PHAGES IN SPACE

Meet our New Faculty
Letters from the Lab
And more
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Cover image: A rocket will carry samples of bacteria and phage to the International Space Station as part of a research project by scientists in the Department of Biochemistry. Their launch is tentatively scheduled for February on a Northrup Grumman rocket from Wallops Flight Facility in Virginia. NASA also issues a patch for each mission and this one, designed by graduate student Chutikarn Chitboonthavisuk in the Raman Lab, features a phage, rocket, and Bucky.

Photo illustration by Robin Davies.
I t is my pleasure to provide these introductory comments to the 2019 edition of Biochemistry InVivo, where we keep current members of the department, and our alumni, supporters, and friends up to date on the most exciting things happening in our research, teaching and service to the world. It is our sincere hope you will find these newsletters engaging, enlightening, and inspiring.

The cover story, titled Phages in Space, introduces an intriguing thought. If humankind is eventually going to travel to other planets, our microbiome is going to have to come with us. So, as we are working out the myriad human viability issues that will arise in this pursuit of the stars, researchers from our department are also addressing issues of microbial viability that might also arise. In experiments that will be carried out on the International Space Station with support from NASA, a team of researchers led by professors Vatsan Raman, Michael Cox, and Michael R. Sussman will carry out a series of foundational experiments, scheduled to begin with a February 2020 launch date. Read the other details contained in the highlight article of this issue.

This edition includes research highlights from three faculty. Dr. Rick Amasino has made a new contribution in the control of flowering in plants, with identification of a gene that kick starts flowering when spring arrives. Dr. Aaron Hoskins has created a “humanized” form of yeast that will accelerate research on the causes of MDS and other diseases. The mass spectrometry research of Dr. Michael R. Sussman is also highlighted, which has led to the identification of new protein biomarkers for colon cancer. From the great research environment provided by all of our faculty and staff, the department had 18 new Ph.D. recipients in 2019. To them, and all of our other M.S. and B.S. graduates, we wish you the best of luck in your future endeavors. Please keep in touch on the great new things you are doing.

We look forward to hearing from you.
Phages in Space

Interstellar Biological Experiments Could Yield Insights into Human Space Travel

If humans are to live in outer space for years at a time, it’s important to understand how the microbes in and on their bodies are affected by space conditions. Humans have trouble performing the most basic tasks when in space thanks to microgravity and they must wear protective gear to safeguard them from the interstellar radiation. But how do microbes experience these effects that aren’t present on Earth?

A team of scientists from the University of Wisconsin–Madison Department of Biochemistry are planning to answer this question by launching tubes of bacteria and bacteriophage — viruses that prey on bacteria — to the International Space Station with help from NASA. Assistant Professor Vatsan Raman is spearheading the project that’s at the forefront of learning how humans could one day colonize space. As scientists and engineers gear up for long-term and commercial space travel, it’s becoming increasingly important to understand how the bacteria in and on humans — many essential for health — function in this environment, Raman says. Their launch is tentatively scheduled for February on a Northrup Grumman rocket from Wallops Flight Facility in Virginia.

Using a protocol carefully crafted by the researchers, they plan for astronauts on the ISS to perform a series of simple experiments to test the effects of space conditions, such as microgravity and radiation, on the microbes and their interactions. Also involved in the project are biochemistry professors Michael Cox and Michael Sussman.

While bacteria and phage have been in space before because they reside on and in humans and other organisms, there haven’t been very many sophisticated experiments on the effects that occur in space. The UW–Madison team’s experiments — supported by the U.S. Defense Threat Reduction Agency (DTRA) — could be some of the most sophisticated biochemistry and microbiology work ever done in space.

“We are interested in the broad differences between how biology performs on Earth versus in space, and we chose to work with *E. coli* bacteria and the phages that infect them because they are the simplest thing to test,” Raman explains. “What’s surprising is there are not a lot of data from controlled experiments done in space that can also be replicated on Earth and allow us to do comparisons.”

The experiments will consist of exposing tubes of bacteria only, phage only, and a mix of the two for different periods of time. While seemingly simple, two graduate students in the Raman Lab — Phil Huss and Chutikarn Chitboonthavisuk — worked to develop experiments that dealt with the many
constraints of doing science in space.

“Every kid wants to be an astronaut, right, so sending samples into space and being at the launch is the next best thing,” Huss says. “It’s a new frontier that we know very little about, especially in terms of microbial interactions, so it’s exciting to start testing this.”

They worked to meticulously document every aspect of the testing and experiments, collaborating with a company called Rhodium Scientific that helps NASA with this kind of work. They will also prepare the samples that will travel to the launch site and then into space and perform quality control tests right up until launch.

“I never thought I’d be involved in a project like this where we get to do science in space,” Chitboonthavisuk says. “It will be interesting to see the results when the microbes are exposed to factors that are not present here on Earth.”

In terms of radiation, that experienced in space is likely different than radiation experienced on Earth and hard to replicate. Cox, a collaborator on this project, studies the effects of radiation on bacterial DNA.

“We want to figure out if there’s anything different between radiation up there and radiation down here,” he explains. “It’s different from something like x-rays we would experience here. These are atoms traveling at pretty close to the speed of light and a lot of them are hydrogen atoms, basically called cosmic rays, and are hard to replicate on Earth.”

The radiation actually interacts with water molecules in a cell, creating what are called reactive oxygen species that are highly reactive and can react with proteins, DNA, and other molecules in the cell and cause damage, such as mutations. The vast majority of these mutations are either benign or deadly to a microbe. However, some of the mutations may allow them to become more resistant to radiation and thrive.

Microgravity might not cause mutations like radiation but it could act as a new stress on the phage and bacteria. For phage in particular, they don’t pursue their bacterial hosts. Instead their random movements cause them to just run into bacterial cells. However, in microgravity that movement will be difficult as the phages float around.

The real work — which will utilize knowledge and techniques from the Cox and Sussman labs — begins when the samples are returned to Earth. Researchers are eager to analyze different aspects of the microbes and compare the data to experiments done on Earth. Their experiments will allow them to compare how quickly or slowly the microbes grow and interact, while other tests will be done that compare the metabolism, RNA, and a variety of other cellular processes to see if they were affected.

By deep sequencing their DNA, they can look for differences between those that experienced radiation and those that did not. The researchers will also use a technology called mass spectrometry, a method of finding molecular identities of proteins based on molecular weights. This will also allow them to look for modifications that possibly occurred.

While small changes in DNA or other cellular mechanics are the most likely, they wonder if the phage, in a rare example, will gain a new function. Perhaps it would be mutated in a way that allowed it to infect a wider range of E. coli than just the strain they sent it to space with. With the rise in bacteria becoming resistant to antibiotics, researchers are turning to phage as a possible alternative to investigate.

No matter their findings, the researchers hope their experiments push the boundaries of the scientific work that is possible to execute in space. As NASA and other organizations conceive of more and more space travel, how microbes behave in this environment will become essential to understand because they play such an important role in human health.

“There is just this curious question we are trying to answer about how the microbiology we know and understand so well works in non-Earth-like conditions,” Raman says. “We expect that the lessons from this study will help us understand and design microbial communities for long-term space applications.”

Mission insignia. NASA has a patch that represents each of its missions. Chutkarn Chitboonthavisuk of the Raman Lab designed this one.
Coyle Searches for Patterns that Govern Complex Cellular Systems

Although cells may seem endlessly complicated, at the end of the day they are machines that aren’t so different from those in daily life — like a Roomba used to vacuum a house. They are just millions of times smaller, made from different components such as proteins, and powered by chemistry rather than electricity.

It’s understanding these cells and the even smaller molecular machines inside them that drive the research of Scott Coyle, a new assistant professor who joined the University of Wisconsin–Madison Department of Biochemistry in September 2019.

Coyle joins the department from a postdoctoral position at Stanford University and scientific consultant for a company he co-founded called CellDesignLabs. He is focused on the microscale machinery of cells and how it’s organized and controlled by nanoscale molecular components. He’s excited to see how that knowledge can be used to engineer new cellular and molecular machines with novel uses.

By gathering data on a complex system like a cell and breaking it up into smaller parts, he is able to see how different types of cells are “different designs assembled from a common toolbox,” Coyle explains. This kind of understanding can lead to insights for basic biology but also for disease states of cells with usefulness in medicine, agriculture, and other areas.

