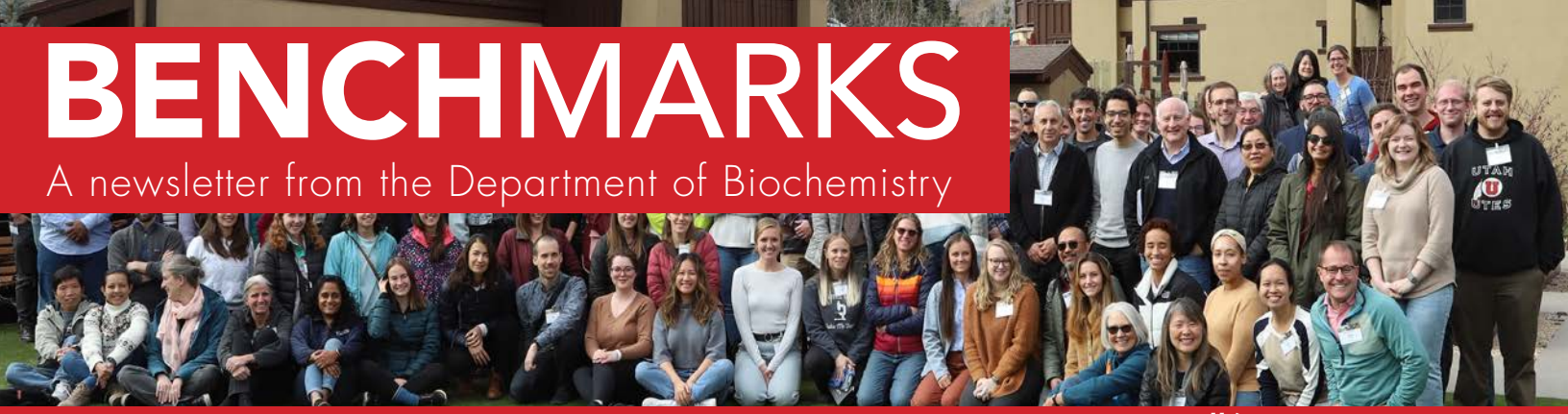
BENCHMARKS

A newsletter from the Department of Biochemistry



Fall/Winter 2023-2024

CONNECTING WITH INDUSTRY

Chair's Message from Wes Sundquist

"If you have genius, industry will improve it"

-Sir Joshua Reynolds, Founder of the Royal Academy of Arts and the 18th century "Grand Style" movement.

Following this advice, our department is embarking on an effort to enhance our ties with industry (even if this isn't exactly what Sir Josh had in mind!). Our efforts are motivated by the fact that industry is typically where innovative ideas are translated into useful cures, products, and services; by the reality that the majority of our trainees go on to great careers in industry; and by opportunities presented by a new Life Sciences Initiative being created by University of Utah President, Taylor Randall, in partnership with the State of Utah, Utah State University, and life sciences industry leaders, with the goals of enhancing training opportunities and helping to keep Utah competitive. We have special opportunities in this space because Utah's job growth in life sciences was the highest in the country from 2012 to 2021, yet leading life science companies in Utah and throughout the US require even more well trained scientists.

Excellence in foundational biochemical research will always be our forte, and this will not change. Moreover, when we ask our industry colleagues what they look for in new employees, they inevitably tell us "great scientists with critical thinking skills". I think we already do a good job of honing those skills in our very talented trainees. Our departmental efforts naturally focus on the academic end of the research spectrum, however, and we are therefore now also exploring ways in which to create tighter links to industry and provide even more relevant preparation for successful industry careers.

We're just getting started, but it has already been a busy year. We've begun by making important new connections and listening to successful industrial scientists and venture capitalists. At our November retreat, Justin English organized a very informative panel discussion from six outstanding representatives from the private sector: Marion Dorsch, President and CSO of Atavistik; Leah Frautschy, VP of Manufacturing at Denali Therapeutics; Mike Grey, Venture Partner and Biotech CEO of Pappas Capital; Kate Lansu, Senior Director of Pharmacology at Eli Lilly; Leo Lin, Medical Director at ARUP Laboratories; and Brandon Probst, VP of Biology at Recursion Pharmaceuticals. Their insights were invaluable in helping us to understand their very different scientific and commercial environments. In January, Jared Rutter hosted a special seminar from Tim Kutzkey, Managing Partner at The Column Group, a very prominent biotech venture capital group in San Francisco. Tim relayed several vignettes about companies that he helped to found, including Carmot Therapeutics (recently acquired by Roche), which has developed very promising GLP1/GIP1 agonists for obesity and diabetes, and Neurona Therapeutics, which is developing neural cell therapies to treat chronic neurological diseases and has exciting clinical data in reducing epileptic seizures. Following Tim's visit, the Column Group decided to return to the University of Utah and hold a "Pitch Day", with the goal of identifying University-based technologies in which they can invest and build companies, potentially in Utah. Finally, on May 29, Vishva Dixit, Vice President and Senior Fellow in Physiological Chemistry at Genentech will give one of our annual JW, Wanda, Nick, and Sheryl Pace Endowed Lectures describing his beautiful work defining and modulating signaling pathways in development, inflammation, innate immunity, cancer, and cell death.

We also continue to build on our departmental tradition of entrepreneurship, and Jared Rutter, Michael Kay, and Justin English have been exceptionally active in this space. Jared has founded five different companies, including Vettore Biosciences, which currently has a promising program in Phase 1 for idiopathic pulmonary fibrosis, and Atavistik Bio, which has recently raised $100M to identify and develop precision allosteric small molecule therapeutics using his powerful MIDAS screening platform. Jared's lab also has a new small molecule program being supported by the U of U Therapeutics Accelerator, he serves on the boards of four companies, and he is leading our departmental efforts to enhance industrial ties. Michael is currently on sabbatical helping to launch a San Francisco-based venture-backed global vaccine startup company, where he serves as Interim VP of Discovery and Scholar-in-Residence. He previously co-founded the D-peptide Division of Navigen Pharmaceuticals, who advanced his work on potent HIV entry inhibitors into phase 1 clinical trials. Last but not least, Justin recently developed a new drug target identification platform called BioTac, founded a company called Evolution Bio based on his VEGAS directed evolution platform, and has received funding from Eli Lilly and Kallyope for his VEGAS and drug development efforts.

Looking forward, we are contemplating interesting ideas for increasing industry-relevant training efforts, including greater experiential learning opportunities, graduate co-mentorship with industrial parners, and even the possibility of a biotechnology-focused graduate training track. We welcome your ideas and input as our department expands into this exciting new dimension and we embrace the Utah State Motto of "Industry"!

L to R: Leah Frautschy, Marion Dorsch, Mike Grey, and Kate Lansu at the Industry panel discussion during the 2023 Biochemistry Retreat. Photo credit: Rachel Merrill.

U GIVING DAY 2024

For U Giving Day 2024 (April 2-3), the Department of Biochemistry is highlighting two important opportunities to support. Both funding causes support the inclusive success and diversity of students and trainees in Biochemistry and in the broader university community. We invite you to learn more about and support our Trainee Emergency Fund and our Utah SACNAS chapter.

The Biochemistry Department created a trainee support fund to provide our trainees with emergency financial assistance in times of unusual need. These funds can make the difference between completing a graduate program or perhaps pausing career goals and aspirations.

