



MEDICAL SCHOOL  
**CELL & DEVELOPMENTAL BIOLOGY**  
UNIVERSITY OF MICHIGAN



# Mapping **the** Brain

*Exploring the Potential Causes and Treatments  
of Neurodegeneration*

**DEPARTMENT NEWSLETTER**

**Fall 2015**

Developing Future Biologists Pilot Takes Off  
Celebrating 10 Years of Bioartography  
Reflections on 160 Years of Excellence

*Brainbow labels neurons in the brain,  
each in a random color to allow the  
highly intermingled and connected  
neurons to be easily distinguished from  
each other.*





## MESSAGE FROM THE CHAIR

### Deb Gumucio, Ph.D.

What an outstanding year! CDB celebrated its 160th anniversary! At a gathering of over 200 faculty, staff, trainees and alumni, we learned about our department's beginnings and the impressive accomplishments of its faculty over decades of evolution in teaching and research. We celebrated innovation with Dr. Manu Prakash (Stanford) and his amazing foldscopes and we learned about the latest achievements in cellular, developmental and neurobiology from experts inside our own department (Drs. Lois Weisman, Doug Engel and Roman Giger) as well as outside (Drs. Dyche Mullins (UCSF), Shahin Rafii (Cornell) and Yuh Nung Jan (UCSF), respectively). President Mark S. Schlissel and Dean James O. Woolliscroft were on hand to help us remember the past and celebrate the future. Even past Chair Corydon Ford (1854–1894) was summoned from the 1850s by means of a time machine to participate in a lively rap battle!



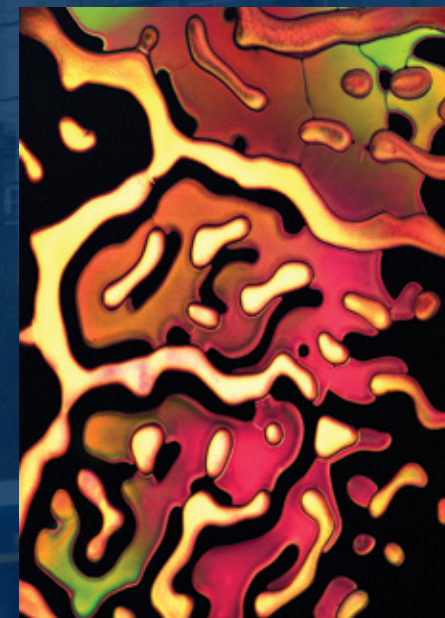
U-M President Mark S. Schlissel

It was great fun to celebrate the past, but it's even more exciting to look to the future. In that regard, we are thrilled to welcome our two newest faculty, Drs. Lei Lei (assistant professor of CDB) and Shiyong Jin (research investigator). They come to us from the Carnegie Institution, where they have both developed active research programs in oocyte development and uterine stem cells, respectively. Dr. Lei was selected through the Reproductive Science Program (RSP) cluster hire; her outstanding research in oocyte maturation will provide active and productive linkages between CDB and RSP. Two new joint faculty also joined our ranks: Drs. Ernestina Schipani (Orthopedic Surgery, Internal Medicine, Endocrinology) and Qing Li (Internal Medicine, Hem/Onc), further strengthening our ties to the clinical research enterprise.

The CDB graduate program also continues to grow as we welcome four new students this year: Titan Shih (Hu Lab), Martha Echevarria-Andino (Allen Lab), Ryan Passino (Giger Lab) and Hao Liu (Ye Lab). Read about eight new postdocs and three more graduate students from other departments inside! And, speaking of growth, nothing is better than increasing the number of CDB endowed chairs, and that is what we have done this year. We welcome our 9th and 10th endowed

Professors, Dr. Roman Giger (the George Linus Streeter Collegiate Professor) and Dr. Bing Ye (the Burton L. Baker Collegiate Professor of Life Sciences), both already approved by the regents.

Meanwhile, our existing faculty, trainees and staff have been quite busy winning awards (pages 22 and 26). There are too many to mention all here (please, do look inside!), but a few highlights include: Lori Longeway's Shining Star Award; induction into the League of Research Excellence for Andrzej Dlugosz, Peter Hitchcock, Ivan Maillard and Kristen Verhey; Sue O'Shea's EBS Teaching Award; Justine Pinskey's PIBS Award for Teaching and Service; Brandon Carpenter's EDGE Award; and Pavi Aravamudhan's dual awards (PIBS award for Excellence in Research and the prestigious Kaluza Prize for Outstanding Research from the American Society of Cell Biology). Wow!



