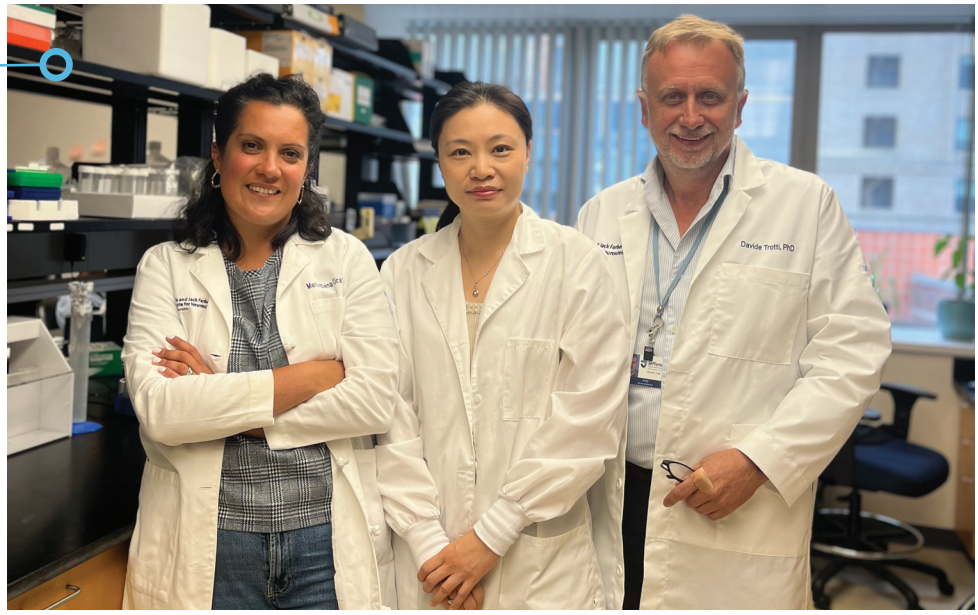


LEFT TO RIGHT: YOHEI KIRINO, PHD, MEGUMI SHIGEMATSU, PHD, DEEPAK DESHPANDE PHD, SUSHRUT SHAH, PHD CANDIDATE, AND JOSHUA RICHARD, RESEARCH ASSISTANT

Dr. Lin Guo Collaborates with Drs. Maria-Elena Cicardi and Davide Trotti of the Jefferson Weinberg ALS Center, to Identify Novel Targets and Strategies for Protecting Nerve Cells from Damage



LEFT TO RIGHT: MARIA ELENA CICARDI, PHD, LIN GUO, PHD, AND DAVIDE TROTTI, PHD

The research teams led by **Lin Guo, PhD,** of the Department of Biochemistry and Molecular Biology, and **Davide Trotti, PhD,** of the Jefferson Weinberg ALS Center, have collaborated for many years to investigate how normal nerve cells become damaged in amyotrophic lateral sclerosis (ALS) and the related neurodegenerative disease frontotemporal dementia (FTD). Their recent work has resulted in two studies that shed light on the protective role of the nuclear import receptor Kapβ2 — best known for transporting molecules into the nucleus — in countering toxic protein fragments produced by the most common genetic cause of ALS/FTD, a C9orf72 gene mutation.

In the first study, published in *Communications Biology* in 2024, the team focused on poly(GR), a particularly toxic protein fragment produced by the C9orf72 mutation. They found that increasing levels of Kapβ2 in neurons reduced poly(GR)-induced damage, while lowering Kapβ2 worsened it — underscoring its protective role. The follow-up study, published in 2025, also in *Communications Biology*, examined whether this protective effect depends on Kapβ2's normal transport function. The researchers created a version of Kapβ2 that cannot carry molecules into the nucleus but still binds toxic fragments. Intriguingly, this modified form protected neurons even more effectively than the normal protein. These results suggest that Kapβ2's ability to neutralize toxic fragments is distinct from its transport role, pointing to new therapeutic strategies that could mimic this specific activity. The collaboration between Drs. Guo and Trotti capitalizes on their complementary expertise in biophysics and neurobiology.

***Cicardi ME**, Kankate V, Sriramoji S, Krishnamurthy K, Markandaiah SS, Verdone BM, Girdhar A, Nelson A, Rivas LB, Boehringer A, Haeusler AR, Pasinelli P, **Guo L**, **Trotti D**. The nuclear import receptor Kapβ2 modifies neurotoxicity mediated by poly(GR) in C9orf72-linked ALS/FTD.* Communications Biology, *2024, 7(1):376.*

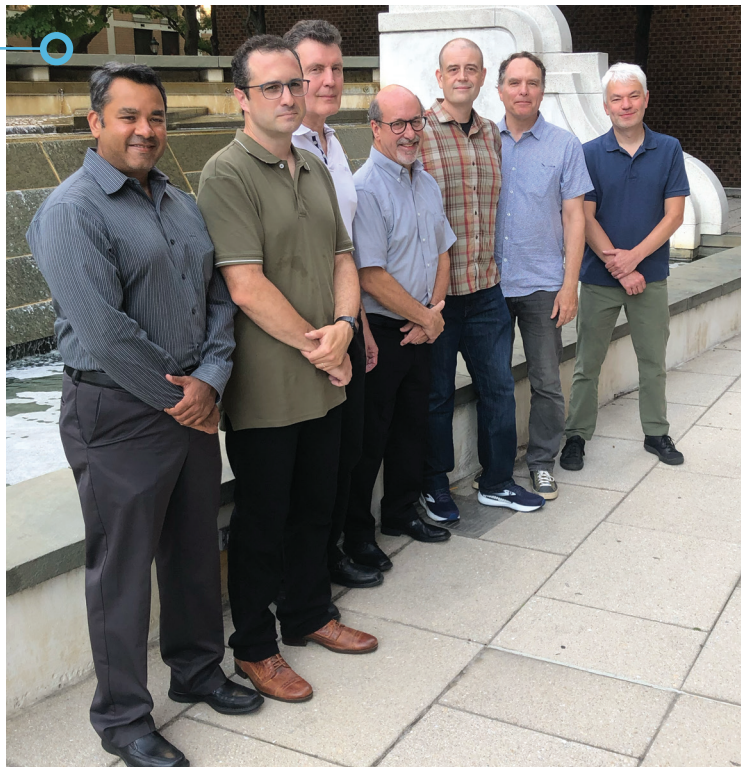
*Kim KM, Girdhar A, **Cicardi ME**, Kankate V, Hayashi M, Yang R, Carey J, Fare CM, Shorter J, Cingolani G, **Trotti D**, **Guo L**. NLS-binding deficient Kapβ2 reduces neurotoxicity via selective interaction with C9orf72-ALS/FTD dipeptide repeats.* Communications Biology, *2025, 8(2).*