SACNAS is an all-inclusive community dedicated to supporting diversity and inclusion in STEM fields and fostering the success of scientists from under-represented backgrounds. Donations to our student-led chapter will help fund activities that promote networking, outreach, and equitable diversity and inclusion in science; professional-development speakers; and student travel to STEM diversity meetings.

You can read more about these two worthy causes in this newsletter.

INVESTING IN FUTURE SCIENTISTS: THE BIOCHEMISTRY TRAINEE SUPPORT FUND

Minna Roh-Johnson

The Biochemistry Department stands by the core values of excellence in research and supporting the diversity of people succeeding in science, recognizing that not everyone has the same level of financial security. Therefore, in early 2023, the Biochemistry Department launched an initiative to support students and postdoctoral fellows who were facing financial emergencies. Several students and postdoctoral fellows were struggling to continue with their studies and research. To meet this need, the department initiated the Biochemistry Trainee Support Fund, a fund first created by personal donations from individuals in the department. After this initial infusion of money, the fund grew through generous donations by friends and family on U Giving Day 2023, and together with a departmental match, the department was optimistic that enough funds were raised to support all students and postdocs in need.

Within six months of establishing the fund, the committee that reviews the Trainee Support Fund applications received a number of requests from students and postdoctoral fellows experiencing a financial crisis. Several of these situations involved caregivers, and the inability to cover childcare expenses for a period of a few months while the caregiver was transitioning between personal situations. “I have been worried about my continuation as a graduate student” wrote one student and that all of the childcare funds that they saved had “been depleted from the expense of this past summer of childcare”. Another student had a parent who was very ill. Upon learning that the parent would likely pass away in less than a week, the student booked travel in less than 24 hours, paying for a costly last-minute flight. They were able to return home before the family member passed away, but since returning to SLC, the student was saddled with credit card debt accrued from travel, creating additional stress during a period of mourning. “It was an expense I was not ready for,” wrote this student. While the department was able to provide assistance to these students and others, it was quickly realized that the need was much more than anyone had anticipated. Thus, the department plans to fundraise again later this Spring, with the hopes of raising enough money to create an endowed fund that will last in perpetuity without the need for yearly fundraising. This fund can then support any student or postdoc facing a financial emergency, allowing these young scientists to continue thriving in our research program.

Trainees can apply for emergency funds through an online application.

SAVE THE DATE!

Join us on May 29, 2024 for a talk by Vishva Dixit, MD (Genentech) as part of the J.W.,Wanda, Nick and Sheryl Pace lecture series. 4pm in the EIHG Gesteland and White Auditorium.

BRIDGING BOUNDARIES, IGNITING POTENTIAL: A PERSONAL ODYSSEY WITH THE SACNAS CHAPTER AT THE UNIVERSITY OF UTAH

Headtlove Essel Dadzie

As an international student from Ghana in West Africa, I understand firsthand the challenges faced by underrepresented minorities in pursuing careers in STEM fields. The journey through a PhD program amidst the isolating effects of virtual learning post-COVID was initially daunting. However, SACNAS (Society for Advancement of Chicanos/Hispanics & Native Americans in Science) emerged as my lifeline – providing a community and a profound sense of belonging that transcended the confines of the online realm. As the sole black student in my cohort, this connection was invaluable, offering solace and understanding in a sea of unfamiliar faces.

My journey with SACNAS began as a participant and evolved into advocacy, culminating in roles such as Historian from 2021-2023 and currently as Vice President for the 2024-26 term. These positions allow me to contribute to the community and empower me to be a voice for underrepresented students in STEM. A pivotal moment in my SACNAS journey occurred at the 2023 NDiSTEM conference in Portland, Oregon. This annual event, organized by SACNAS, serves as a vital gathering for Chicanos/Hispanics and Native Americans in STEM, providing opportunities for networking, workshops, research presentations, mentorship, and access to resources to advance careers and foster diversity and inclusion.

The immersive experience, knowledge gained, and invaluable networking opportunities at the NDiSTEM conference amplified my sense of belonging within the SACNAS community. However, the impact of SACNAS extends beyond personal growth – it shapes the future of STEM by empowering underrepresented voices and fostering a more inclusive academic landscape.

Your support as sponsors and donors is critical in fueling SACNAS's initiatives and ensuring its continued success in empowering diversity in STEM, especially at the University of Utah. By investing in SACNAS, you're investing in transforming lives and creating a brighter, more equitable future for all. Your generosity enables SACNAS to provide vital resources, support, and opportunities to underrepresented students, helping them overcome barriers and achieve their full potential in STEM.

Join us in this journey of empowerment. Your donation to SACNAS echoes far beyond financial contributions – it shapes the narrative of representation in STEM and fosters the leaders of tomorrow.

Together, let's celebrate the impact of SACNAS and work towards a future where inclusion is at the forefront of scientific innovation.

Headtlove Essel Dadzie is a 4th year graduate student in the Snyder Lab in the Department of Oncological Sciences.

SACNAS officers. First row (L to R): Headtlove Essel Dadzie, Taylor Stevens, Daniela Tamayo Jaramillo, Precious Opurum, Shai-Anne Nalder, Neetu Singh, Paola Fonseca-Romero, Deirdre Mack. Second row (L to R): Jesse Velasco, Jessica Pita-Aquino, Luis Cedeño-Rosario, Paul Sigala. Photo credit: Rachel Merrill.

SAVE THE DATE!

Daniel Colón-Ramos, PhD (Yale University/HHMI) will be giving a keynote talk following the Graduate Student Rising Stars symposium on May 20, 2024, co-sponsored by the J.W., Wanda, Nick and Sheryl Pace lecture series.

2023 POSTDOCTORAL RISING STARS SYMPOSIUM

Paul Sigala

2023 Postdoc Rising Stars with keynote speaker Dale Abel (2nd from right). Photo credit: Jason Shepherd.

The 2023 Postdoctoral Rising Stars Symposium was held on September 28-29 and featured 20 speakers in four half-day sessions centered around Cellular Metabolism, Microbiology and Immunology, Molecular Neurobiology, and Cell Biology and Cancer. These sessions were collaboratively planned by the Department of Biochemistry together with Oncological Sciences, Nutrition and Integrative Physiology, Pathology (Division of Microbiology and Immunology), and Neurobiology. In addition to the outstanding science presented by the 20 highly accomplished postdocs at this year's event, we were especially pleased with the diversity of speakers that included 60% females and >40% individuals from racial, ethnic, and LGBTQ backgrounds that are underrepresented in science. As our department grows, it remains an important goal to diversify our faculty to mentor our diverse graduate student body effectively. We consider this year's event to have been a major success and to have substantially advanced our efforts to recruit outstanding and diverse faculty to the University of Utah Dept. of Biochemistry.

The keynote speaker for this year's symposium was Dr. Dale Abel, who is a former faculty member at the University of Utah and is currently Chair of the Department of Medicine at UCLA. Funding for the event was provided by a grant from the Burroughs Wellcome Fund, the Senior Vice President for Health Sciences Research Unit, and by the partnering departments. We look forward to another exciting Postdoctoral Rising Stars Symposium on Sept. 26-27, 2024!