“Although these behaviors may seem very complex, if we collect information about everything that the cell is doing over time, then we can start to find patterns in that data that teach us about the ‘programs’ that are driving the behaviors,” he says. “This is a highly interdisciplinary challenge that requires thinking about biological, chemical, and molecular systems on many different scales and figuring out ways to make connections between different fields.”

Understanding these “programs” is the first step in being able to engineer cells and molecular machines with novel functions, such as detecting disease in the human body or sensing chemicals in the environment. It’s something Coyle says he fell in love with while getting his undergraduate degree at Berkeley and continued in his Ph.D. at UCSF.

“I became fascinated with the fact that everything in biology, even me, is somehow just a consequence of biochemistry,” he says. “This fascination has motivated me to push myself to connect biochemistry to different scales at every stage of my career, such as applying this understanding to engineer new cell behaviors in immune cells at CellDesignLabs, which was acquired by Gilead in 2017.”

Through his teaching he hopes to instill foundational knowledge but also educate students on the latest developments in areas such as coding and machine learning. He also enjoys incorporating real-world examples into class lectures, he says.

“I was blown away by how absolutely outstanding a university like UW–Madison is and how good a fit it is for my research interests and the program I’d like to develop,” Coyle says. “The biochemistry department has an amazing history and is full of incredible scientists — both senior and junior — who are earnest and genuine about helping new faculty achieve great science and education.”

Molecular engineers. A unicellular hunter, known as Lacrymaria olor, in the act of striking and capturing its prey. Cells like these are one of many remarkable “microscopic robots” that Coyle studies to understand how nanoscale biochemical components can be organized and controlled to produce sophisticated microscale molecular machines.

Image courtesy of Scott Coyle.
Kirchdoerfer Joins Department and Campus Virology Community to Utilize Cryo-EM Technologies

When Robert Kirchdoerfer was offered a faculty position in the University of Wisconsin–Madison Department of Biochemistry, it was a bit of a homecoming. The 2006 undergraduate alumnus and Oregon, Wisc., native arrived back on campus in mid-August — this time as an assistant professor in Biochemistry and the Institute for Molecular Virology. Following his Bachelor of Science with majors in biochemistry and genetics, Kirchdoerfer earned his Ph.D. in biophysics at Scripps Research Institute in Southern California and continued there as a postdoctoral scholar before coming back to UW–Madison. During graduate school he became fascinated by viruses while working on the flu virus and it’s an interest that guides his research today.

“Viruses are so fascinating to study because they defy expectations,” he explains. “For every rule and trend in biology, there is a virus out there that somehow breaks it. This means that viruses have a lot to teach us about what biological systems are capable of.”

In his role, Kirchdoerfer will play a key part in bridging the virology community to the newly established UW–Madison Cryo-EM Research Center. Using cryo-electron microscopy (cryo-EM) technology allows him and other virologists to get an extremely detailed look at viruses and how they work, which is an important piece of the puzzle when exploring therapies and vaccines.

“One of the most straightforward ways of figuring out how something works is by looking at it,” he says. “My research uses structural biology methods like cryo-electron microscopy and X-ray crystallography combined with more traditional biochemistry approaches to examine the protein machines of viruses in incredible detail. By viewing how these viral machines are put together and function, we can identify vulnerable points in the virus where we can intervene with new vaccines and antiviral drugs. Bringing high-resolution cryo-EM to bear on important questions in virology builds on UW–Madison’s existing strengths in structural biology and virology.”

In order to infect a host, viruses must follow several steps, including binding to the host cell, entering it, and then replicating their genetic material, either RNA or DNA. Each of these stages offers possibilities for intervention to shut down infection, and Kirchdoerfer and his lab will study each of them.

Specifically, Kirchdoerfer studies coronaviruses, a common type of virus. Most are not harmful and some cause mild flu-like symptoms. However, some are more dangerous, especially, he says, those that jump between animal species and find their way into humans.

His work in vaccines and antivirals doesn’t stop with humans. He explains that since coronaviruses affect a large variety of animal species — many kept as pets or important agricultural livestock — the research has broad potential to aid human, animal, and economic wellbeing by preventing or battling outbreaks.

“Viruses like SARS-CoV and MERS-CoV both originated in bats before eventually moving into humans,” he explains. “Infection with these highly pathogenic human coronaviruses can lead to a severe and sometimes fatal respiratory disease. Developing vaccines and treatment strategies will help the world prepare for the next coronavirus outbreak.”

Cryo-EM in action. The structure of the SARS-CoV nsp12 polymerase complex. Being able to visualize the structure of viruses and their parts is an important step in finding vaccines and antivirals.

Image courtesy of Robert Kirchdoerfer.
In high school, Judith Simcox pored over scientific literature to try to understand the link between her sister’s Down Syndrome and type 1 diabetes. It was the first time she asked a question that didn’t have an answer yet — and it led her down the path of answering unknown questions as a metabolism researcher and advocate for diversity in science.

Simcox, whose work specifically focuses on how organs communicate through lipid signaling to respond to the energy demands of cold exposure, joined the University of Wisconsin–Madison Department of Biochemistry as an assistant professor in February 2019.

“Madison is an incredible environment that cultivates creativity and innovation while having a firm appreciation for the historical discoveries in research,” she says. “Any field I ventured into, even during my undergraduate, seemed to have leaders from the department. It is surreal that I will be starting my lab in the same building as researchers who have left me star struck as a young student.”

She joins Biochemistry from a postdoctoral fellowship at the University of Utah, where she also earned her Ph.D. in 2014. She spent her undergraduate years at Carroll College.

She explains that mammals must maintain a body temperature that is favorable to biochemical reactions and when experiencing extreme cold, this becomes more energy demanding. This requires coordination between several organs that store excess energy and those that can utilize this energy to generate heat. Her work looks to understand how these organs communicate using lipid signaling, with mice as a model.

The work on these basic pathways can aid researchers in understanding health issues such as obesity. Also, studying cold response lends itself to looking at the effects of hypothermia in mice. Information on these thermoregulatory pathways that she and her team find could be applied to livestock exposed to extreme temperatures.

“From a scientific level, I find it fascinating how rapidly organisms are able to integrate signals from their environment into changes in metabolic outcome,” says Simcox, who is also an affiliate in the Department of Nutritional Sciences. “Studying metabolism at this time is incredibly important because it allows us to understand how we will respond to continued shifts in our environment, develop early diagnostic markers of metabolic disease, and discover treatments for these metabolic diseases.”

In addition to metabolism research in the lab, Simcox — who hails from Montana and has mixed Filipino and Native American Apsáalooke (Crow) heritage — is passionate about members of minority groups being involved in science.

“My hope is that with openness people will realize that all journeys in science are unique but share elements like failure, fortitude, and curiosity,” she says. “Part of what attracted me to Madison is that there is a great support system with the resources and desire to reach out to the rural community, indigenous communities, and other underserved minority populations around the state.”
Sure, the Human Genome Project may have ended — but it didn’t yield all of the answers scientists need to understand what’s happening inside cells. This is because, while each cell in an organism contains the same genetic information, each is creating, modifying, and using a unique and extremely vast set of proteins that’s difficult to determine and understand.

Amy Weeks, who joined the University of Wisconsin-Madison Department of Biochemistry in September 2019 as an assistant professor, is focused on developing tools to map this dynamic proteome. Before coming to UW-Madison, Weeks was a postdoctoral scholar at the University of California, San Francisco.

While the more commonly known “genome” describes the collection of all of the genes encoded in human DNA, the “proteome” is the set of proteins encoded in the genes present in a cell at any given time. Unlike the static genome, the proteome is dynamic and tricky to characterize.

“We often think of one gene as encoding one protein, but the reality is much more complex,” she explains. “After proteins are made, they can be modified in many different ways that impact their functions, so a big challenge following the completion of the Human Genome Project is to define the ways in which the proteins encoded by each gene are modified and what the biological consequences are. We are tackling this question by engineering enzymatic tools that enable us to capture specific protein forms to identify them and to probe their functions.”

These modifications to proteins allow cells to respond rapidly to changes in their environment and errors in these processes often lead to disease. Understanding the proteome and mapping these modifications can not only provide basic insights into their function but help scientists look for new drug targets, for example.

Her interest in the proteome and enzymes — one of the tools she uses to study the proteome — began during her undergraduate years at MIT and continued during her Ph.D. at the University of California, Berkeley, where she studied how an unusual soil bacterium synthesizes natural products.