A Thirty-Year Collaboration Continues to Drive Progress Against Airway Disease

The long-standing collaboration between the laboratories of **Dr. Jeffrey Benovic** in the Department of Biochemistry and Molecular Biology and the laboratory of **Dr. Raymond Penn** from the Center for Translational Medicine (CTM) in the Department of Medicine is an outstanding example of the power and benefits of synergy between independent scientists coming together to attack a shared problem or disease. This collaboration began more than 30 years ago, when Dr. Penn joined Dr. Benovic's laboratory as a post-doctoral fellow. Dr. Penn was well-trained in airway physiology from his doctoral studies, which made him invaluable in expanding the Benovic research team's expertise beyond molecular pharmacology towards clinical translation. Dr. Penn rapidly established his own independent research program and ultimately became the Director of CTM and lung research within the Jane and Leonard Korman Lung Center at Jefferson. The partnership that Drs. Benovic and Penn established also began to attract other scientists, with each bringing new expertise and enthusiasm to the team. The collaborative group now includes **Dr. Tonia Pera**, an expert in airway pharmacology; **Dr. Deepak Deshpande,** whose group focuses on airway physiology; **Dr. Charles Scott,** with expertise in high-throughput screening; **Dr. Roger Armen,** who adds expertise in computational chemistry; and **Dr. Ajay Nayak,** whose expertise includes pre-clinical animal models of airway disease.

Collectively, this team has been remarkably productive, with over 50 publications to date, and a firmly established international reputation that places them among the most prominent centers for airway pharmacology. They have also attracted tens of millions of dollars in federal funding to support their innovative team. At SKMC, Dean Said Ibrahim recently recognized the team with the 2025 Dean's Award for Faculty Team Achievement, as highlighted elsewhere in this newsletter.

Ippolito M, De Pascali F, Hopfinger N, ***Komolov KE****, Laurinavichyute D, Reddy PAN, Sakkal LA, Rajkowski KZ,* ***Nayak AP****, Lee J, Lee J, Cao G, Donover PS, Reichman M, An SS, Salvino JM,* ***Penn RB****,* ***Armen RS****,* ***Scott CP****,* ***Benovic JL****. Identification of a β-arrestin-biased negative allosteric modulator for the β2-adrenergic receptor.* Proc Natl Acad Sci USA. *2023 Aug;120(31):e2302668120. doi: 10.1073/pnas.2302668120. Epub 2023 Jul 25.*



LEFT TO RIGHT: AJAY NAYAK, PHD, TONIO PERA, PHD, RAYMOND PENN, PHD, JEFFREY BENOVIC, PHD, ROGER ARMEN, PHD, CHARLES SCOTT, PHD, AND KONSTANTIN KOMOLOV, PHD

The Department Welcomes New Colleagues

MICHAEL J. ROOT, MD, PHD

Professsor

The Department of Biochemistry and Molecular Biology welcomes the return of Dr. Michael J. Root to our faculty. Dr. Root rejoins SKMC from The Ohio State University College of Medicine. He earned his AB, PhD, and MD degrees from Harvard University and conducted fellowship training at MIT. Prior to joining OSU in 2020, Dr. Root was a faculty member at Jefferson. His research utilizes biophysical approaches to understand the mechanisms by which HIV enters human cells, with publications appearing in *PNAS, Science,* and *PLOS Pathogens*.

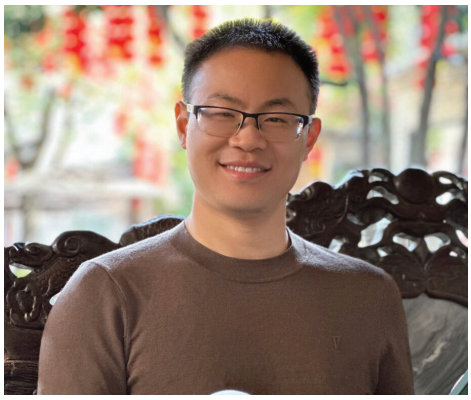
Beyond research, Dr. Root has also held significant leadership roles in graduate and medical education at both Thomas Jefferson University and OSU. At Jefferson, he served as the Assistant Dean for Graduate Affairs in the Jefferson College of Life Sciences, was a member of the Steering Committee that led to the JeffMD curricular redesign within SKMC, and served as Director of the Integrated Structural Biology Facility within the Sidney Kimmel Comprehensive Cancer Center. Similarly, Dr. Root held a number of leadership roles at OSU, including as Director of the Master's Program in Medical Sciences. In addition to his role in the Department of Biochemistry and Molecular Biology, Dr. Root will assume roles in both graduate and medical education at Jefferson.

MICHAEL SONIAT, PHD

Assistant Professsor

Dr. Michael Soniat recently joined Jefferson as an Assistant Professor of Biochemistry and Molecular Biology. Dr. Soniat earned his PhD in Molecular Biophysics from the University of Texas Southwestern, where he used structural biology and biophysics to define how histones are imported into the nucleus by transport receptors during nucleosome biogenesis. As a postdoctoral fellow at the University of Texas at Austin, he utilized single-molecule microscopy to directly measure the dynamic assembly of distinct repair enzymes at DNA breaks. This work provided key advances in our understanding of the regulation of the molecular machines required for efficient repair of DNA damage.

By understanding DNA repair and telomere maintenance mechanisms using single-molecule and structural biology, Dr. Soniat's team will focus on how genome instability contributes to aging and age-related diseases, including cancer and neurodegeneration. His recent research has appeared in *Molecular Cell, Science Advances,* and *PNAS,* and his laboratory has received funding through a K99/R00 Pathway to Independence Award from the National Institute of Aging. Since joining the Department, Dr. Soniat has already obtained a second NIH award, entitled "Elucidating the mechanisms underlying DNA double-strand break repair", which provides over $1.5M in research support.