RIBOSOME GALA AT THE NATURAL HISTORY MUSEUM OF UTAH

Wes Sundquist

This past fall, the stars aligned to create a gala event celebrating Venki Ramakrishnan's groundbreaking research on the ribosome at our beautiful Natural History Museum of Utah (NHMU). It all began when Professor David Goldenberg (Biology), invited former Biochemistry faculty member Venki Ramakrishnan to give the Frontiers of Science Lecture- the oldest and most prestigious science lecture at the University of Utah- on his amazing structural studies of the ribosome. His work provided remarkable insights into how the ribosome functions, and ultimately led to the 2009 Nobel Prize in Chemistry. At about the same time, Ray Gesteland (former chair of Human Genetics Department) was working with John Atkins (Human Genetics), Janet Iwasa (Biochemistry), Tim Lee (NHMU Director of Exhibits), and Sarah Kurrus (donor) to create a new ribosome exhibit, that would include a feature on Venki. In parallel, we were thinking about how best to hold the 2023 James and Kathleen McCloskey Endowed Lecture, which honors Jim McCloskey's legacy here in our Biochemistry and Medicinal Chemistry Departments. Jim cared deeply about the RNA in the ribosome and was a good friend of Venki's. So we found we were all creating a word cloud with just two words – "Venki" and "Ribosome" – and decided to combine forces to create one big celebration, which included a dinner reception for participating departments and friends of the NHMU, a ribbon cutting ceremony that officially opened the ribosome exhibit, and a packed-house lecture in which Venki wonderfully described his own personal journey through our department and, ultimately, to the structure of the ribosome. You can read more about Venki in his NHMU interview, and about the scientific twists and turns in the race for the ribosome in his now-classic book, Gene Machine.

A joyful ribbon-cutting ceremony celebrating the opening of the ribosome exhibit. From left to right: Janet Iwasa, Ray Gesteland, Sarah Kurrus, Venki Ramakrishnan, Tim Lee, Jason Cryan (at podium), Kay McCloskey, and Wes Sundquist.

The lasting legacy of the evening is a wonderful ribosome exhibit, which was designed to appeal to different audiences and age groups. A large, colorful animation of the eukaryotic cytosol is projected along the back of the exhibit and shows numerous ribosomes at work. An interactive physical model of a ribosome allows museum visitors to insert a mRNA into a ribosome and crank it through, producing a lit-up peptide chain. The complex structure of the ribosome is highlighted by a detailed 3D printed atomic model, and a close-up view of the bacterial ribosome is displayed on a monitor. Visitors can push buttons to view bacterial translation at real time (around 20 amino acids per second!) and to see how antibiotics can inhibit translation. Finally, a section of the exhibit displays a Nobel Prize medal, and describes Venki's contribution to solving the structure of the ribosome.

Tim Lee (3rd from left) demonstrates features of the ribosome exhibit to museum visitors during the ribosome gala.

A HISTORY OF THE BIOCHEMISTRY DEPARTMENT: PART 2

Dana Carroll

The first installment of this recounting of our history focused on our founding Chair, Leo Samuels. The other member of the Samuels family who had a major impact on the department was Leo's wife, Barbara. She worked with Leo and the department in a number of capacities. She was a capable research chemist and was a gracious host to the many visitors who came to work with Leo. With the community of biomedical science being a tiny fraction of its current size, researchers frequently traveled among labs and institutions to learn new approaches and techniques in their fields. The Biochemistry Department had a rich parade of visitors and trainees, many of whom had prominent careers in countries around the world.

Barbara was born in 1911 and grew up in Hollywood, California – not amidst its glamour, she claims. She got both bachelor's and master's degrees in history from UCLA, but gave up a Ph.D. program when she married Leo in 1935. She volunteered extensively in Salt Lake City, including teaching English to non-native speakers at the Guadalupe Center, and serving as a member and/or board member of Friends of the University Library, the UofU Women's Club, the Aztec Club (a town-and-gown organization), the ACLU, NAACP, Common Cause and Planned Parenthood.

Barbara K. Samuels, 1910-2009.

After Leo's death, Barbara established the Leo T. and Barbara K. Samuels Presidential Endowed Chair in Biochemistry, a post currently held by Wes Sundquist. She was kind and modest and a great supporter of the department. The University gave her an honorary doctorate in 1985. She used to come to the department picnics until her health prevented that, and she died in 2010 at the age of 99.

Marjorie Riches Gunn, 1928-2023.

The Department also provided an early home for Marge Gunn, who was hired in her twenties as a secretary before moving to the Department of Medicine. Her long association with the School of Medicine was further solidified by her marriage to Francis Gunn, who was then the Chair of the Department of Pathology. Marge was a generous donor and good friend to our department up to her death in 2023.

The Samuels years also saw the beginning of protein biochemistry research in the department, due to the arrival of Emil Smith. Maxwell Wintrobe, the Chair of Internal Medicine who was hired in 1943, obtained the very first NIH research grant for a project to study inherited diseases, including muscular dystrophy. To pursue that research, Smith was hired in 1946 and joined the Biochemistry Department as his natural academic home. The grant provided generous funds to remodel space in old Fort Douglas buildings, to purchase high-end (for that time) equipment, to buy supplies and hire personnel. Among the purchases was the second commercial analytical ultracentrifuge ever made. Smith established an outstanding research program based on protein purification, protein sequencing, and enzymology, and attracted domestic and international visitors, including outstanding students and postdocs. He was also an excellent teacher who linked lessons in biochemistry to medical conditions and processes.

The department was quite small in those early years. The University catalog for 1951-52 lists only four tenure-track faculty members, just three of whom ran research groups, plus a range of research track appointees and fellows. Nonetheless, a number of prominent biochemists received early training here during that time.

Bill Rutter received a master's degree in 1950 and went on to a very distinguished career in academic science and the private sector. He brought the Department of Biochemistry and Biophysics at UCSF to prominence as chair from 1969-1982. In 1981, he co-founded Chiron Corporation, one of the most successful early biotech companies. He founded and still runs the biotech incubator company, Synergenics, which has provided support for the commercialization efforts of his nephew and current Biochemistry faculty member, Jared Rutter. Bill is a very generous donor to our department and the U.

Among Emil Smith's trainees were graduate student Alex Glazer (Ph.D., 1960) and postdocs Rufus Lumry and Bob Hill. Glazer was a postdoc with Fred Sanger in Cambridge, UK, then had faculty positions at UCLA and UC Berkeley. Lumry had a distinguished career at the University of Minnesota, and Hill was the long-time chair of Biochemistry at Duke. Emmanuel Margoliash spent two years as a visitor in Smith's lab, where he determined the first sequence of a cytochrome c. Rutter, Glazer, Hill, Margoliash and Smith himself were all elected to the National Academy of Sciences.

Emil L. Smith, 1911-2009.

Emil Smith expressed an interest in becoming department chair after Leo Samuels retired, but he wasn't considered for the job and instead moved to UCLA as chair in 1963. Given his prominence in protein biochemistry, this was our loss.

Dana Carroll is Distinguished Professor Emeritus of Biochemistry and is one year older than the Department.