“I find enzymes endlessly interesting, and I think it’s even more exciting when we can build from their functions to develop tools that can advance our understanding of biology,” she says. “The tools that my group is developing will enable us to identify disease-associated modifications that we can potentially target with drugs. They will also help us to understand whether certain protein modifications could serve as biomarkers of disease states.”

When it comes to teaching, she says her core values are integrating research and education, equipping students with tools for success, and creating an inclusive learning environment.

“The UW-Madison campus itself always seems to be buzzing with incredible energy, and I’m also a big believer in accessible public higher education so I’m excited to contribute,” Weeks says. “I hope that the outcomes of my research will influence and improve human health by advancing our basic biological understanding, which fits in with the Wisconsin Idea.”

To read more about the department’s new faculty go to biochem.wisc.edu/faculty
If you’ve ever grown carrots in your garden and puzzled over never once seeing them flower, don’t blame a missing green thumb. Carrots, beets, cabbage and many other plants won’t flower until they’ve gone through winter. Sensing the extended cold of winter gives them the signal to flower quickly once spring arrives, providing the plants an edge in the race to produce seeds.

But cold isn’t the only way some plants sense winter. In the 1930s, two English scientists discovered that some crops in the grass family, like rye or wheat, can use short days instead of cold to perceive when winter has come. “But nothing was known about how it works,” says Rick Amasino, a professor of biochemistry and genetics at the University of Wisconsin–Madison.

Now, more than 80 years later, Amasino’s group has finally discovered how grasses count the short days of winter to prepare for flowering. In most plants, a protein called florigen induces flowering when it is expressed during the lengthening days of spring and summer. Grasses have multiple copies of the florigen gene, thanks to ancient duplications in their genomes. One of those copies has been repurposed to be expressed during the short days of winter, giving some grasses a new way to prepare for spring.

To get at the use of day length as a winter signal, Amasino’s group, also part of the Great Lakes Bioenergy Research Center at UW–Madison, turned to Brachypodium, a grass used in the lab that is related to crops like corn, rice and wheat. They found that some varieties of Brachypodium could sense short days as a sign of winter whereas others could not, and the cause of this difference was a single letter change in a single gene that is one of 14 duplicates of the florigen gene.

The team found that the duplicate, named FTL9, has evolved to act as a sort of inverse of its parent gene florigen. Where florigen builds up in leaves during long days to cause flowering, FTL9 accumulates during the short days of winter. While enough florigen makes flowering inevitable, FTL9 only makes flowering possible, by releasing the brakes on the florigen gene once spring arrives.

Better understanding how plants have evolved systems to mark the end of winter may help scientists keep crops productive, especially in a warming climate. Because as growing regions heat up, crops that follow the sun will always reliably track the seasons, even if winter’s chill falters.

“Mechanisms of floral induction. This picture shows a cabbage plant that was grown in the greenhouse for five years. (For size comparison Amasino’s daughter, who was the same age as the cabbage, is shown. The small plant in the girl’s hands is a summer annual variety of B. oleracea that flowers rapidly without vernalization.) Cabbage is a biennial and requires exposure to the environmental cue of prolonged winter cold in order to flower the second spring after planting. This promotion of flowering by cold is called vernalization. The large cabbage has never been vernalized and cannot flower.

Additional Reading

Ancient Gene Duplication Gave Grasses Multiple Ways to Flower Once Spring Arrives

Professor Rick Amasino

Story by Eric Hamilton for University Communications.
Biochemistry associate professor Aaron Hoskins is searching for new treatments for myelodysplastic syndromes — a type of blood cancer — by being able to screen for RNA splicing inhibitors using “humanized” yeast.

Myelodysplastic syndromes (MDS) arise when bone marrow has defects in producing red blood cells, which can cause anemia or even blood cancers like acute myeloid leukemia. Treatments for the disorder are limited.

Many patients with MDS have mutations in the spliceosome, the molecular machine responsible for taking out sections of RNA and putting what remains back together in a process called RNA splicing. The spliceosome acts like a film editor, removing some scenes and joining, or splicing, together others to make a complete movie. RNA splicing allows for a large diversity of proteins to be made from a relatively small number of DNA genes and occurs in all eukaryotes including humans and yeast, but not bacteria.

Cells unable to splice RNA properly are considered “splicing sick,” and it just so happens that the mutations that cause this also make the cells susceptible to new therapies that target the spliceosome.

“The splicing machinery has emerged as a potential therapeutic target for a number of human diseases but especially cancers,” Hoskins explains. “Many cancer cells have stressed their splicing machinery to its limit and small perturbations in splicing can lead to cancer cell death. This means that low doses of splicing inhibitors could potentially be used in cancer chemotherapy.”

Currently, only a few drug options are available that target the spliceosome. Many groups are trying to discover new molecules that inhibit the splicing machinery, which requires screening the effectiveness of hundreds of thousands of chemicals. This would normally be very expensive and time-consuming.

The key to Hoskins’ experiments will be “humanized” yeast his lab has genetically engineered. The yeast use human splicing proteins, some of which are associated with MDS, in place of their own.

With sophisticated lab work they’ve gotten the yeast to use these human proteins and ensured they are susceptible to known splicing inhibitors. It is the culmination of work done by former Integrated Program in Biochemistry (IPiB) graduate students Tucker Carrocci and Sarah Hansen, as well as former undergraduate Doug Zoerner. The project is now being led by several Hoskins Lab members, including graduate students Sierra Love and Karli Lipinski and lab manager Josh Paulson.

Because yeast is so cheap and quick to grow, they now plan to screen about 200,000 different drug candidate compounds to see if they inhibit the growth of the “humanized” yeast, with funding from a recent grant from the Edward P. Evans Foundation. Other work in the lab will investigate how spliceosome inhibitors function using a technique that lets them sequence all of the RNA present in a cell at a point in time and assess changes.

“Our approaches are particularly powerful because they let us connect splicing inhibition to yeast growth and to simultaneously conduct a counter-screen using a non-mutated yeast strain,” Hoskins says. “This is dramatically cheaper, faster, and easier to interpret than carrying out splicing assays in vitro or in human cells.”

Unraveling the spliceosome’s mysteries. Genetics graduate student Sierra Love (left) and lab manager Josh Paulson are currently leading this project in the Hoskins Lab.

To read more about the department’s research go to biochem.wisc.edu/news
Scientists at the University of Wisconsin–Madison have identified blood-based fingerprints — human protein markers — associated with the pre-cancerous forms of colon cancer that are most likely to develop into disease. They say their findings are a promising start to what could ultimately lead to a new blood test for the cancer.

The lab of biochemistry professor Michael R. Sussman, in collaboration with researchers at the McArdle Laboratory for Cancer Research and UW–Madison School of Medicine and Public Health, used a technique called mass spectroscopy to isolate biomarkers in mouse and rat models of the disease and then test patient blood for the same markers. The researchers presented their newest advancements in the spring of 2019 in the Proceedings of the National Academy of Sciences.

“The most commonly used technologies such as colonoscopy are highly invasive or utilize stool samples for testing, which may not be appealing to patients,” Sussman says. “Because colon cancer is highly curable if detected early enough, setting up tests for the earliest signs of colon cancer to provide as many early diagnostic options as possible is critical.”

Since nearly all cases of colon cancer are curable if caught early enough, this should make screening tests straightforward. However, this is not the case because colon cancer screening suffers from a paradoxical combination of low compliance rates and what is called ‘over-screening’ with colonoscopies.

While the gold standard for colon cancer screening is a colonoscopy, patients must complete a day-long prep to empty their bowels before undergoing an invasive procedure — factors that contribute to low screening compliance. On the other hand, research from UW–Madison shows many of the polyps found and biopsied during a colonoscopy are regressing or static and not at risk of being harmful. A blood test that can detect if a polyp is growing or cancerous would give a better indication that a colonoscopy is needed.

“It would not be meant to replace a colonoscopy in any way,” says Melanie Ivancic, the study’s lead author. “But the blood test could serve as a pre-screen to detect polyps that have the greatest propensity to turn into cancer.”

This work in the Sussman Lab was started more than a decade ago by Ed Huttlin while he was a biochemistry graduate student and was continued by Ivancic. Although far from commercialization, their findings provide a proof of concept for a future test that could use these biomarkers to determine patients’ need for a colonoscopy. Their ultimate goal is to provide another option to screen for colon cancer and help diagnose the disease when it is most treatable.