U-M's Bioartography Program celebrates its 10th year (page 12)

It's been nothing short of a stellar year for grants! In addition to a whole slew of fellowship awards, listed inside, we send congratulations on their new funding to Drs. Ben Allen (x2), Kristen Verhey (x2), Billy Tsai (x2), Dawen Cai, Bing Ye, Roman Giger (x3), Daniel Lucas and Kate Walton.

Inside this newsletter, you will learn more about the exciting research that fascinates and engages our current CDB faculty and their trainees (page 4). They are leaders and shapers of their fields. Collectively, they published >80 manuscripts this year, many in the highest impact journals, including *Cell*, *Nature*, *Nature Medicine*, *Nature Cell Biology*, *Cell Stem Cell*, *Nature Neuroscience*, *Journal of Cell Biology*, etc. As we look to the future, we see huge opportunity for continued growth and success in our department. However, pursuing important and highly competitive scientific challenges depends more and more on philanthropic support. Inside this newsletter, you can learn about several new funds that support training and research in our department. Please, help us continue to make the Michigan Difference!

.....its so hard to be humble when your department is so awesome.....  
Go BLUE!

Deb Gumucio

**21**  
Primary Faculty

“Students get to learn from faculty who are defining the leading edge of human knowledge and curiosity; and the imagination and energy of our students contribute to the research enterprise.”

— Mark S. Schlissel, M.D., Ph.D.

**18**  
Joint Faculty

**15**  
National ranking of Cell Biology Departments 2014



## 5

## FIVE RESEARCH AREAS IN CDB

Faculty in the Department of Cell & Developmental Biology are studying a variety of areas of groundbreaking science. In each of these areas, they're seeking to understand the basic biology that leads to abnormalities in the way cells function. By getting a strong understanding of the mechanisms that lead to disease, they're able to find ways to address what's gone wrong. This will lead to treatments for many vexing diseases in the future that today have no effective remedy. Here are just five important areas.

### Reversing Neurodegeneration

Diseases of the brain and nervous system can be devastating, since patients suffer and loved ones must grapple with the fact that there is often no effective treatment. CDB scientists are exploring potential treatments of ALS, multiple sclerosis and Parkinson's disease. To do this, they are trying to better understand the function of the nervous system with the goal of unlocking the mysteries of the brain. Faculty are exploring how neurons communicate with each other, and how that communication is impacted in disease.

**REVERSING NEURODEGENERATION IS THE FEATURE IN THIS ISSUE. READ MORE ON PAGE 4!**

### Watching Molecules at Work Building Technologies for the Future

This field focuses on how diseases can be caused by mutations in proteins or by chemical imbalances. CDB faculty are employing new technologies to label individual brain cells and use biosensors to track how molecules and cells work together in the body. Researchers are studying how changes in the way cells interact can promote the growth of cancer, epilepsy and schizophrenia.

### Decoding Cellular Conversations How Miscommunication Leads to Disease

Scientists are examining changes in cell-to-cell communication that occur in diseases like Down syndrome, depression and diabetes. Faculty are mapping connections between hundreds of different nerve cells to understand how connections form and are modified during development, learning and memory, so that communication can be reestablished following traumatic brain injury, in aging, seizures or stroke.

### Cellular GPS Getting There on Time

Each cell has a system to sort proteins, sending them to the proper locations at the proper time. Errors in this cellular GPS system can lead to neurodegenerative diseases like Alzheimer's disease, as well as to cancer, diabetes and Parkinson's. Researchers are trying to better understand how this traffic system works, in particular, abnormalities in transport along the microtubule train tracks, which provide the critical "rails" for transport to different destinations in the cell. They are also studying the impact of deprivation of oxygen or essential nutrients, with implications for treating heart attacks or stroke and improving organ transplants.

### Regenerative Medicine

Advances in stem cell biology hold promise for treating diseases ranging from spinal cord injury to multiple sclerosis, Alzheimer's and Parkinson's disease. Following an injury, stem cells play a crucial role in the healing process, so learning how to activate them could speed up that process. Stem cells also provide an opportunity to study the impact of various therapies in a culture dish. By taking adult cells from the skin, then turning them into embryonic-like stem cells, then into neurons, scientists are able to see how cells from individuals with bipolar disorder behave differently than controls, and how lithium made them behave more like a neuron from a healthy individual. Being able to try out therapies on stem cells is paving the way for individualized medicine.