BIOCHEMISTRY FACULTY PLAY A KEY ROLE IN THE NEW MD PROGRAM

Janet Lindsley, Morgan Nelson, and Tim Formosa

The Spencer Fox Eccles School of Medicine at the University of Utah has more than a new name. In August 2023, the Mission-Driven Medical Degree (or MD) Program was launched, and Biochemistry faculty have played a large role in many aspects of designing and rolling out this program.

The Need for a New Mission-Driven Medical Degree Program

In 2009, Biochemistry faculty members Janet Lindsley and Tim Formosa were both involved in a major medical school curriculum update that integrated separate department-based courses (e.g., anatomy, biochemistry, physiology) into disease-based courses (e.g., cancer, infectious disease, diabetes). They and other faculty members tried many innovative teaching methods, gained insights into what works, and made more than a few mistakes! The COVID-19 pandemic created significant challenges to all forms of education, notably highlighting the existing disparities and flaws in both medical education and in the healthcare system this training is meant to support. Together, these experiences revealed the need for another, more substantial change in the design of our curriculum.

During a year-long effort involving the existing teaching faculty, current and past students, and the school administration, every aspect of the process for training physicians was examined and reconsidered. Major issues that emerged included:

- The traditional medical school curriculum typically consists of two years of classroom-based courses stuffed with science facts followed by two years of clinical rotations. This divorces the foundational sciences underlying medicine from the clinical practice of medicine, making these intertwined topics look and feel like separate entities.
- Treating medical students as if they are empty vessels that we attempt to fill with a firehose of expanding biomedical knowledge is incongruous with how learning happens, and often drowns innate student curiosity. Educational research instead shows that most adults learn best by actively doing something that feels useful (as opposed to sitting in a classroom for 4-8 hours per day).
- Teaching facts in one context and clinical practice in another doesn't help students learn to use evidence-based scientific processes for improving the delivery of healthcare.
- In 2022 the United States Medical Licensing Exam Step 1 (basic science, multiple-choice exam) changed from reporting a numeric to a pass/fail score. The goal of helping students achieve the highest possible score on this exam has changed to helping them pass it with competency.
- The traditional system of training physicians has failed to achieve a unified, equitable healthcare system whose practitioners understand, value, and reflect the diversity of their patient population.

A New Approach

In retrospect, while the changes implemented in 2009 felt significant, they were more of an update compared to the complete overhaul introduced in the 2023 MD program. As shown in Figure 1, a first year medical student (MS1) in our new MD program has a weekly schedule that includes a 4-hour shift at one of five student-led clinics located throughout the Salt Lake valley, three 2-hour sessions of interactive small group work with a faculty facilitator in Problem-Based Learning (PBL) modules (described below), and only about 3 hours of more traditional lectures. This schedule provides time for flexibility and individualization – all of the self-directed learning time (lime green) is left to the students, who might use it for studying, conducting research that fans their curiosity, participating in a project that they are passionate about, or just attending to their wellness!

Example weekly schedule for first year medical student in the new MD program

	Monday	Tuesday	Wednesday	Thursday	Friday
8 AM	Self-directed learning	Student-Led Clinic shift	Self-directed learning	Self-directed learning	Problem-based learning (PBL)
10 AM	Problem-based learning (PBL)		Problem-based learning (PBL)		Team-based learning (TBL)*
12 PM	Lunch (and travel)	Lunch (and travel)	Lunch (and travel)	Lunch (and travel)	Lunch (and travel)
1 PM	Self-directed learning	Large group learning & lectures*	Doctoring 1*	Lab	Self-directed learning
3 PM					

*Activities that occur at the same time for all students

Figure 1: Note that only a few of these activities occur at the same time for all students.

Problem-Based Learning (PBL)

A major change in the new MD Program is that much of the "content" is managed by the students themselves in PBL sessions. Here, a group of 7-8 students receives the bare outlines of a clinical presentation each Monday, with only the patient's picture and their chief concern. A faculty member facilitates the session, acting as the patient as the students must advance the case by asking questions to learn more about this patient's situation and symptoms. Once students have interviewed the patient, they articulate the gaps in their knowledge to identify a list of "learning issues" that they need to know more about to proceed with diagnosis and treatment.

Students then research their topic independently and come to class on Wednesday prepared to teach their teammates what they learned. After student presentations, the group determines what to focus on during a physical exam and what lab tests and/or imaging to order to narrow their differential diagnosis. Once provided with the results they request, they identify new learning issues (e.g. how does that test work? How sensitive and specific is it?), complete another round of research, and teach each other again on Friday.

As the case wraps up, the students collectively synthesize their shared understanding of how each symptom and diagnostic finding

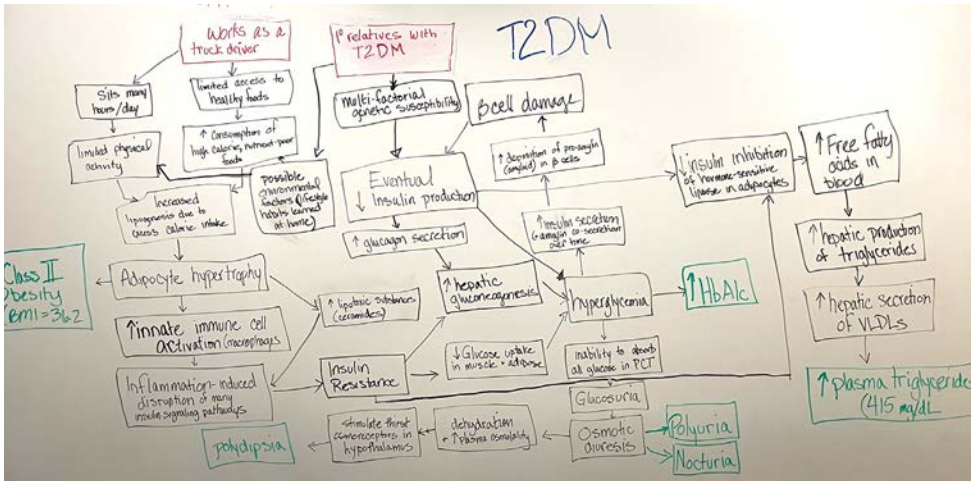


Figure 2. Example of a student-generated Mechanism of Disease map for a patient with type 2 diabetes.

results from a combination of biologic, environmental, social, and psychological risks or inciting factors in the form of a complex Mechanism of Disease map. In drawing these maps, students are learning how to integrate social determinants of health with both known and as-yet-unknown pathophysiologic mechanisms. This process breaks down the silos found in traditional curricula, aligning the "facts" with their relevance in a clinical scenario, enhancing both the stability and the utility of the learning. Several Biochemistry faculty (English, Formosa, Hawkins, Kay, Lindsley, Liu, Nelson) have been PBL facilitators this year.

For example, a PBL case might start as a 57-year-old man who is coming to clinic with a concern of fatigue. From their comprehensive history interview, they learn that this patient is a long-haul truck driver with limited dietary options, little opportunity to access healthcare, and is experiencing unintentional weight loss, along with other symptoms. After a week of research and ordering appropriate diagnostic tests, the students ultimately diagnose this patient with type 2 diabetes. Their Mechanism of Disease map then attempts to explain how his risk factors contributed to his acquiring diabetes, how this condition causes the signs and symptoms he presents with, and how the treatment options are designed to support his health. Figure 2 shows part of a student-generated map, showing the level of sophistication they acquire to integrate their understanding of the case.