“We believe that using our test in combination with other marketed tests, such as the stool DNA tests developed by Exact Sciences in Madison, WI, will provide an orthogonality in which the tests complement each other,” Sussman says. “The reasons you might get a false positive from one kind of test are different from the false positive you might get from a blood test. Being able to have multiple options can be very helpful for catching colon cancer early.”

See the story online for more on this research: go.wisc.edu/l761du.

Award-winning research. Left to right: Jennifer Pleiman, Melanie Ivancic, and Michael Sussman. In 2015, the group won an Innovation Award from the Wisconsin Alumni Research Foundation (WARF) to support their work on biomarkers for colon cancer.

Photo courtesy of WARF.
Postdoc Remembers Research Skills and ‘Science Family’ That Helped Launch Faculty Career

As a postdoc in the lab of Professor Elizabeth Craig, Jill Johnson saw her repertoire of scientific knowledge and techniques, as well as her “science family,” grow. Today, she’s approaching 20 years as a professor at the University of Idaho.

Johnson grew up in Kansas and received her undergraduate degree from the University of Michigan, before earning her Ph.D. in biochemistry and molecular biology from the Mayo Clinic. She then joined Craig’s lab in 1994 after learning throughout her Ph.D. about Craig’s work on molecular chaperones as one of the original researchers in the field.

“Betty’s lab was much bigger than the lab I had been in for my Ph.D. studies, so I got a lot more exposure to different types of techniques and projects,” Johnson says. “I also really loved living in Madison.”

The Craig Lab studies molecular chaperones, which recognize misfolded proteins and help them fold and are also involved in protein transport. Using yeast as a model, the lab uses genetic approaches to study their function and inner workings. While in the lab she was exposed to different biochemical techniques that allowed her to combine both genetic and biochemical approaches. She also taught courses, attended scientific conferences, and built relationships with other scientists.

In 2002, Johnson started as an assistant professor at Idaho, where her current role is 50% teaching/service and 50% research. Her research focuses on the molecular chaperone Hsp90, which requires more than a dozen accessory proteins as it helps other proteins function. To study this complex system, she utilizes a genetic approach in yeast to identify distinct regulatory steps in the pathway — working with collaborators to find specific biochemical defects.

While Hsp90 is required for many cellular functions, many of the proteins that drive growth of cancer cells require Hsp90, Johnson explains. Inhibiting Hsp90 inhibits growth of many different types of tumor cells, but unfortunately Hsp90 is so vital to a cell it’s very toxic to completely disable it. Johnson’s goal is that by learning more about how this molecular chaperone works, she and others could find a specific target to drug that would inhibit the worst functions like promoting cancer but leave the others intact.

“Hsp90 is a big complicated puzzle and it will require lots of researchers using different techniques and approaches to figure it out,” she says. “I love the general field of biochemistry and molecular biology because new techniques are constantly being developed and it is fun to learn about research other people are doing and think about how to use new techniques to answer different questions.”

For Johnson, her postdoc was a chance to develop her own research projects and learn about the benefits of different approaches to science, especially, she adds, because many of the most groundbreaking studies are collaborative and multi-disciplinary.

“As a postdoc, it’s good to set goals of what you hope to gain from your experience, as well as take advantage of the opportunity to get to know your lab mates and others in other labs,” she says. “I have been very lucky that I am still in regular contact with many of the people in my ‘science family’ that I first met while in graduate school and Betty’s lab.”

“I love the general field of biochemistry and molecular biology because new techniques are constantly being developed and it is fun to learn about research other people are doing and think about how to use new techniques to answer different questions.”
—Jill Johnson, Biochemistry Postdoc ’94-02
Biochemistry Alumnus Combines Interest in Science and Humanities in Career as Patent Agent

Dan Blasiole’s career is a synthesis of his two intellectual passions: the sciences and the humanities. After honing his science knowledge with a Ph.D. in biochemistry from the lab of professor Alan Attie, he found the perfect combination of these two interests as a patent agent.

Originally from Pennsylvania, he attended Franklin and Marshall College intending to get a degree in a science field. Instead, he left with a degree in philosophy and headed to the University of California, San Diego for a master’s degree in the philosophy of science. After spending several years researching molecular epidemiology in a Department of Defense lab in California he moved to Madison for his Ph.D. in biochemistry with Attie, which he finished in 2008, and discovered the patent field.

Through networking with professionals at the Wisconsin Alumni Research Foundation (WARF), he learned of the patent field and got interested. As a patent agent he specializes broadly in biotechnology. Patent agents are the negotiating liaisons between inventors and the United States Patent and Trademark Office (USPTO). Blasiole often works with WARF in his role.

UW–Madison researchers who want to patent an invention, some even from the Department of Biochemistry, first approach WARF. WARF then connects patent attorneys and agents like Blasiole with the inventors. Blasiole then drafts a patent application on the technology, files the application at the USPTO, and negotiates with the USPTO to get the application approved as a patent.

“The negotiation with the USPTO is an extremely challenging but stimulating process that requires a mix of scientific and legal reasoning,” he says. “As a patent agent you never know what is going to come your way, and you’ve got to be able to master it and talk about it cogently with the experts in the area. My graduate education at UW prepared me to do this effectively and efficiently.”

The patent process is very important, says Blasiole, because if investors are going to invest millions of dollars into a technology, they want to make sure that the intellectual property is protected.

He adds how the breadth of the UW–Madison Department of Biochemistry in general, and Attie’s lab in particular, prepared him for the career.

““What I appreciate about my graduate education is how much I learned not only about biochemistry and molecular biology but also the biosciences across the board,” he says. “As a patent agent you never know what is going to come your way, and you’ve got to be able to master it and talk about it cogently with the experts in the area. My graduate education at UW prepared me to do this effectively and efficiently.”

“As a patent agent you never know what is going to come your way, and you’ve got to be able to master it and talk about it cogently with the experts in the area. My graduate education at UW prepared me to do this effectively and efficiently.”

—Daniel Blasiole, Ph.D. Biochemistry ’08
Biochemistry and Medical Training Leads to Exciting Career in Oncology Research and Development

Dr. Kevin Sokolowski

Biochemistry is the foundation of what Kevin Sokolowski does every day in his career. Armed with an undergraduate degree in biochemistry from the University of Wisconsin–Madison, as well as an M.D., he has embarked on a unique alternative career as a Senior Medical Science Liaison for Solid Tumor Oncology Development at AbbVie.

Sokolowski came to UW–Madison in 2000, after a year at UW–La Crosse, and graduated in 2003 before heading to medical school. He says he was drawn to Madison because of the university’s history and strength in biochemistry.

In his role at AbbVie, Sokolowski works to develop and support the company’s solid tumor oncology research and development pipeline. In addition, he works with academic and community physicians to educate them on solid tumor disease states. He says is it an exciting, novel, and challenging alternative career path for those with a medical or pharmacy degree or a Ph.D.

“This position is very rewarding as it allows me to combine both my passion for medicine as well as my excitement for research,” he says. “My biochemistry background at UW has enabled me to understand and grasp the complexities of cellular signaling as well as provide input in oncology development.”

While an undergraduate in the department, Sokolowski participated in the biochemistry undergraduate association — now a student chapter of the American Society for Biochemistry and Molecular Biology (ASBMB) — as well as student organizations in CALS and the pre-medicine society. He says his advisor and now-Emeritus Professor David Nelson, as well as the lab of Herbert Chen where he did undergraduate research in oncology, played an integral role in exposing him to research and opportunities he was interested in.

“Understanding the role of signaling pathways in cancer and mechanisms of disease resistance, and then leveraging these concepts to develop novel therapies, is critical to my current role,” explains Sokolowski, a native of Mukwonago, Wisc. “Furthermore, part of my role is staying up to date on all the advances in solid tumor medicine. Having a strong biochemical foundation allows me to efficiently review manuscripts and generate thought-provoking discussions.”

He continues to leverage his medical background and passion for science on a daily basis, he adds, as well as relationships he’s built over time. In his role he works with academic and community partners, including some at the University of Wisconsin Carbone Cancer Center.

“My goal is to improve the lives of patients and their families through my research and development,” he says. “It’s a team approach, but when I prepare for each day, I think of what I can do today that can help patients. It is very rewarding and humbling to know that we are working on developing new technology that has the potential to help patients and their families.”