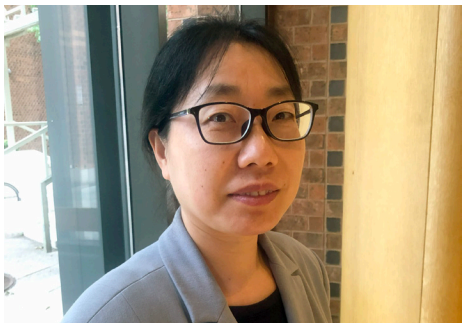


ZHENG RUAN, PHD

Assistant Professsor

The Department of Biochemistry and Molecular Biology welcomes Zheng Ruan, PhD as a new faculty member. Dr. Ruan joins the Department as an Assistant Professor after a highly successful fellowship studying ion channel biophysics at the Van Andel Institute in Grand Rapids Michigan. Prior to his fellowship training, Dr. Ruan earned his PhD at the University of Georgia in Bioinformatics, focusing on understanding the role of epidermal growth factor receptor mutations in human cancer. At Sidney Kimmel Medical College, his research will focus on understanding membrane protein signal transduction in both normal and disease settings, using a combination of structural, biochemical, and cellular approaches. In particular, Dr. Ruan has extensive experience with state-of-the-art structural methods that include single particle Cryo-EM.

Dr. Ruan's achievements have been published in high-profile journals, including *Nature, Nature Structural and Molecular Biology, PNAS, PLoS Genetics,* and *Cell Reports*. His work is currently funded by a Pathway to Independence Award from the National Institute for Neurological Disorders and Stroke at NIH. Dr. Ruan has also received funding from the American Heart Association.



QIAOLI (LILI) LI, PHD

Research Professor

Dr. Li's research primarily focuses on ectopic calcification disorders that affect soft connective tissues. Her work involves investigating the molecular mechanisms underlying these conditions, particularly in relation to diseases like pseudoxanthoma elasticum and calcinosis cutis. She utilizes expertise in cell biology, biochemistry, and molecular biology, and works with both in vitro and in vivo models, including rodent models, to study these disorders.

MARIA ELENA CICARDI, PHD

Research Instructor

HIDEHARU HASHIMOTO, PHD

Research Instructor

GURU CHANDRAMOULY, PHD

Research Instructor

KONSTANTIN KOMOLOV, PHD

Research Instructor

Professor James B. Jaynes, PhD Retires from Jefferson after 33 years

After more than 33 years at Jefferson, **Dr. James Jaynes** has retired as of July 2025. Dr. Jaynes began his career as a biologist with undergraduate and PhD training at the University of Washington in Seattle. After fellowship research with Dr. Patrick O'Farrell at the University of California-San Francisco, he joined Thomas Jefferson University, where he has remained a faculty member and active scientist since 1992. Dr. Jaynes' research career has had a broad impact on our understanding of one of the most fundamental processes in biology, i.e., the molecular mechanisms that dictate contextual patterns of gene expression. His discoveries have important implications for developmental biology, as well as for human disease. Many of his landmark publications have been cited hundreds of times by other scientists. Beyond his scientific contributions, Dr. Jaynes has made important contributions to graduate education at Jefferson, via leadership roles in the Jefferson College of Life Sciences curriculum, and having trained more than a dozen PhD students.

2024

Welcome New 2024 - 2025 BMP Students

KATHLEEN TILL

UNDERGRADUATE INSTITUTION
University of Scranton
HOMETOWN
Newtown Square, PA

INTERESTS: DNA repair mechanisms, neurodegenerative diseases, family gatherings, and running

TISHA KALPESH DESAI

UNDERGRADUATE INSTITUTION
Shree M. & N. Virani Science College
HOMETOWN
Jetpur, India

INTERESTS: Biology, tackling biomedical challenges, cooking, and research seminars

RILEIGH OWENS

UNDERGRADUATE INSTITUTION
Ursinus College
HOMETOWN
Newark, DE

INTERESTS: Yoga, music, reading, and my cats

RYAN MAGUIRE

UNDERGRADUATE INSTITUTION
University of Scranton
HOMETOWN
Chester Springs, PA

INTERESTS: Chemical and biological interplay, protein design and function, skiing, biking, and hiking

MUSTAFA SHAKIR

UNDERGRADUATE INSTITUTION
Saint Joseph's University
HOMETOWN
Downingtown, PA

INTERESTS: RNA and medicinal chemistry, exploring the city, and spending time with friends and family

HANNA CAMPBELL-IRWIN

UNDERGRADUATE INSTITUTION
McGill University
HOMETOWN
Quebec, Canada

INTERESTS: Biomedical research and playing tennis

2025

COLTIN ALBITZ

UNDERGRADUATE INSTITUTION
Dickinson College
HOMETOWN
Pottsville, PA

INTERESTS: Drug discovery, DNA damage sensing, rock climbing, hiking, and cooking

MARK CASSIDY

UNDERGRADUATE INSTITUTION
Johns Hopkins University
HOMETOWN
Washington Township, NJ

INTERESTS: Cooking, exercising, and traveling

ANNA PAULSON

UNDERGRADUATE INSTITUTION
University of Maryland
HOMETOWN
Rockville, MD

INTERESTS: Drawing, painting, swimming, and playing with my pets

MIGUEL PRYSAKAR

UNDERGRADUATE INSTITUTION
University of Delaware
HOMETOWN
Lancaster, PA

INTERESTS: Figure skating

JOHN QUADARELLA

UNDERGRADUATE INSTITUTION
Northeastern University
HOMETOWN
Boston, MA

INTERESTS: Food critiques, wine tasting, figure skating, and ballet

THEODHORA QYSHKOLLARI

UNDERGRADUATE INSTITUTION
Cabrini College
HOMETOWN
Broomall, PA

INTERESTS: Taking long walks with music, relaxing with TV shows, and baking

JILLIAN SHELLY

UNDERGRADUATE INSTITUTION
University of Delaware
HOMETOWN
Lansdale, PA

INTERESTS: Neurodegenerative diseases and therapies, music, dance, fitness, and musicals

LILY TAYAG

UNDERGRADUATE INSTITUTION
Thomas Jefferson University
HOMETOWN
Okinawa, Japan

INTERESTS: Hiking and roadtrips

Thomas Jefferson University College of Life Sciences Day 2025

On Monday, May 19th, the College of Life Sciences celebrated its 2025 Annual Class Day, recognizing outstanding achievements of students and faculty in its training programs. Two of the most prestigious awards that are conferred on students at Class Day are the Alumni Thesis Prize, and the Frederic Rieders Family Foundation Student Recognition Award.