Figure 3: MS1s working in small groups to diagnose metabolic disease patient cases.

Student-Driven Science Learning

Even as one of the designers of this curriculum, Janet Lindsley found it seemingly impossible to fit the necessary metabolism content into the allotted teaching time in the MD curriculum. Fortunately, she and some colleagues recently completed a research study on the role of basic science education in physician professional identity development. One finding from this work suggested that science faculty can help catalyze the transformation of a medical student into a developing physician by acting as "travel guides." In this analogy, a truly effective tour guide can make a lasting impact on a traveler, not by having them memorize the local laws, history and street names, but instead by showing them a few favorite places with appropriate context, giving them a map, and allowing them to further explore and discover.

Janet Lindsley and Morgan Nelson decided to test this idea in January 2024 with the first-year medical students (MS1s). After a lecture introducing core concepts of human metabolism and a metabolic map, the MS1s were instructed to diagnose six patients with inborn errors of metabolism using the reported lab findings and the map. These were difficult cases that had previously challenged MS2s in the prior curriculum (now known as the "legacy curriculum"). The MD Program MS1s treated the metabolic map and patient cases as a treasure hunt, and they correctly diagnosed the six patients and accurately explained their diagnoses within an hour. Based on initial quiz score analysis, this cohort of MD program students is better able to answer metabolism questions compared to students in our legacy curriculum, despite fewer hours of metabolism instruction. While the new modalities can be chaotic (or perhaps *because* they are chaotic) student learning through self-discovery appears to be superior to traditional methods even with less "coverage" of the content.

Looking to the future

The entire MD Program curriculum is illustrated below; places of current or envisioned biochemist involvement are highlighted. (This year, only the MS1s are in the MD Program curriculum, while the MS2s-MS4s remain in the legacy curriculum.) Subsequent years maintain the philosophy that students best learn medicine through integration of foundational sciences with clinical exposure. Students therefore engage in their major clerkship year as MS2s (instead of as MS3s in the legacy curriculum), which includes a weekly foundational science component. In their third and fourth years, after having the opportunity to see a range of specialties, they take a deep dive into topics that will support their differentiation into specific practice areas, including advanced science courses.

To highlight a few of the exciting areas where biochemistry faculty are already involved:

- A few MS1s have been awarded NIH training grants for summer research in Biochemistry department labs (Keren Hilgendorf and Jared Rutter).
- Janet Lindsley is collaborating with clinical faculty to develop the weekly pathophysiology team-based learning sessions that the MD Program MS2 students will start next year as part of their Longitudinal Integrated Clerkships (LICs).
- Our newest faculty member, Morgan Nelson, is working with Janet Lindsley and Juliana Simonetti, co-director of the U's Comprehensive Weight Management Program, to develop an MS3/MS4 Advanced Integrated Science Course called "Beyond BMI: a multidisciplinary approach to obesity".

We've come a long way since the 2008 stand-alone Medical Biochemistry course with 67 hours of lectures! Biochemistry remains highly relevant to educating future physicians, and our department remains committed to helping catalyze the transformation of medical students into thoughtful, knowledgeable, and skillful physicians.

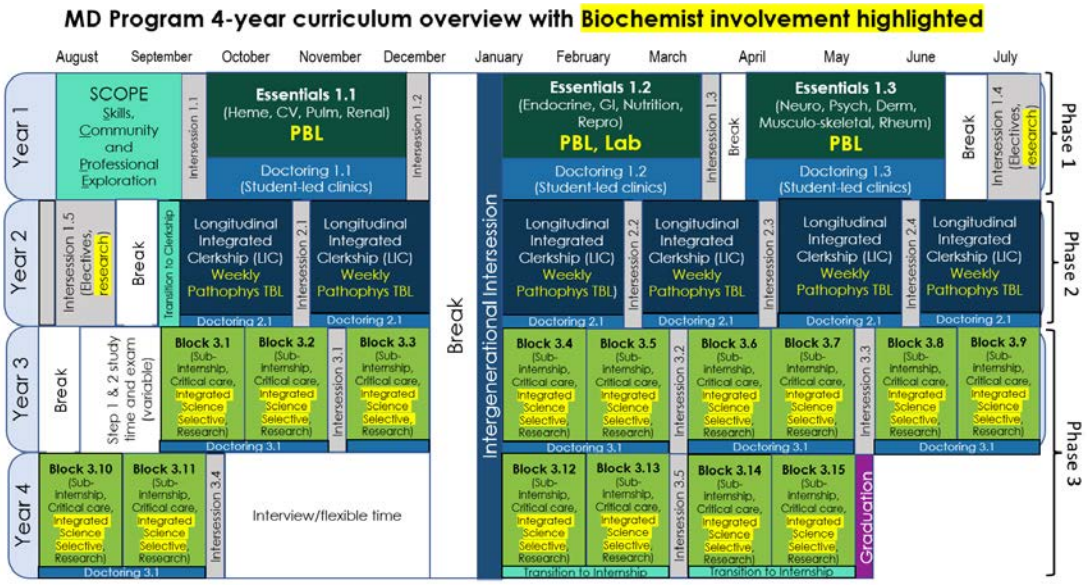
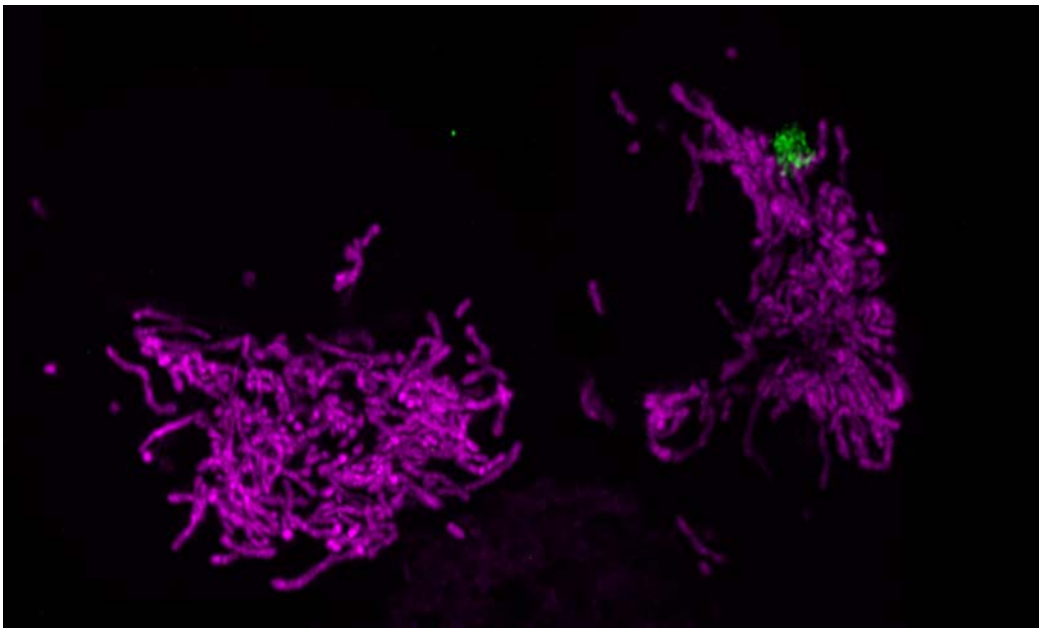


Figure 4. Graphic illustration of new MD Program curriculum with biochemist involvement highlighted.