His advice for undergraduate students, particularly those interested in medicine, is to network and build relationships by being involved and meeting others. He benefited from joining the pre-med society and contacting UW physicians to ask about their career paths. Additionally, keeping his mind open to alternative career paths allowed him to land his current rewarding position.

“Remember, we all started on the same road,” he says. “Don’t be afraid to ask questions, ask for help, ask for support. Finally, remember that the path to success is never a straight line. It is the obstacles, failures, disappointments that make you successful. As I reflect on my career, it is those failures that made me who I am today.”

“Part of my role is staying up to date on all the advances in solid tumor medicine. Having a strong biochemical foundation allows me to efficiently review manuscripts and generate thought-provoking discussions.”

—Kevin Sokolowski, B.S. Biochemistry ’03
<table>
<thead>
<tr>
<th>Degree</th>
<th>Name (Major Professor)</th>
<th>Thesis Title</th>
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<tbody>
<tr>
<td>PhD</td>
<td>Sandra Tseng (Ansari)</td>
<td>Regulation of RNA synthesis and decay via the C-terminal domain of Pol II</td>
</tr>
<tr>
<td>PhD</td>
<td>Erin Weisenhorn (Coon)</td>
<td>An analysis of dynamic proteomes with enhanced sample preparation and computation</td>
</tr>
<tr>
<td>PhD</td>
<td>Anastasia Lindahl (Denu)</td>
<td>The role of Acetyl-CoA and Acetyl-CoA synthesis pathways in regulation of nuclear acetylation</td>
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<tr>
<td>PhD</td>
<td>Markus Nevil (Harrison)</td>
<td>Mechanisms regulating the highly conserved transcription factor Grainy head during Drosophila melanogaster development</td>
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<tr>
<td>PhD</td>
<td>Sarah Hansen (Hoskins)</td>
<td>Intron recognition by the pre-spliceosome</td>
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<tr>
<td>PhD</td>
<td>Katarzyna Dubiel (Keck)</td>
<td>Elucidating structural and cellular mechanisms of bacterial single-stranded DNA binding proteins (SSB)</td>
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<tr>
<td>PhD</td>
<td>Andrew Votter (Keck)</td>
<td>Mechanisms of G-quadruplex unwinding and repair</td>
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<tr>
<td>PhD</td>
<td>Kimberly Haupt (Kimble)</td>
<td>The self-renewal regulatory hub in C. elegans</td>
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<tr>
<td>PhD</td>
<td>Beth Shen (Landick)</td>
<td>Structure of Escherichia coli H-NS and mixed H-NS filaments and their effect on transcription elongation by RNA polymerase</td>
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<tr>
<td>PhD</td>
<td>Dominik Hoelper (Lewis)</td>
<td>Nucleosome-independent functions for the histone H3.3 variant in retroelement and gene repression</td>
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<tr>
<td>PhD</td>
<td>Ellen Crummy (Martin)</td>
<td>Characterization of CAPS interactions with dense core vesicles</td>
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<td>PhD</td>
<td>Molly McDevitt (Pagliarini)</td>
<td>Systems biochemistry investigations into lipid metabolism and lipid-metabolizing enzymes</td>
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<td>PhD</td>
<td>Michael Andreas (Rayment)</td>
<td>Coiled coil fusion proteins facilitate structural studies of the cardiac myosin rod and thick filament</td>
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<tr>
<td>PhD</td>
<td>Karl Wetterhorn (Rayment)</td>
<td>Enzymatic inactivation of trichothecene mycotoxins in Fusarium head blight of wheat</td>
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<td>PhD</td>
<td>Samantha Anderson (Senes)</td>
<td>Understanding the GAS_{reg} motif: Sequence, structure, and stability</td>
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<td>PhD</td>
<td>Thao Nguyen (Sussman)</td>
<td>Crosslinking mass spectrometry reveals a mechanism for regulating the Arabidopsis plasma membrane proton pump</td>
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<tr>
<td>PhD</td>
<td>Hugo Medina-Muñoz (Wickens)</td>
<td>Tagging as a probe for localization</td>
</tr>
<tr>
<td>PhD</td>
<td>Michael Kelliher (Wildonger)</td>
<td>The critical role of kinesin-1 autoinhibition in the regulation of intracellular transport in neurons</td>
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<tr>
<td>MS</td>
<td>Julie Cheung (Bednarek)</td>
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<tr>
<td>MS</td>
<td>Delia Scoville (Raman)</td>
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</tr>
<tr>
<td>MS</td>
<td>Anne Schwarzwalder (Rayment)</td>
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**Biochemistry Advisor Degrees 2019**

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<tr>
<td>PhD</td>
<td>Hongbo Chen</td>
<td>Biophysics</td>
<td>NMR study of an engineered temperature-sensitive Shaker K+ channel</td>
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<td>Nov 2019</td>
<td>(Henzler-Wildman)</td>
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<tr>
<td>PhD</td>
<td>Indro Neil Ghosh</td>
<td>CMB</td>
<td>Optimizing gene expression signals for metabolic enzymes enables maximizing metabolic pathway fluxes</td>
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<tr>
<td>Feb 2019</td>
<td>(Landick)</td>
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<tr>
<td>PhD</td>
<td>Yanding Li</td>
<td>BSE</td>
<td>Lignin Hydrogenolysis</td>
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<tr>
<td>Aug 2019</td>
<td>(Ralph)</td>
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<tr>
<td>PhD</td>
<td>Munish Chhabra</td>
<td>Biophysics</td>
<td>Fluorescence-detected intermediates in open complex formation by E. coli RNA polymerase: Analysis of large-scale conformational changes and effects of Lipiarmycin</td>
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<tr>
<td>Aug 2019</td>
<td>(Record)</td>
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</table>

**Degrees Dec. 1, 2018 - Nov. 30, 2019**

**BSE**: Biological Systems Engineering  
**CMB**: Cellular & Molecular Biology

**IPiB Graduates** (Sandra Tseng not pictured)

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**We heard from you!**

Below are some notes we got after our last issue or some alumni news we spotted online. Have something you’d like to share with us? **Contact**: alumninews@biochem.wisc.edu.

**Jackson J. W. Clemmons**, B.S. ’48, M.S. ’49 & Ph.D. ’56 (Link), received an honorary Doctor of Science degree from the University of Vermont during their May 2019 commencement.

**Michael C. Flickinger**, B.S. ’73 (Garver), M.S. ’75 & Ph.D. ’77 (Perlman), is celebrating his retirement as Professor of Chemical and Biomolecular Engineering and Director of Academic Programs at the Biomanufacturing Training and Education Center (BTEC) at North Carolina State University. He led a prosperous career filled with leadership positions, groundbreaking research, and training and mentoring numerous young scientists.

**Sanjeev Jain**, Ph.D. ’90 (Sundaralingam) & M.D., was named “Patient Preferred Immunologist of the Year” representing the state of California for 2019.

**Squire Booker**, Postdoc ’95-99 (Frey), was elected to the National Academy of Sciences (NAS) in 2019. He is the Evan Pugh University Professor of Chemistry at Penn State.

**Elle Kielar Grevstad**, Ph.D. ’11 (Martin), had her microscopy image of a single grain of corn selected as one of ten winners in the 2019 UW–Madison Cool Science Image Contest.