The Alumni Thesis Prize is awarded based upon thesis committee recommendations for important original contributions to the scientific literature, superior academic performance, outstanding public oral defense, a well written and organized thesis, and a private oral defense before their thesis committee demonstrating breadth and depth of understanding and discussion as a peer.

Tyler Fenstermaker, PhD from the laboratory of Dr. Alex Mazo was recognized with the Alumni Thesis Prize from the Genetics, Genomics and Cancer Biology Ph.D. program.

Justin Gumas, PhD, from the laboratory of Dr. Yohei Kirino was selected as the Alumni Thesis Prize winner from the Biochemistry and Molecular Pharmacology Ph.D. program.

The Rieders Foundation Graduate Student Recognition Award was established to honor students in the Jefferson College of Life Sciences who have made outstanding contributions to the University environment above and beyond academic achievement. Students are recognized for outstanding commitment to Jefferson and to their peer community.

GERALD B. GRUNWALD, PHD, DEAN, JEFFERSON COLLEGE OF LIFE SCIENCES, PICTURED WITH ELIZABETH MCDUFFIE, PHD

Elizabeth McDuffie, PhD was recognized with the Fredric Rieders Family Foundation Award for her service to her peers as an officer and president of the Business and Biotechnology (BizBio) student interest group, for her service as a student liaison and interviewer for Jefferson College of Life Sciences graduate programs, for her contributions as a student representative on the search committee that selected Dr. Susan Aldrich as the seventh President of Thomas Jefferson University, for her award winning representation of Jefferson at regional and national scientific meetings and for her contributions to science policy and science advocacy at the national level during her tenure in the graduate program.

Selected Recent Publications

The role of G protein-coupled receptors and receptor kinases in pancreatic β-cell function and diabetes. Varney MJ, **Benovic JL**. *Pharmacol Rev.* 2024 Feb 13;76(2):267-299. **https://pubmed.ncbi.nlm.nih.gov/38351071/**

Two DOT1 enzymes cooperatively mediate efficient ubiquitin-independent histone H3 lysine 76 tri-methylation in kinetoplastids. Frisbie VS, **Hashimoto H**, Xie Y, De Luna Vitorino FN, Baeza J, Nguyen T, Yuan Z, Kiselar J, Garcia BA, **Debler EW**. *Nat Commun.* 2024 Mar 19;15(1):2467. **https://pubmed.ncbi.nlm.nih.gov/38503750/**

Single acetylation-mimetic mutation in TDP-43 nuclear localization signal disrupts importin α1/β signaling. Ko YH, Lokareddy RK, Doll SG, Yeggoni DP, Girdhar A, Mawn I, Klim JR, Rizvi NF, Meyers R, Gillilan RE, **Guo L**, Cingolani G. *J Mol Biol*. 2024 Oct 15;436(20):168751. **https://pubmed.ncbi.nlm.nih.gov/39181183/**

Engineered NLS-chimera downregulates expression of aggregation-prone endogenous FUS. Hayashi M, Girdhar A, Ko YH, Kim KM, DePierro JA, Buchler JR, Arunprakash N, Bajaj A, Cingolani G, **Guo L**. Nat Commun. 2024 Sep 10;15(1):7887. **https://pubmed.ncbi.nlm.nih.gov/39251571/**

NLS-binding deficient Kapβ2 reduces neurotoxicity via selective interaction with C9orf72-ALS/FTD dipeptide repeats. Kim KM, Girdhar A, **Cicardi ME**, Kankate V, Hayashi M, Yang R, Carey JL, Fare CM, Shorter J, Cingolani G, Trotti D, **Guo L**. *Commun Biol*. 2025 Jan 2;8(1):2. **https://pubmed.ncbi.nlm.nih.gov/39747573/**

Unraveling RNA conformation dynamics in mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episode syndrome with solid-state nanopores. Namani S, Kavetsky K, Lin CY, Maharjan S, **Gamper HB**, Li NS, Piccirilli JA, **Hou YM**, Drndic M. *ACS Nano*. 2024 Jul 2;18(26):17240-17250. **https://pubmed.ncbi.nlm.nih.gov/38906834/**

Post-transcriptional methylation of mitochondrial-tRNA differentially contributes to mitochondrial pathology. Maharjan S, **Gamper H**, Yamaki Y, Christian T, Henley RY, Li NS, Suzuki T, Suzuki T, Piccirilli JA, Wanunu M, Seifert E, Wallace DC, **Hou YM**. *Nat Commun*. 2024 Oct 18;15(1):9008. **https://pubmed.ncbi.nlm.nih.gov/39424798/**

Genome-wide profiling of tRNA modifications by induro-tRNAseq reveals coordinated changes. Nakano Y, **Gamper H**, McGuigan H, Maharjan S, Li J, Sun Z, Yigit E, Grünberg S, Krishnan K, Li NS, Piccirilli JA, Kleiner R, Nichols N, Gregory BD, **Hou YM**. *Nat Commun*. 2025 Jan 26;16(1):1047. **https://pubmed.ncbi.nlm.nih.gov/39675712/**

A kinetic model for compound heterozygous pathogenic variants in tyrosyl-tRNA synthetase gene YARS2-associated neonatal phenotype. Christian T, Maharjan S, Yin S, Yamaki Y, **Masuda I**, Li F, Muraresku C, Clever S, Ganetzky RD, **Hou YM**. *J Biol Chem*. 2025 Jan;301(1):108092. **https://pubmed.ncbi.nlm.nih.gov/39865096/**

M6A modification is incorporated into bacterial mRNA without specific functional benefit. Szydlo K, Santos L, Christian TW, Maharjan S, Dorsey A, **Masuda I**, Jia J, Wu Y, Tang W, **Hou YM**, Ignatova Z. *Nucleic Acids Res*. 2025 May 22;53(10):gkaf425. **https://pubmed.ncbi.nlm.nih.gov/40401555/**