BIOCHEMISTRY RESEARCH ADVANCES: TRANSFERRED MITOCHONDRIA PROMOTE PROLIFERATION

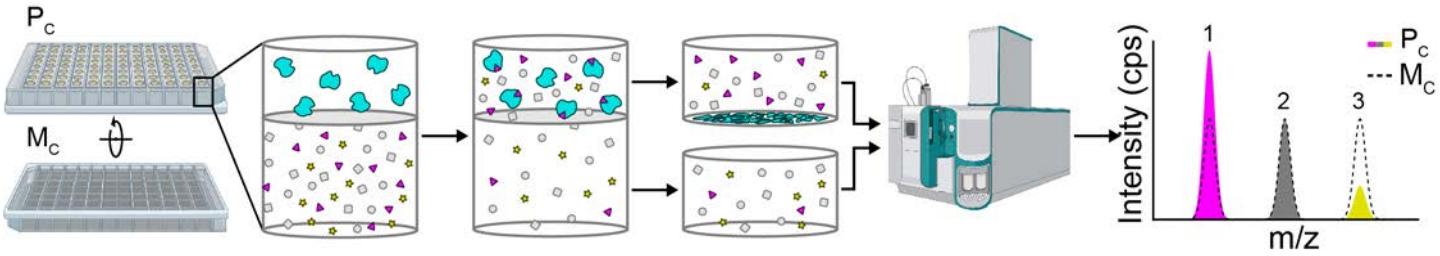
Cancer cells are constantly receiving signals from the local tumor environment that influence decisions regarding whether to die, divide, or metastasize. One cell type in the environment that communicates with cancer cells is the macrophage, an immune sentinel and responsive cell. Paradoxically, even though they are a part of the immune system, macrophages promote many steps of cancer metastasis. Roh-Johnson and colleagues discovered that one way macrophages promote cancer progression is by transferring their own mitochondria, the cellular organelle that provides energy for the cell, into the cancer cell. They and others initially hypothesized that cancer cells might meet the energetic demands of metastasis by "stealing" mitochondria from neighboring cells like macrophages, but surprisingly, they found instead that the transferred macrophage mitochondria are dysfunctional. Rather than providing energy, transferred macrophage mitochondria instead activate signaling pathways and promote cancer cell proliferation. This discovery could ultimately have clinical impacts given the importance of cancer cell metastasis and the fact that mitochondrial transplantation is an emerging therapeutic approach for treating critical illnesses, particularly ischemia reperfusion injury.



Two cells showing: 1) a breast cancer cell with its own mitochondria labeled in red that has been injected with purified green macrophage mitochondria (right cell, green cluster on the top right corner of the cell), and 2) a control un-injected breast cancer cell (left cell).

Transferred mitochondria accumulate reactive oxygen species, promoting proliferation. Kidwell CU, Casalini JR, Pradeep S, Scherer SD, Greiner D, Bayik D, Watson DC, Olson GS, Lathia JD, Johnson JS, Rutter J, Welm AL, Zangle TA, Roh-Johnson M. Elife. 2023 Mar 6:12:e85494. Also highlighted in: Researchgate.

BIOCHEMISTRY RESEARCH ADVANCES: THE MIDAS PLATFORM



Schematic depiction of the MIDAS platform. A purified protein of interest is subjected to equilibrium dialysis against a library of ~400 metabolites. Those metabolites that bind to the protein are enriched, as detected by mass spectrometry (purple). Metabolites that are consumed by the protein, or otherwise depleted from the protein chamber, are colored yellow.

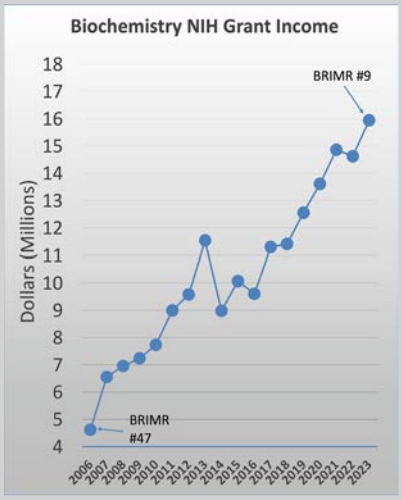
Direct interactions between proteins and small molecule metabolites mediate a majority of the enzymatic, regulatory, and signaling events that occur in human cells and tissues. Despite their obvious importance, there is a relative absence of methodologies available for high-throughput and systematic protein-metabolite interactomics. To address this limitation, the Rutter lab and colleagues developed and validated a unique technological platform (MIDAS) with unprecedented power to identify protein-metabolite interactions systematically. Through implementation of MIDAS, they discovered numerous interactions in human metabolic and signaling pathways. They also further validated a number of novel substrates, activators, inhibitors, and post-translational modifications. These discoveries have resulted in 10 new structures of novel metabolite-protein interactions. The MIDAS platform has the potential to provide a transformative advance in our understanding of metabolic regulation of fundamental and disease-relevant pathways and to catalyze the development of novel pharmacological interventions.

Protein-metabolite interactomics of carbohydrate metabolism reveals regulation of lactate dehydrogenase. Hicks KG, Cluntun AA, Schubert HL, Hackett SR, Berg JA, Leonard PG, Ajalla Aleixo MA, Zhou Y, Bott AJ, Salvatore SR, Chang F, Blevins A, Barta P, Tilley S, Leifer A, Guzman A, Arok A, Fogarty S, Winter JM, Ahn H-C, Allen KN, Block S, Cardoso IA, Ding J, Dreveny I, Gasper C, Ho Q, Matsuura A, Palladino MJ, Prajapati S, Sun P, Tittmann K, Tolan DR, Unterlass J, VanDemark AP, Vander Heiden MG, Webb BA, Yun C-H, Zhap P, Wang B, Schopfer FJ, Hill CP, Nonato MC, Muller FL, Cox JE, and Rutter J, Science. 2023. Mar 10;379(6636):996-1003.

Also highlighted in @THEU, UU Innovation Impact Award.

TOP 10!

Every year, the Blue Ridge Institute for Medical Research (BRIMR) ranks US academic departments doing biomedical research based on the total level of NIH funding that they receive. The 2023 NIH BRIMR rankings just came out, and the University of Utah Department of Biochemistry is now ranked #9 of 96 national biochemistry departments - our highest ranking ever! Source: https://brimr.org/brimr-rankings-of-nih-funding-in-2023/.