**JoAnne Stubbe**, former department faculty, was named the 2020 Priestly medalist by the American Chemical Society, one of the organization's most prestigious awards.
Honors & Awards

Faculty

Jason Cantor  NIH/NCI Career Transition Development Award - 2019-2022
Elizabeth Craig  Cell Stress Society International Medallion Career Achievement Award
Brian Fox  DOE Grant: Creation of an Acyltransferase Toolbox for Plant Biomass Engineering (with J. Ralph)
Aaron Hoskins  EvansMDS Grant: Humanized Yeast for Discovery of New Splicing Modulators for Treatment of MDS
Judith Kimble  WARF Named Professorship
David Pagliarini  H.I. Romnes Fellowship
2020 Earl and Thressa Stadtman ASBMB Young Scholar Award
Ann Palmenberg  2019 Sir Michael Stoker Award, Center for Virus Research
2019 Distinguished Scientist Award, National Jewish Health
John Ralph  2019 Clarivate Analytics highly cited researcher, one of 10 at UW-Madison
DOE Grant: Creation of an Acyltransferase Toolbox for Plant Biomass Engineering (with B. Fox)
Philip Romero  2019 WARF Innovation Award (with O. Venturelli, R. Hsu, J. W. Tan)
Ophelia Venturelli  2019 WARF Innovation Award (with P. Romero, R. Hsu, J. W. Tan)
Grand Challenges Grant from the Bill & Melinda Gates Foundation
Army Research Office Grant: Investigating energy efficiency, information processing and control architectures of microbial community interaction networks
“Future of Biochemistry: the International Issue” list in the journal Biochemistry

Marvin Wickins  CALS Excellence in International Activities Award
Andrew Buller  (Biochemistry Affiliate) NIH Director’s New Innovator Award

Staff

Craig Bingman  Crystallography Core  Marine Aquarium Society of North America Lifetime Achievement Award
Ryan Hsu  Venturelli  2019 WARF Innovation Award (with O. Venturelli, P. Romero, J. W. Tan)
Woonghee Lee  Markley  NSF Grant: Integrative Computational Platform for Biomolecular Solid-State NMR
Eric Montemayor  Wright  NIH National Center for Cryo-EM Access and Training (NCCAT) Award
Lynne Prost  Faculty Associate  Professional Development Grant from Office of the Secretary of the Academic Staff

Postdoctoral Staff

Kate Henderson  Record  Paul Boyer Award for Postdoctoral Excellence in Biochemistry
Ryan Clark  Venturelli  Genomic Sciences Training Program (GSTP)
Emily Cushing  Attie  Cardiovascular Research Center National Research Service Award
2018 F32 Grant from the NIH
Rachel Guerra  Pagliarini  Accelerator Award from the United Mitochondrial Disease Foundation (UMDF)

Graduate Student Awards

Evan Glasgow  Fox  Denton Award for Graduate Student Excellence in Teaching & Mentoring
Nathan Thomas  Henzler-Wildman  Denton Award for Graduate Student Excellence in Teaching & Mentoring
Andrew Voter  Keck  Sigrid Leirmo Memorial Award in Biochemistry
Jin Wen Tan  Venturelli  2019 WARF Innovation Award (with O. Venturelli, P. Romero, R. Hsu)
Graduate Student Fellowships

Kyle Nishikawa Raman Robert & Katherine Burris Biochemistry Fellowship
Nathan Thomas Henzler-Wildman CALS Wisconsin Distinguished Graduate Student Fellowship
Dylan Plaskon Record Dr. James Chieh-Hsia Mao WI Distinguished Graduate Fellowship
Dana Dahhan Bednarek Arthur B. Michael Fellowship
Harriet Saunders Wildanger Arthur B. Michael Fellowship
Brian Carrick Kimble NSF Graduate Research Fellowship Program
Tina Lynch Kimble NSF Graduate Research Fellowship Program
Nathan Murray Pagliarini NSF Graduate Research Fellowship Program
Kyle Robinson Pagliarini NSF Graduate Research Fellowship Program
Jonathan Tai Pagliarini National Institute of Health Fellowship
Bianca Chavez IPiB Rotator Science and Medicine Graduate Research Scholars (SciMed GRS)
Miguel Osorio Garcia Cox Science and Medicine Graduate Research Scholars (SciMed GRS)
Edrees Rashan Pagliarini Science and Medicine Graduate Research Scholars (SciMed GRS)
Zachary Romero Cox Science and Medicine Graduate Research Scholars (SciMed GRS)
Zack Kemmerer Pagliarini Denis R. A. & Martha Washburn Wharton Fellowship

Graduate Student Training Grants

Andrew Sung Pagliarini Biology of Aging T32 Training Grant
Abigail Bartlett Pagliarini Biotechnology Training Program (BTP)
Nina Bonde IPiB Rotator Biotechnology Training Program (BTP)
Andrea Killian IPiB Rotator Biotechnology Training Program (BTP)
Johnson Saba Landick Biotechnology Training Program (BTP)
Ross Soens IPiB Rotator Biotechnology Training Program (BTP)
Christine Hustmyer Landick Chemistry-Biology Interface Training Program (CBI)
Gilbert Loiseau Senes Chemistry-Biology Interface Training Program (CBI)
Laura Steenberge Pagliarini Chemistry-Biology Interface Training Program (CBI)
Samantha Anderson Senes Computation and Informatics in Biology and Medicine Training Program
Kimberly Huggler Cantor Genomic Sciences Training Program (GSTP)
Juan Diaz Rodriguez Romero Genomic Sciences Training Program (GSTP)
Sonali Gupta Venturelli Molecular Biosciences Training Grant (MBTG)
Saeed Roschdi Butcher Molecular Biosciences Training Grant (MBTG)

Undergraduate Awards

Michael Gilpin Simcox American Indian Science & Engineering Society Travel Award
Claire Evensen Record Astronaut Scholarship
Mary Donoghue Sarah Doughty Record Biochemistry Mary Shine Peterson Award
Claire Evensen Record Biochemistry Mary Shine Peterson Award
Hallie Hanson Henzler-Wildman Biochemistry Mary Shine Peterson Award
Megan Hazen Artun Kadar Record Biochemistry Mary Shine Peterson Award
Mckayla Miller McKayla Miller Biochemistry Mary Shine Peterson Award
Allison Schiffman Landick Biochemistry Mary Shine Peterson Award
Charles Schneider Hoskins Biochemistry Mary Shine Peterson Award
Cerise Siamof Biochemistry Mary Shine Peterson Award
Travis Drow Artun Kadar Biochemistry Undergraduate Summer Research Award
Ryan Kempen Ansari Biochemistry Undergraduate Summer Research Award
Stella Ma Saeed Roschdi Biochemistry Undergraduate Summer Research Award
Saveda Majesty Seamus McWilliams Biochemistry Undergraduate Summer Research Award
Benjamin Palatnik Record Biochemistry Undergraduate Summer Research Award
Abbey Ragan Biochemistry Undergraduate Summer Research Award
Abigail Watson Cox Biochemistry Undergraduate Summer Research Award

Samantha Anderson (left) & undergrad
Zack Kemmerer
Dana Dahhan
Evan Glasgow (right) & high school student
## Undergraduate Awards

### Undergraduate Fellowships

<table>
<thead>
<tr>
<th>Name</th>
<th>Award</th>
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<td>Ann Curme</td>
<td>Hilldale Undergraduate Research Fellowship</td>
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<td>Sonam Dolma</td>
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<td>Mary Donoghue</td>
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<td>Eric Geunes</td>
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<td>Megan Hazen</td>
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<td>Vansh Jain</td>
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<td>Isabel Monti</td>
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<td>Charles Schneider</td>
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<td>Calvin Spolar</td>
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<td>Peter Volkert</td>
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<td>Alyssa Walker</td>
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<td>Luke Zangl</td>
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<td>Keer Zhao</td>
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<td>Haiyang Zheng</td>
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<td>Jessica Liu</td>
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<td>Jarod Moyer</td>
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<td>Jinan Sous</td>
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<td>Mary Donoghue</td>
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<td>Emma Groblewski</td>
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<td>Hallie Hanson</td>
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<td>Artun Kadaster</td>
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<td>Cerise Siamof</td>
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<td>Allison Schiffman</td>
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<td>Abbey Stoltenburg</td>
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<td>Michael Kierski</td>
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</table>

## Undergraduate Awards

- Luke Zangl: Biochemistry Undergraduate Summer Research Award
- Haiyang Zheng: Biochemistry Undergraduate Summer Research Award
- Claire Evensen: Biophysical Society National Meeting Poster Award
- Mitchell Keith: Ginsberg Family Award
- Claire Evensen: Barry Goldwater Scholarship
- Anna Larsen: Jack Gorski Scholarship
- Grace Carlson: ACS-Hach Land Grant Undergraduate Scholarship
- Claire Evensen: Marshall Scholarship
- Abbey Stoltenburg: Trewartha Senior Thesis Award
- Jacob Olson: University Bookstore Academic Excellence Award
- Michael Palo: University Bookstore Academic Excellence Award
- Wenqi Shen: University Bookstore Academic Excellence Award

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*2019 Biochemistry Undergraduate Summer Research Awards sponsored by Dr. Shang-Chen Pan Fund in Biochemistry, E.W. Hopkins Fund, and Henry A. Lardy Undergraduate Research Fund.*
Construction Progresses on UW-Madison Cryo-Electron Microscopy Research Center

Construction is well underway in the Hector F. DeLuca Biochemical Sciences Complex for the UW-Madison Cryo-Electron Microscopy Research Center, which will house four microscopes and other equipment in two buildings. The facility, directed by biochemistry professor Elizabeth Wright, pictured lower right, will house the powerful Titan Krios 300 kV transmission electron microscope (TEM). In the same building, a smaller 120 kV TEM will be located in the Biochemistry Optical Core (BOC) and Biophysical Instrumentation Facility (BIF) nearby.