Defining the true native ends of RNAs at single-molecule level with TERA-Seq. **Ibrahim F**, Mourelatos Z. *Methods Mol Biol*. 2025;2863:359-372. **https://pubmed.ncbi.nlm.nih.gov/39535720/**

Stem-loop and circle-loop TADs generated by directional pairing of boundary elements have distinct physical and regulatory properties. Ke W, **Fujioka M**, Schedl P, **Jaynes JB**. *Elife*. 2024 Aug 7;13:RP94114. **https://pubmed.ncbi.nlm.nih.gov/39110491/**

Chromosome structure in drosophila is determined by boundary pairing not loop extrusion. Bing X, Ke W, **Fujioka M**, Kurbidaeva A, Levitt S, Levine M, Schedl P, **Jaynes JB**. *Elife*. 2024 Aug 7;13:RP94070. **https://pubmed.ncbi.nlm.nih.gov/39110499/**

The homie insulator has sub-elements with different insulating and long-range pairing properties. **Fujioka M**, Ke W, Schedl P, **Jaynes JB**. *Genetics*. 2025 Apr 17;229(4):iyaf032. **https://pubmed.ncbi.nlm.nih.gov/39999387/**

Immunostimulatory short non-coding RNAs in the circulation of patients with tuberculosis infection. Gumas J, Kawamura T, **Shigematsu M**, **Kirino Y**. *Molecular Therapy Nucleic Acids*, 35 (1): 102156, 2024. **https://pubmed.ncbi.nlm.nih.gov/38481936/**

The tRNAVal half: A strong endogenous toll-like receptor 7 ligand with a 5′-terminal universal sequence signature. Pawar K, Kawamura T, **Kirino Y**. *Proceedings of the National Academy of Sciences, USA*, 121 (19): e2319569121, 2024. **https://pubmed.ncbi.nlm.nih.gov/38683985/**

Immunoactive signatures of circulating tRNA- and rRNA-derived RNAs in chronic obstructive pulmonary disease. **Shigematsu M**, Kawamura T, Deshpande DA, **Kirino Y**. *Molecular Therapy Nucleic Acids*, 35 (3): 102285, 2024. **https://pubmed.ncbi.nlm.nih.gov/39220268/**

Angiogenin-catalyzed cleavage within tRNA anticodon-loops identified by cP-RNA-seq. **Shigematsu M**, Matsubara R, Gumas J, Kawamura T, **Kirino Y**. *Bioscience, Biotechnology, and Biochemistry*, 89 (3): 398-405, 2025. **https://pubmed.ncbi.nlm.nih.gov/39658364/**

cP-RNA-seq for tRNA half sequencing. **Shigematsu M**, Gumas J, **Kirino Y.** *Methods in Enzymology*, 711: 135-153, 2025. **https://pubmed.ncbi.nlm.nih.gov/39952701/**

TaqMan RT-qPCR for tRNA half quantification. **Shigematsu M**, Kawamura T, **Kirino Y.** *Methods in Enzymology*, 711: 155-170, 2025. **https://pubmed.ncbi.nlm.nih.gov/39952703/**

A hormone-dependent tRNA half promotes cell cycle progression via destabilization of p21 mRNA. Kawamura T, **Shigematsu M**, **Kirino Y.** *PLoS Biology*, 23 (6): e3003194, 2025. **https://pubmed.ncbi.nlm.nih.gov/40471969/**

more >

Magnesium decreases urine supersaturation but not calcium oxalate stone formation in genetic hypercalciuric stone-forming rats. **Li Q**, Krieger NS, Yang L, Asplin J, Bushinsky DA. *Nephron.* 2024;148(7):480-486. **https://pubmed.ncbi.nlm.nih.gov/38262368/**

Novel treatment for PXE: Recombinant ENPP1 enzyme therapy. Jacobs IJ, Obiri-Yeboah D, Stabach PR, Braddock DT, **Li Q**. *Mol Ther.* 2024 Nov 6;32(11):3815-3820. **https://pubmed.ncbi.nlm.nih.gov/39342427/**

Norganic pyrophosphate plasma levels in patients with GGCX-associated PXE-like phenotypes. **Li Q**, Troutman C, Peckiconis M, Wurst T, Terry SF. *Front Genet.* 2024 Sep 27;15:1429320. **https://pubmed.ncbi.nlm.nih.gov/39399214/**

Non-redundant roles for the human mRNA decapping cofactor paralogs DCP1a and DCP1b. Vukovic I, Barnada SM, Ruffin JW, Karlin J, Lokareddy RK, Cingolani G, **McMahon SB**. *Life Sci Alliance.* 2024 Sep 10;7(11):e202402938. **https://pubmed.ncbi.nlm.nih.gov/39256052/**

Somatic p53 mutations that are markedly overrepresented in lung cancer confer resistance to ROS-induced cell death. Tracewell MA, Karlin JE, Barnada SM, McDuffie EL, **Scott CP**, Barta JA, **McMahon SB**. *Carcinogenesis*. 2025 Jun 3:bgaf027. **https://pubmed.ncbi.nlm.nih.gov/40458924/**

Differentially disrupted spinal cord and muscle energy metabolism in spinal and bulbar muscular atrophy. DeBartolo D, Arnold FJ, Liu Y, Molotsky E, Tang HY, **Merry DE**. *JCI Insight.* 2024 Mar 5;9(7):e178048. **https://pubmed.ncbi.nlm.nih.gov/38452174/**

Blocking the dimerization of polyglutamine-expanded androgen receptor protects cells from DHT-induced toxicity by increasing AR turnover. Lisberg A, Liu Y, **Merry DE**. *J Biol Chem.* 2024 May;300(5):107246. **https://pubmed.ncbi.nlm.nih.gov/38556081/**

Mutant androgen receptor induces neurite loss and senescence independently of ARE binding in a neuronal model of SBMA. Karliner J, Liu Y, **Merry DE**. *Proc Natl Acad Sci U S A*. 2024 Jul 16;121(29):e2321408121. **https://pubmed.ncbi.nlm.nih.gov/38976730/**