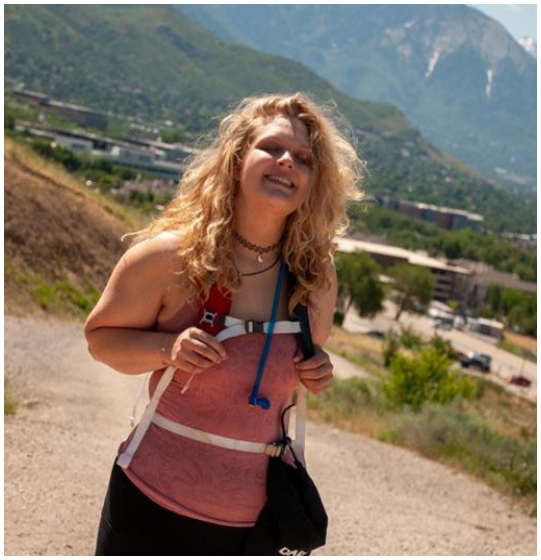


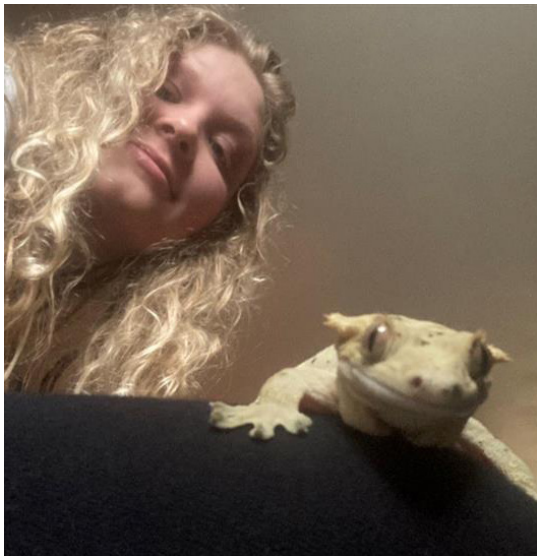
STAFF HIGHLIGHT: MEET HANNAH LOGAN

As the Executive Secretary for the Department of Biochemistry, Hannah Logan helps department members with a wide array of tasks, including making conference room reservations, updating our website, ordering office supplies, and managing the monthly birthday board announcements. She particularly enjoys working with students and helps them throughout their training, from posting their bio on a lab website, to setting up rooms for their thesis defense.

Prior to working in Biochemistry, Hannah worked at a pediatric clinic as a patient relations specialist. She received a Bachelor's degree in Anthropology from the U, where her favorite courses included forensic anthropology and primatology.

A SLC native, Hannah grew up in nearby Cottonwood Heights and has long enjoyed the local outdoors. In the summertime, she often goes on hikes after work on the foothills behind the Biochemistry building. Hannah also enjoys cooking and baking (and recently tried her hand at making char siu bao) as well as drawing (including a mouse that was featured on the most recent Biochemistry retreat T-shirt). She has a pet crested gecko named Schmeckels. On the weekends, you might see Hannah working the register at the Pie Pizzeria (and if you do, she'll be sure that you get the 10% U of U discount!)





Left: Hannah Logan enjoying a hike in the foothills, and (right) hanging out with Schmeckels the crested gecko.

FACULTY HIGHLIGHT: MEET MORGAN NELSON

Morgan Nelson with sons Wes (left) and Cal (right) and husband Eric.

Morgan Nelson, who grew up in Bountiful, Utah, says she disliked science until the 8th grade. An elective science course she took, taught by an engaging teacher, made her see science differently. She enjoyed the hands-on activities, including testing and building bottle rockets and trebuchets, as well as a memorable field trip to the Huntsman Cancer Institute, where she and her classmates took cheek swabs and isolated their own DNA. Encouraged by her teachers, she went on to participate in science clubs and spent a summer in high school doing a summer internship in Charlie Murtaugh's lab (U of U Human Genetics). By the end of high school, Morgan knew she wanted to major in a scientific field.

At BYU, Morgan took courses in molecular biology and worked in a lab for over two years studying the development of asthma in Utahns. Although she had initially thought a science major would lead her to medical or dental school, her experience in the lab made her realize that going to graduate school for a PhD was a viable path for her. Since Morgan's husband, Eric, graduated a year ahead of her and had started the dentistry program here at the U, Morgan decided to stay local and apply to the U's Molecular Biology graduate program.

Having gained an interest in RNA and transcriptional regulation during her undergrad years, Morgan decided to join the lab of Ryan O'Connell (Pathology), where she initially studied the anti-inflammatory microRNA miR-146a and its role in obesity and metabolic syndrome. After noticing that mice lacking miR-146a were predisposed to developing fatty liver and cancer, Morgan's follow-up research project described how the immune system plays an important role in protecting the liver from tumor development. Her time in graduate school, however, was disrupted when the COVID pandemic hit.

While the lab was mostly shut down, Morgan worked on writing a review, but still had free time and wanted to try her hand at science communication. Dismayed by the misinformation she was seeing regarding the COVID vaccine, Morgan created an Instagram account and started creating videos about the risks and benefits of vaccinations. Her posts led to interesting interactions over social media and an invitation to teach about vaccines to a local high school health class. After realizing how much she enjoyed this teaching experience, Morgan decided to apply for a Higher Education Teaching Specialist (HETS) program at the U, and balanced this coursework with her research. As part of the certification program, she worked with Scott Hale (Pathology) on a graduate course on immunology. Later, she worked as a teaching assistant for a metabolic regulation course with Janet Lindsley, taught a microbiology course as an adjunct professor at Westminster College, and participated in the Science Communication Fellowship program at the Natural History Museum of Utah.

Shortly after she completed her PhD work with Ryan in early 2023, Morgan learned about a newly created position that was opening in the School of Medicine and decided to apply for it. Now, as a lecturer in Biochemistry, Morgan is broadly involved in the medical curriculum at the U. She currently facilitates problem-based learning and case-based learning, and will be a director for a medical course called “Beyond BMI: a multidisciplinary approach to obesity” in the new curriculum. She continues to be involved in local science outreach efforts, such as teaching biology to youth in custody as part of the STEMCAP program and continuing annual vaccine presentations to local high school classes.

In her free time, Morgan enjoys spending time with her two boys, Cal (5 yo) and Wes (2 yo), and her husband, Eric. Having played on soccer teams for much of her life, she now acts as a coach for Cal's team. She also enjoys running, biking, and hiking.

Morgan gave a workshop as part of the Science Communication Fellowship program at the Natural History Museum of Utah.

ALUMNUS HIGHLIGHT: MEET JUDITH SIMCOX

The Simcox lab (with Judi in the 4th row on the left) enjoying the 2023 Ugly Sweater Christmas Party.