In the basement of the historic Hector F. DeLuca Biochemistry Building, the facility will have two more microscopes — a Talos Arctica 200 kV TEM and an Aquilos cryo-FIB-SEM — specimen prep equipment, and lab space for UW-Madison investigators, external collaborators and industry partners. The construction on phase two began in July 2019.

Cryo-electron microscopy (or cryo-EM, for short) is the latest essential tool for biologists trying to visualize and understand structures at the atomic scale. Cryo-EM flash-freezes biological samples at lightning speeds, without creating ice crystals that would warp the specimen. The result is a biological sample captured in its native state.

Construction and installation is complex because the rooms need temperature and humidity control and sophisticated shielding to make sure the microscopes are vibrationally isolated. Vibrations from nearby passing trains or elevators, as well as magnetic fields from other research equipment, can all interfere with the microscopes.

Even without the facilities open, the researchers have been spreading the word about cryo-EM, laying the groundwork for collaborations, and gathering preliminary data at other facilities. Groups contributing funding to the $15 million-plus initiative include Biochemistry, the Morgridge Institute for Research, the School of Medicine and Public Health and its departments of biomolecular chemistry and neuroscience; and the Office of the Vice Chancellor for Graduate Research and Education. The new facility is expected to open in 2020. More information at cryoem.wisc.edu.

Pair of Emeritus Professors to Celebrate 90th Birthday

The year 2020 will mark an important and impressive occasion for two Emeritus Professors in the Department of Biochemistry. Both Julius Adler and Hector DeLuca will celebrate their 90th birthdays.

Adler received his Ph.D. under Henry Lardy and then became a faculty member in 1960. In 1996 he became Emeritus. DeLuca earned his Ph.D. under Harry Steenbock and became a faculty member in 1959. He became an Emeritus Professor in 2011.

Both can still be found gracing the department regularly, and they send their regards to all.
Letters from the Labs

We’ll be including a selection of faculty members each issue of Biochemistry InVivo.

Attie Lab

Our lab has had a good year harvesting the results of a genetic screen we conducted over several years using outbred mice. We recently published an article in The Journal of Clinical Investigation where we show many loci that play a role in insulin secretion. Postdoctoral fellow Chris Emfinger has carried out exciting studies on a transcription factor we identified that, when knocked out, leads to a marked increase in insulin secretion. Another postdoc, Emily Cushing, is working on a protein tyrosine phosphatase that affects insulin secretion and, surprisingly, is expressed in macrophages. Tanja Schallshmidt is spending a year in our lab after having earned her Ph.D. in Düsseldorf, Germany. She too is working on genes that emerged from our genetic screen. Nicolas Calo is working on genes that cause hepatic steatosis (fatty liver). Donnie Stapleton and Shane Simonett are a terrific team carrying out our work on islets, from physiological studies to genomic studies looking at chromatin accessibility. Shane is working with Mark Keller on a terrific manuscript on the role of the transcription factor NFATC2 on β-cell insulin secretion. Finally, Kiki Schueler is marking her 25th year in our lab. She has co-authored 33 published papers during that time. Melkam Kebede is doing well in her position as an assistant professor at the University of Melbourne. She has several grants funded and big manuscripts under review. Sushant Bhatnagar is also doing well in his assistant professor position at the University of Alabama. He has won several grants and published his first two independent articles in the past year.

Cox Lab

The lab is filled with people and activity. A collaborative grant focused on the metabolism of postreplication gaps cements our ties with the group of Antoine van Oijen in Wollongong, Australia, and with Myron Goodman at USC. This work complements our effort to study the molecular basis of extreme resistance to ionizing radiation. The latter effort is enhanced by internal collaboration with Mike Sussman, and all of our work is enhanced by our collaboration with Jim Keck.

Our most recent departure is Tyler Stanage, who’s a postdoc with Simon Boulton at the Crick Institute. Meanwhile, the lab has expanded. Liz Wood and Sindhu Chitteni-Pattu remain constants. Steve Bruckbauer defended his thesis but stayed on to continue his work on IR resistance as a postdoc. Camille Henry continues postdoctoral work on the RecF protein. A recent postdoctoral arrival from Japan, Takeshi Shinohara, joins Steve on the IR resistance project. A visitor from China, Jing Zhu, bolsters the IR resistance studies until the end of this year.

Three graduate students are pushing the frontiers of enzymology in postreplication gaps. These include Zachary Romero (whose first paper on the proteins Uup and RadD just appeared in NAR), Miguel Osorio Garcia (holding down our efforts to elucidate the structures of RadD and DNA polymerase V), and Kanika Jain (advancing our understanding of the RarA protein). The enzymes we are seeing in postreplication gaps seem to be doing things that nobody ever expected an enzyme might do, and the work becomes more exciting every day. The graduate students are assisted by two former lab undergrads, Neema Mbele and Serena Wan, who are working with us for a year as they prepare for their next career steps. Our energetic undergraduates include Hope Beyer, Emma Steigerwald, Jasmine Lancaster, Jessica Liu, Abby Watson, Omar Quadri, Christine Wolfsmith, and Hannah Sweetman. Carol Pfeffer holds all together.

The link with Australia has opened opportunities, not only to apply new technologies to our research problems but to provide training in those new technologies. Annual visits are now routine, and the Wollongong group has integrated itself into ours. The trips are scientifically rewarding. This is our new normal as we approach 2020.

Last, but not least, Mike is a grandfather for the first time. Son Thomas and wife Sarah, living in Cambridge, UK, presented Beth and me with a granddaughter, Lucy Rose, on September 10, 2019. Lucy Rose is thriving.

Kimble Lab

At the time of our last letter in 2016, we had not pulled together our understanding of molecular regulation of germline stem cell self-renewal, one of our big questions since the lab started a few decades ago. The late ’80s revealed Notch signaling from the niche, the early ’00s uncovered RNA-binding proteins, FBF-1 and FBF-2 (collectively FBF), and the mid-’10s brought two key direct Notch target genes, lst-1 and sygl-1. All are critical self-renewal regulators, and Notch and FBF are conserved regulators across phylogeny. However, LST-1 and SYGL-1 were mysterious – both novel and largely disordered – and these various regulators did not fit together in the network. We now find that LST-1 and SYGL-1 proteins interact with FBF and that amino acids stapling their partnerships are essential for continued stem cell self-renewal. And we found, finally, that two more PUF (for Pumilio and FBF) RNA-binding proteins were missing. So a combinatorial “PUF hub” (four PUF proteins and two PUF partners) is responsible for driving self-renewal in the stem cell regulatory network. In addition, we made major progress understanding the sperm fate decision, Notch transcriptional activation and FBF target RNAs. The overarching theme is that RNA regulators are the primary drivers of the regulatory network balancing stem cell self-renewal and differentiation.

Our “we” includes a cast of smart, creative, committed and wonderfully collegial people. Several have moved on since the last letter. Two IPiB students, Dr. Heaji Shin and Dr. Kimberly Haupt, completed Ph.D.s. Heaji is now a postdoc at MIT, working on vertebrate stem cells and metabolism. Kim works at Promega and is delving into the corporate world. One IPiB student, Brandon Taylor, left the program early and has blossomed as a creative writer. Two postdocs are now leading their own labs as Assistant Professors, Dr. ChangHwan Lee at University at Albany in New York and Dr. Scott Aoki at Indiana University School of Medicine. Undergraduates and “postbacs” have also moved on: Jon Doenier, Amy Enright, Charlotte Kanzler and Annie Ryan to Ph.D. programs at Stanford (JD), UT-Southwestern (AR) or UW-Madison (AE, CZ); Sindhu Battula to Medical School, UW-Madison; Tim Guthrie to Medical College of Wisconsin - Green Bay; Garret Gunderson to School of Pharmacy, UW-Madison; and Kim Law to Vet School, U Penn. Finally, our Administrative Assistant, Anne Helsley-Marchbanks, retired when we transitioned from HHMI back to UW in September 2019.