Structural and molecular basis of PCNA-activated FAN1 nuclease function in DNA repair. Li F, Phadte AS, Bhatia M, Barndt S, Monte Carlo III AR, Hou CD, Yang R, Strock S, **Pluciennik A**. *Nat Commun*. 2025 May 14;16(1):4411. **https://pubmed.ncbi.nlm.nih.gov/40368897/**

4'-ethynyl-2'-deoxycytidine (EdC) preferentially targets lymphoma and leukemia subtypes by inducing replicative stress. Calbert ML, **Chandramouly G**, Adams CM, Saez-Ayala M, Kent T, Tyagi M, Ayyadevara VSSA, Wang Y, Krais JJ, Gordon J, Atkins J, Toma MM, Betzi S, Boghossian AS, Rees MG, Ronan MM, Roth JA, Goldman AR, Gorman N, Mitra R, Childers WE, Graña X, Skorski T, Johnson N, Hurtz C, Morelli X, Eischen CM, **Pomerantz RT**. *Mol Cancer Ther*. 2024 May 2;23(5):683-699. **https://pubmed.ncbi.nlm.nih.gov/38064712/**

Discovery of a small-molecule inhibitor that traps Polθ on DNA and synergizes with PARP inhibitors. Fried W, Tyagi M, Minakhin L, **Chandramouly G**, Tredinnick T, Ramanjulu M, Auerbacher W, Calbert M, Rusanov T, Hoang T, Borisonnik N, Betsch R, Krais JJ, Wang Y, Vekariya UM, Gordon J, Morton G, Kent T, Skorski T, Johnson N, Childers W, Chen XS, **Pomerantz RT**. *Nat Commun*. 2024 Apr 5;15(1):2862. **https://pubmed.ncbi.nlm.nih.gov/38580648/**

PARG is essential for Polθ-mediated DNA end-joining by removing repressive poly-ADP-ribose marks. Vekariya U, Minakhin L, **Chandramouly G**, Tyagi M, Kent T, Sullivan-Reed K, Atkins J, Ralph D, Nieborowska-Skorska M, Kukuyan AM, Tang HY, **Pomerantz RT**, Skorski T. *Nat Commun*. 2024 Jul 11;15(1):5822. **https://pubmed.ncbi.nlm.nih.gov/38987289/**

Structural basis for a Polθ helicase small-molecule inhibitor revealed by cryo-EM. Ito F, Li Z, Minakhin L, **Chandramouly G**, Tyagi M, Betsch R, Krais JJ, Taberi B, Vekariya U, Calbert M, Skorski T, Johnson N, Chen XS, **Pomerantz RT**. *Nat Commun*. 2024 Aug 14;15(1):7003. **https://pubmed.ncbi.nlm.nih.gov/39143110/**

Structural basis for Polθ-helicase DNA binding and microhomology-mediated end-joining. Ito F, Li Z, Minakhin L, Khant HA, **Pomerantz RT**, Chen XS. *Nat Commun*. 2025 Apr 19;16(1):3725. **https://pubmed.ncbi.nlm.nih.gov/40253368/**

Structural basis for substrate binding and selection by human mitochondrial RNA polymerase. Herbine K, Nayak AR, **Temiakov D**. *Nat Commun*. 2024 Aug 20;15(1):7134. **https://pubmed.ncbi.nlm.nih.gov/39164235/**

Structural basis for intrinsic strand displacement activity of mitochondrial DNA polymerase. Nayak AR, Sokolova V, Sillamaa S, Herbine K, Sedman J, **Temiakov D**. *Nat Commun*. 2025 Mar 11;16(1):2417. **https://pubmed.ncbi.nlm.nih.gov/40069189/**

Maackia amurensis seed lectin structure and sequence comparison with other M. amurensis lectins. Nayak AR, Holdcraft CJ, Yin AC, Nicoletto RE, Zhao C, Zheng H, **Temiakov D**, Goldberg GS. *J Biol Chem*. 2025 May;301(5):108466. **https://pubmed.ncbi.nlm.nih.gov/40158854/**

The guanine nucleotide exchange factor Ric-8A regulates the sensitivity of constitutively active Gαq to the inhibitor YM-254890. Dwyer MB, Luo J, Todd TD, Blumer KJ, Tall GG, **Wedegaertner PB**. *J Biol Chem*. 2025 May;301(5):108426. **https://pubmed.ncbi.nlm.nih.gov/40118458/**

The MAPK homolog, Smk1, promotes assembly of the glucan layer of the spore wall in S. cerevisiae. Lee-Soety JY, Resch G, Rimal A, Johnson ES, Benway J, **Winter E**. *Yeast*. 2024 Jul;41(7):448-457. **https://pubmed.ncbi.nlm.nih.gov/38874213/**

Recent Grant Awards

Department faculty secured the following new extramural funding (2023–2025)