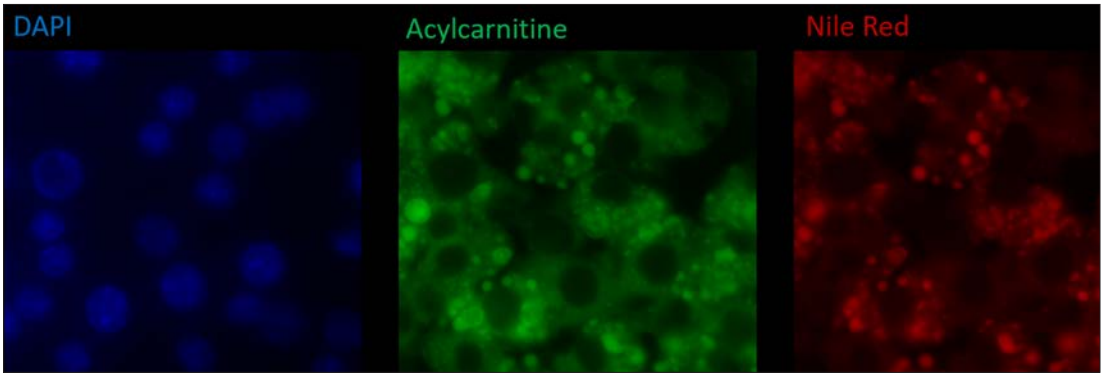
Judi Simcox grew up in Huntley, Montana, a small rural community with a population less than 500 which was close to a Crow reservation where many members of her extended family live. She developed an interest in the natural world over the course of many hiking, fishing, and hunting trips in her youth. Her interest in biomedical research was also piqued at a young age by her younger sister, Jan. Jan was born with Down's syndrome, and developed diabetes when she was 6 years old. In order to put Jan at ease with the new process of having her blood glucose levels regularly monitored, Judi volunteered to have her blood glucose checked before Jan. Judi soon became interested in understanding how her measurements were impacted by her diet, and would experiment by eating different foods and checking her blood glucose levels afterwards. When Judi was in high school, she was tasked with writing a research paper for a science class. She chose to write about Down's syndrome and diabetes risk, having observed a seemingly high prevalence of diabetes among other children in her community with Down's syndrome. Immersed in this research, the 4-page paper ended up as a 20-page report describing several prevalent hypotheses.

At Carroll college, a small liberal arts college in Montana, Judi initially thought that she would pursue a career in medicine. She was inspired, however, by a seminar by Jerry Shields, a faculty member in biology studying speciation, and ended up spending 4 years in his lab doing research. Although she had started thinking about attending graduate school by her junior year, she felt she needed more time to think about her path, and decided to work as an analytical chemist at a environmental science company near her hometown. This experience gave her the insight that she did want to pursue a career in research, and also provided skills that proved useful later in her career.

Judi joined the Molecular Biology graduate program at the U, joining Don McClain's lab. Her research focused on how iron and other dietary components impact metabolism and circadian rhythm. While a graduate student, Judi actively sought out teaching opportunities

and was able to balance her work in the lab with an adjunct position at Westminster College teaching genetics. Although she enjoyed teaching, she realized that she was more motivated by lab research, and decided to do a postdoc. Joining Claudio Villanueva's lab, then in Biochemistry (and now at UCLA), Judi's project focused on aging and brown adipose tissue. After her initial story was scooped, she almost decided to quit the lab. Digging into her lipidomics data, however, led to a new story -- Judi found that in mice exposed to cold, the liver produces acylcarnitines that can fuel thermogenesis by brown fat.

Judi is currently a HHMI Freeman Hrabowski Scholar and Assistant Professor in the Biochemistry Department at the University of Wisconsin-Madison. Her lab is focused on identifying and characterizing different classes of lipids, and understanding the mechanisms by which these can contribute to human health and disease in diverse populations. She offers these words of advice to students: "Your unique perspective and passion are valuable to science. Be sure to understand your personal value, and to ask for what you need or want."



The Simcox lab uses fluorescently labeled lipids to track uptake into cells. This image shows the uptake of a fluorescently labeled acylcarnitine localized to the lipid droplet (stained with nile red) in adipocytes.

HONORS, GRADUATIONS, AND TRANSITIONS

MAJOR FACULTY AWARDS & RECOGNITIONS

Kevin Hicks and **Jared Rutter** won the Inaugural University of Utah Innovation Award in the "Innovation Impact" category (for their development of MIDAS technology).

Adam Hughes' discovery of the Mitochondrial Derived Compartment (MDC) was feature in an article on cellular organelle biogenesis in Knowable Magazine.

Minna Roh-Johnson's work on mitochondrial transfer in cancer was referenced in National Geographic Magazine.

MAJOR GRADUATE STUDENT & POSTDOC AWARDS

Caroline Craig (Starr lab) was awarded a spot on the Genetics T32 training grant.

Mark Lee in the Hilgendorf lab received a T32 predoctoral training grant in metabolism.

Meghan Curtin in the Hilgendorf lab received the trainee award at the Metabolic Breast Cancer Research Conference.

Ahmad Cluntun (Rutter lab) received a K99/R00 grant.

Kristina Seiler (Rutter lab) received a postdoctoral fellowship from the Swiss National Science Foundation.

Luis Cedeno-Rosario (Rutter lab) received a postdoctoral fellowship from the Burroughs-Wellcome Foundation and was selected to be part of the 2023 National SACNAS postdoc leadership institute and as a University of U-HELM scholar

Libby Mumby (English lab) was accepted to the T32 Pitch Training Grant Program.

Alexa Gormick (English lab) was named a UROP scholar for the Summer 2023 and Fall 2023 semesters and was also awarded the College of Science Dean's Scholarship and the School of Biological Sciences Continuing Education Scholarship for 2023-2024.

Kade Loveridge (Sigala lab) won a "best talk" award at the MD/PhD retreat and was selected for funding on the STARS Research Translation T32 training grant.

Nate Krah (Rutter lab), was awarded the Quagliana Endowed Fellowship from the Department of Internal Medicine.

Ashish Toshniwal (Rutter lab) won the first-place poster prize at the 2023 DMRC retreat.

Anna Gilstrap (Shen lab) was selected to present her research as part of the Research on Capitol Hill (ROCH) event.

Sangeetha Balasubramaniam (Hughes lab) was awarded a Travel Scholarship to attend the upcoming Keystone Symposia on Mitochondria Signaling and Disease.

Julio Fierro (Roh-Johnson lab) was selected to give a keynote address at a symposium sponsored by the Salt Lake Community College.

Ashish Toshniwal (Rutter lab) was awarded an American Heart Association postdoctoral fellowship.

Graduate students **Kade Loveridge** and **Jessica Pita-Aquino** and postdoc **Radek Omelianczyk** (Sigala lab) were awarded 2-year fellowships from the American Heart Association.

Ryan Andrews, a postdoc in the Bass Lab, received an NIH F32 postdoctoral fellowship.

Amber Vogel (Hill Lab) received a postdoctoral fellowship from the Juvenile Diabetes Research Foundation.

Aldo Garcia-Guerrro (Sigala lab) was selected as a University of Utah U-HELM scholar.

GRADUATIONS & TRANSITIONS

Qian Xue (Roh-Johnson lab) started a postdoc at Stanford University.

Joey Casalini (Roh-Johnson lab) accepted a position at Paterna Biosciences.

Austin Bender (Ducker lab) was accepted into Pharmacy School.

Megan Okada (Sigala lab) started a Master's in Public Health Program at the U.

Sarah Hansen (Bass lab) accepted an Assistant Professor position at The University of Wisconsin - Eau Claire, in the Chemistry and Biochemistry Dept.

The following students completed their degrees since the last publication of the newsletter in Spring/Summer 2023: Magnus Creed, Kathryn Davis, and Samuel Hickenlooper (all graduating from the Franklin lab).

CHANGING YOUR NEWSLETTER COMMUNICATION PREFERENCES

We release two newsletters a year, and send out both print and email versions. If you currently receive a print version but would prefer an electronic version (or vice versa), or if you would prefer to opt out of either or both, please visit this link and scroll to the bottom to indicate your preferences:

https://medicine.utah.edu/biochemistry/newsletters

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Group photo from the Biochemistry Department Retreat held at Deer Valley on November 2-3, 2023. Photo credit: Tim Formosa.