Despite departures, the Kimble Lab continues to be a great place to do science. Three IPiB students, Brian Carrick (joint with Wickens Lab), Tina Lynch and Ahlan Ferdous, and one Genetics student, Sarah Robinson-Thiewes, continue to tackle new aspects of stem cell regulation, and four postbacs and one undergraduate, Cazza Czerniak, Sadie Jackson, Kyle Krueger, Jen Woodworth and Mingyu Xue, are cutting their research teeth with aims of med or grad school. Senior Scientist Sarah Crittenden continues to hold us together and advance all projects. And superb technical assistance from Peggy Kroll-Conner and administrative support from Carol Pfeffer make our work possible. It has been a great few years and we still have much to learn.

Pagliarini Lab

Hello from the Pagliarini Lab! This year we celebrated our 10th anniversary of being an independent lab and a part of the Morgridge/UW-Madison community. We have had another exciting year with much to celebrate and many happenings within the group. Our group continues to focus on three general themes:

1. Systematic functional annotation of the mitochondrial proteome. We were awarded a NIH MIRA Award to continue our systematic approach to defining mitochondrial protein function.
2. Elucidating the mechanisms of coenzyme Q biosynthesis. Our manuscript describing the role of COQ9 in enabling CoQ biosynthesis, led by Danielle Lohman, and in collaboration with the Dal Peraro group in Lausanne, was published in Molecular Cell.
3. Regulation of mitochondrial function and biogenesis. Our manuscript describing an essential mitochondrial matrix protein phosphatase, led by Natalie Niemi, was published in Nature Communications. We also successfully renewed our NIDDK R01 for work on protein phosphatases.

We are grateful for the recognition of our work through various awards and honors. These include one new Hilldale awardee (Keith Kamer), one Denis R. A. and Martha Washburn Wharton Fellowship (Zachary Kemmerer), a UMDF...
Pagliarini Lab continued

Accelerator Award (Rachel Guerra), among others. Three traineeships were also awarded this year to Laura Steenberge (Chemistry-Biology Interface Training Program (CBI) T32), Andrew Sung (Biology of Aging and Age-Related Disease T32) and Jonathan Tai (F31 Predoctoral Fellowship from the National Institute on Aging). I (Dave) was fortunate to be recognized by a UW H. I. Romnes Faculty Fellowship and the 2020 Earl and Thressa Stadtman Young Scholar Award from the American Society for Biochemistry and Molecular Biology.

Coming and Goings: The world of academia by nature results in the ever-changing composition of our laboratory with people coming and going. Two graduate students successfully defended their Ph.D. theses: Mike Veling moved to Boston to join Dr. Pamela Silver’s laboratory as a postdoc at Harvard Medical School and the Harvard Wyss Institute, and Molly McDevitt is now a Senior Scientist at PPD in Middleton, WI. Jon Stefely moved to Boston to start his residency at Massachusetts General Hospital - Clinical Pathology Specialty. Three undergraduates (Lainy Von Bank, Sheila Johnson, and Amy Lin) moved onto their respective graduate programs and post baccalaureate intramural research traineeship at the NIH. While we had to say “see you soon” to a number of lab members, we have been privileged to have Daniel Pensinger (postdoctoral fellow), Caroline Fecher (postdoctoral fellow), and Alana Caldwell (undergraduate student) join the lab.

Finally, we were honored to host U.S. Senator Tammy Baldwin in the lab in early October. We enjoyed showcasing the strong connection between the history of her grandfather’s work (David Green) and our current research ambitions. What a rewarding experience for everyone involved. For more news and updates from the lab, check out our laboratory website: https://morgridge.org/research/metabolism/pagliarini-lab/.

Record Lab

Hello from the Record Lab! There are many transitions involving accomplished lab members this year to recount. Postdoctoral fellow Kate Henderson, who received the departmental Paul Boyer Award for her research into the chemical and biophysical mechanisms of transcription initiation and promoter escape and the Sigrid Leirmo Award for mentoring many undergraduates, accepted a scientist position at Illumina in Madison. 2019 graduates from our terrific group of undergraduate researchers are Sarah Dyke (Medical School – MCW), Rezwana Karim (Graduate School – Cornell), Guanyu (Gary) Liao (Graduate School – Princeton), Jack Prazich (Graduate School – UT Austin), Rebecca Tang (Biotech industry), and Jamie Schuberth (Chem Eng industry). Biophysics graduate student Munish Chhabra obtained his Ph.D. for fluorescence kinetic studies of the role of promoter DNA wrapping on RNA polymerase in the mechanism of open complex formation in initiation. Munish moved to a scientist position at Molecular Assemblies in San Diego.

These projects are being continued by IPiB graduate students Dylan Plaskon (a previous Biotechnology trainee and current departmental scholarship recipient) and Max Rector, scientist Irina Shkel, Biophysics graduate student Hao-Chewang, BME undergraduate Krysta Stronek and Biochemistry undergraduates Claire Evensen, Sarah Doughty, Artun Kadaaster, Taka Ishikuri, Ben Palatnik, Will Langford, Jiayan Tang, Quinn McBride, and Savannah Peterson. Another research team (Irina Shkel, specialist Emily Zytkiewicz and undergraduates Keer Zhao, Kate McClure, Armor Rupanya, and Loron Cipala) is continuing our research into the strengths of weak interactions of C, N and O atoms of amides and other biochemical solutes, relative to interactions with water. These interactions are responsible for effects of these solutes on protein processes, and collectively drive biopolymer self-assembly. These studies allow use of amides like urea and other small solutes as probes of large conformational changes in protein processes.

Our current undergraduates have earned more than a dozen scholarships and awards in the past year, including Claire Evensen’s Goldwater, Astronaut, and Marshall scholarships, as well as a Biophysical Society National Meeting poster award for her research into how pyrophosphate (product) concentration affects transcription initiation. Congratulations to everyone!
William ‘Bill’ Hoekstra — Nutritional Biochemistry Pioneer, Thoughtful Mentor

University of Wisconsin–Madison Professor Emeritus of Biochemistry and Nutritional Sciences and Ph.D. alumnus William G. “Bill” Hoekstra died on Monday, Nov. 4, 2019 at 91. For nearly four decades, he was a faculty member with expertise in the role of trace minerals in human and animal nutrition. He made seminal contributions to both departments and helped found the Department of Nutritional Sciences during his time in the UW–Madison College of Agricultural and Life Sciences.

Hoekstra was born in Colorado and obtained a bachelor’s degree at Colorado State University. He then headed to graduate school at UW–Madison and obtained a master’s degree in biochemistry and animal science in 1952 and his Ph.D. in biochemistry under Paul H. Phillips in 1954.

He then joined the faculty after his Ph.D. and retired in 1990. He had appointments and students from both Biochemistry and Nutritional Sciences throughout his career. He also had students from the Department of Animal Sciences. Forty-four Ph.D. and 21 master’s students graduated with Hoekstra as their advisor.

Among other significant contributions, his lab was the first to discover the role of selenium, a trace element, in human and animal nutrition. Hoekstra was known foremost as a teacher and mentor to his students. His career was filled with awards and service to the fields of nutrition and biochemistry. He held both national and international positions, published many research articles, and received numerous awards of distinction.

“We were graduate students at the same time, in labs right across the hall, so we got to become great friends and also started as assistant professors together,” says Hector DeLuca, a Biochemistry Professor Emeritus. “He was a wonderful friend, colleague, and collaborator who helped shape CALS into what it is today.”
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A special thank you to those who contributed.

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United States Patent
Ralph et al.
Patent No.: US 10,286,504 B2
Date of Patent: May 14, 2019

SYNTHESIS OF PARACETAMOL (ACETAMINOPHEN) FROM BIOMASS-DERIVED P-HYDROXYBENZAMIDE

Relieving two headaches with one process. The lab of biochemistry professor John Ralph, who is a member of the Great Lakes Bioenergy Research Center housed in the Wisconsin Energy Institute, has been awarded a patent for a method to synthesize acetaminophen — the active ingredient in Tylenol — from a natural compound derived from plant material. The approach offers a renewable alternative to the current manufacturing process, which uses chemicals derived from coal tar. It also creates a useful product from an abundant but difficult-to-manage component of plant cell walls called lignin. The patent was filed by the Wisconsin Alumni Research Foundation (WARF). The researchers are now working on refining the process to improve the yield and purity of the plant-derived acetaminophen.