PRINCIPAL INVESTIGATOR	SPONSOR	TYPE	AWARD TITLE	TOTAL AWARD
Emad Alnemri, PhD	NIH through University Of Alabama at Birmingham	R01	Dysregulation of cardiac signaling in disease and stress	$44,979
Jeffrey Benovic, PhD	NIH/NHLBI	P01	Discovery/signaling core	$1,406,000
Erik Debler, PhD	NIH/NIAID	R01	Chromatin biology of the African trypanosome – equipment supplement	$93,937
Lin Guo, PhD	NIH/NINDS	R01	Developing RNA oligonucleotides to mitigate aberrant FUS phase transition in FTD/ALS	$780,000
Ya-Ming Hou, PhD	NIH through The Jackson Laboratory	U24	Probing RNA conformational dynamics through a solid-state nanopore with sub-100 nanosecond time resolution	$85,000
Ya-Ming Hou, PhD (with Lorraine Iacovitti, PhD)	NIH/NICHD	R03	A cell model of YARS2-associated childhood-onset mitochondrial disease	$67,067
Ya-Ming Hou, PhD	NIH/NIA	R21	The tRNA pool in C9-ALS/FTD	$444,696
Ya-Ming Hou, PhD	NIH/NHGRI	R01	Twice reading of RNA by direct nanopore sequencing	$3,106,916
Ya-Ming Hou, PhD	NIH through Northeastern University	R01	Synthetic mRNA control set for nanopore-based pseudouridine modification profiling in human transcriptomes	$854,067
Ya-Ming Hou, PhD	NIH / NIGMS	R35	tRNA in codon usage	$2,730,000
Fadia Ibrahim, PhD	NIH/NIGMS	R01	Mechanism for post-transcriptional gene regulation by ribothrypsis	$1,638,000
Fadia Ibrahim, PhD	NIH/NIGMS	R01	Mechanism for post-transcriptional gene regulation by ribothrypsis – equipment supplement	$97,050
Yohei Kirino, PhD	NIH/NIAID	R21	Endogenous single-stranded RNA ligands for endosomal toll-like receptors	$429,000
Yohei Kirino, PhD	NIH/NHLBI	R01	Role of tRNA- and rRNA-derived RNAs in acute lung injury	$1,360,848
Yohei Kirino, PhD	NIH/NIGMS	R35	Biogenesis and function of cyclic phosphate-containing RNAs	$2,144,994
Qiaoli Li, PhD	PXE International, Inc.		Establishment of PXE international center of excellence in research and clinical care	$100,320
Qiaoli Li, PhD	Sanifit		Testing the effects of SNF610 and INS-3001 on ectopic calcification in an Abcc6-/- mouse model of PXE	$129,168
Qiaoli Li, PhD	CSL Vifor		Testing the effects of SNF610 (CSL960) on ectopic calcification in an Abcc6 -/- mouse model of PXE	$126,048
Qiaoli Li, PhD	NIH/NIDDK	R01	Hypercalciuria and abnormal bone in the genetic hypercalciuric stone-forming rats	$2,227,105
Qiaoli Li, PhD	NIH/NIAMS	R21	Gene therapy for PXE: breaking the barrier of ectopic calcification	$377,520
Alexander Mazo, PhD	Pennsylvania Department Of Health		De-condensing H3K27me3-marked chromatin is essential for novel AML therapies	$81,469
Steven McMahon, PhD	NIH/NIEHS	R01	METTL3 in chromium-induced angiogenesis and carcinogenesis	$2,426,058
Diane Merry, PhD	argenx BV		Therapeutic effects of MuSK agonistic antibody ARGX-119 in vitro and in vivo models of SBMA	$364,724
Diane Merry, PhD	NIH/NINDS	R37	The role of the AR interactome in SBMA	$2,543,887

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PRINCIPAL INVESTIGATOR	SPONSOR	TYPE	AWARD TITLE	TOTAL AWARD
Diane Merry, PhD	NIH/NINDS	R21	Therapeutic strategies to rescue metabolic deficiencies in spinal and bulbar muscular atrophy	$429,000
Diane Merry, PhD	NIH/NINDS	R21	The mechanism and role of androgen receptor serine 16 phosphorylation in SBMA	$429,999
Diane Merry, PhD	NIH/NINDS	R21	Somatic instability of CAG repeats in spinal and bulbar muscular atrophy	$429,000
Diane Merry, PhD	Kennedy's Disease Association, Inc.		KDA student travel grant to attend KDA conference (student: Medha Sengupta)	$1,000
Anna Pluciennik, PhD	NIH/NIGMS	R01	Crosstalk between DNA repair pathways in repeat instability	$1,248,000
Anna Pluciennik, PhD	NIH/NIGMS	R01	Crosstalk between DNA repair pathways in repeat instability – equipment supplement	$139,966
Anna Pluciennik, PhD (Pre-doctoral fellowship award to Lily Thompson)	NIH/NIEHS	F31	Uncovering the impact of oxidative stress on centromere integrity	$97,948
Richard Pomerantz, PhD	NIH/NIGMS	R35	Novel mechanisms and regulation of mammalian double-strand break repair	$3,597,800
Richard Pomerantz, PhD (with Christine Eischen, PhD)	NIH/NCI	R01	A next-generation nucleoside prodrug for diffuse large B-cell lymphoma	$1,565,395
Richard Pomerantz, PhD (with Wayne Childers, PhD —Temple University)	NIH/NCI	R01	Development of best-in-class pol-theta inhibitors	$1,401,850
Richard Pomerantz, PhD	Dr. Ralph and Marian Falk Medical Research Trust		PROTACs for targeting BRCA-deficient cancers	$999,999
Richard Pomerantz, PhD	Department Of Defense		Second-generation precision medicine for BRCA-mutant ovarian cancer	$756,897
Michael Root, MD-PhD	NIH/NIAID	R21	Function of HIV-1 env cytoplasmic tail domain	$392,995
Zheng Ruan, PhD	NIH/NINDS	R00	Structural and functional studies on proton-activated chloride (PAC) channel	$739,527
Seyed Shekarabi, PhD (Merry Lab)	Kennedy's Disease Association		Identification and characterization of kinase(s) responsible for androgen receptor phosphorylation at serine 16	$100,000
Megumi Shigematsu, PhD	NIH/NHLBI	R21	Circulating immunoactive small RNAs in COPD as biomarkers	$234,000
Michael Soniat, PhD	NIH/NIGMS	R35	Elucidating the mechanisms underlying DNA double-strand break repair	$1,950,000
Michael Soniat, PhD	NIH/NIA	R00	Molecular mechanisms of Werner syndrome helicase in genome stability and aging	$746,997
Michael Soniat, PhD	American Cancer Society		Mechanisms of telomere length regulation in ALT cancers	$40,000
Dmitry Temiakov, PhD	NIH/NIGMS	R35	Molecular mechanisms of mitochondrial transcription and replication	$2,720,950
Philip Wedegaertner, PhD	Department Of Defense		Targeted degradation of mutant GNAQ/11 in uveal melanoma cells	$780,000

Thesis Defenses

The following students earned doctoral degrees as members of Biochemistry and Molecular Biology Department laboratories and/or as members of the Biochemistry and Molecular Pharmacology Program.

STUDENT	ADVISOR	THESIS TITLE
Oghenerukevwe Akpoghiran	Kyunghee Koh, PhD	Molecular, behavioral, and disease-linked circadian regulation in drosophila melanogaster
Samantha Barnada	Steven McMahon, PhD / Marco Trizzino, PhD	Uncovering molecular mechanisms underlying human developmental gene regulation
Benjamin Barnhart	Rajanikanth Vadigepalli, PhD	Partial hepatectomy as a model of liver regeneration: network-based profiles
Gina Buchel	Dmitry Temiakov, PhD	Fidelity of DNA synthesis by human mitochondrial replication machinery
Moriah Cunningham	Steven McMahon, PhD	Evaluating the impact of community outreach and clinical PARP inhibitors in prostate cancer
Qingqing Cao	Andrew South, PhD	The role of type VII collagen in mediating extracellular matrix protein secretion in recessive dystrophic epidermolysis bullosa
Steven Doll	Gino Cingolani, PhD	Recognition of the TDP-43 nuclear localization signal by importin $\alpha 1/\beta$
Morgan Dwyer	Philip Wedegaertner, PhD	Understanding sensitivity of oncogenic, constitutively active $G\alpha q$ to the inhibitor YM-254890
Tyler Fenstermaker	Alexander Mazo, PhD	Epigenetic bookmarking during DNA replication by the RNA polymerase II complex
Victoria Frisbie	Erik Debler, PhD	Mechanism of cooperative histone H3 lysine 76 methylation by two DOT1 enzymes
Justin Gumas	Yohei Kirino, PhD	Characterization of immunostimulatory short non-coding RNAs: uncovering a novel pathway for immune modulation
Karl Herbine	Dmitry Temiakov, PhD	The structural basis for human mitochondrial transcription
Eden Hornung	Rajanikanth Vadigepalli, PhD	Spatiotemporal molecular characterization of brain-body neuromodulatory processes in autonomic health and disease
Stephano Iglesias	Gino Cingolani, PhD	Structural and biochemical studies of phage biomedicines
Jordyn Karliner	Diane Merry, PhD	Investigating the molecular mechanisms of neurite loss in spinal and bulbar muscular atrophy
Natalie Laspata	Elise Fouquerel, PhD	Investigating the role of poly (ADP-ribose) polymerase 1 (PARP1) in the prevention of R-loop-mediated genomic instability
Allison Lisberg	Diane Merry, PhD	Identifying the mechanism behind the role of the AR N/C interaction in SBMA
Elizabeth McDuffie	Charles Scott, PhD	Muscarinic acetylcholine 3 receptor signals through g12/13 and RhoA to induce human airway smooth muscle shortening
Elana Molotsky	Diane Merry, PhD	The impact of androgen receptor polyglutamine expansion on the motor unit in SBNA: NMJ pathology, motor unit vulnerability, and neurofilament dysregulation
Clinita Randolph	Philip Wedegaertner, PhD	The influence of membrane localization on constitutively active $G\alpha q$ signaling
Abhimannyu Rimal	Edward Winter, PhD	ISC10, a developmentally regulated inhibitor of non-canonical mapk signaling
Hannah Schapiro	Michael Root, MD, PhD	Dissecting how interactions at the apex of HIV-1 Env modulate epitope exposure at the distant base of the glycoprotein
Mason Tracewell	Steven McMahon, PhD	Roles of a class of p53 mutants enriched in lung cancer
Matthew Varney	Jeffrey Benovic, PhD	G Protein-coupled receptor kinase 6 (GRK6) regulation of insulin processing and secretion
Ivana Vukovic	Steven McMahon, PhD	Non-redundant roles for the human mRNA decapping cofactor paralogs DCP1a and DCP1b
Ruoyu Yang	Gino Cingolani, PhD	Multifaceted role of importins in virus nuclear import and antiviral response

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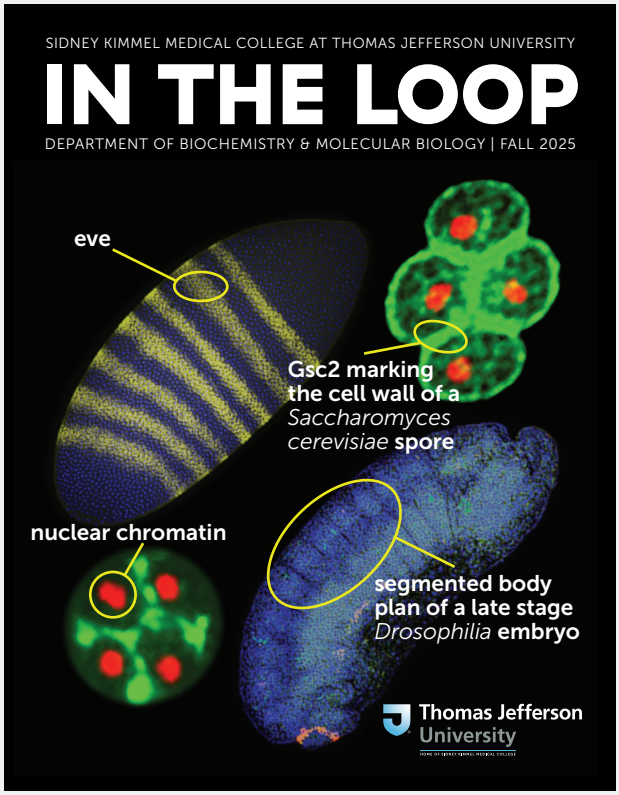

FROM THE COVER:

The power of model organisms in understanding human biology.

Drs. Jim Jaynes and Miki Fujioka have spent decades using the fruit fly *Drosophila melanogaster* as a model for dissecting precisely how gene expression patterns are established and maintained. In both humans and *Drosophila*, the ability of different cells to have different gene expression patterns underlies the creation of distinct tissue types. Having a spectrum of functionally distinct tissue types is a defining feature of complex organisms like flies and humans. Images on the cover show the very early striped expression patterns for a gene termed eve (yellow), which controls the development of the segmented body plan in the *Drosophila* embryo later in development.

Like Dr. Jaynes, Dr. Winter and his group have spent decades studying an organism that has yielded tremendous insights into human health and disease. This important model is the baker's yeast *Saccharomyces cerevisiae*. Specifically, they have discovered a series of signaling pathways that regulate meiosis, the process that leads to the creation of sperm and eggs in humans, and spores in yeast. The cover shows images of yeast that have undergone sporulation and which are stained for the cell wall protein Gsc2 (green), and for chromatin proteins in the yeast nucleus (red).

These genetically tractable model organisms have served as a platform for experiments that have led to groundbreaking advances in treatments for human diseases like neurodegeneration, cardiovascular disease, and cancer.

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