Explore some of the questions that drive research and the faculty in CDB starting on page 18.



**ONLINE** There is so much more information about these exciting areas of research on the CDB website: [medicine.umich.edu/dept/cdb/research](http://medicine.umich.edu/dept/cdb/research)



# Mapping the Brain

*Exploring the Potential Causes and Treatments of Neurodegeneration*

## CONNECTING THE DOTS

**A**mong all human diseases, neurodegenerative disorders have proven most vexing to researchers who have yet to find a cure. Neurodegeneration involves death of neuron cells and a loss of nerve structure and function that causes a loss of cognitive abilities, such as memory and decision making. In order for the neurons to function properly, there must be constant signaling both between the neurons and between neurons and muscles; when that signaling is disrupted, it can lead to neurodegenerative diseases. The number of those suffering from these types of diseases is large and growing. More than 12,000 people in the U.S. have a definite diagnosis of amyotrophic lateral sclerosis (ALS), while one million Americans and an estimated seven to 10 million people worldwide are living with Parkinson's disease; 5.3 million Americans have Alzheimer's disease today and that figure is expected to reach 16 million by 2050.

A cure has been elusive because there is still a general lack of knowledge about how the brain works and how the central and peripheral nervous systems function, says Ben Allen, an assistant professor in the Department of Cell and Developmental Biology. He says that so many interconnections are involved, it's difficult to isolate the one connection causing the problem and fix it, as you would do by replacing a diseased kidney with a healthy one through a transplant. "You can't transplant part of a person's brain, so we really have to figure out how to fix the problem at the site of the disease," he said. Making the situation even more complicated, particularly in the case of ALS, is that a single motor neuron can innervate multiple muscle fibers, so unlocking the mysteries to a cure is a daunting process.

But seven researchers in the University of Michigan Medical School's Department of Cell and Developmental Biology are making significant progress. By closely studying the patterns of neurons in the brain and the way they connect to each other, they hope to better understand how a normally functioning brain works and compare it to a brain of an individual suffering from a neurodegenerative disease to determine what has gone awry. This could pave the way for new treatments.

### \* DAWEN CAI: BRAINBOW

One way of doing this is by exploring how various neurons in the brain connect to each other. Dawen Cai, an assistant professor of Cell and Developmental Biology in the University of Michigan Medical School with a joint appointment in biophysics in the College of Literature,

Science, and the Arts, is focused on developing and using sophisticated genetic labeling, microscopic imaging and computer software to map the structure of neurons in the brain and how neurons communicate with each other. He explains that most mental disorders and neurodegenerative diseases are caused by neuron miswiring in the brain. There are hundreds to thousands of neurons that connect to each other to form a microcircuit but "we have almost no

define the circuit at the cellular level in a healthy mouse brain and then compare that to a diseased mouse brain.

Cai developed software, called nTracer, which traces the processes of each colorful neuron within a densely labeled network, as you would trace a spaghetti noodle in a plate to define what and where it connects, providing a three-dimensional digitized neural network blueprint. It's similar to



Dawen Cai

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knowledge about what exactly this circuit means, which neurons are included in a circuit and how neurons connect to each other at the cellular level," he said. He's using a genetic labeling technology, called Brainbow, that labels neurons in the brain, each in a random color to allow the highly intermingled and connected neurons to be easily distinguished from each other. Cai explains that since neurodegenerative diseases cause neural circuits breaking down at the cellular level, leading to a malfunction of the brain, his approach to understand the physical basis of these diseases is to first

a three-dimensional map you can see of highways through a satellite. "We try to identify these highways and piece them together and figure out the junctions and connections in a scale that has never been achieved before," he said. This is the first time that the complete input and output patterns of a small fraction of important circuits have been directly measured, Cai said. His work may help to better understand the mechanism of the progress of neurodegenerative disease, especially at the point of diagnosis, because in the early phase of the disease, it normally involves



subtle miswiring between neurons before severe neuronal cell death occurs.

“This could lead to better understanding the mechanism that triggers the disease and finding a way to try and fix it,” he said. The information can also be used to simulate the impact on the entire circuit when one cell dies. Ultimately, it could lead to more targeted, localized therapies that can treat the problem at the precise place where the disease originates instead of treating the entire brain, significantly reducing the potential for side effects, he added.

The tracing software was presented at the annual meeting of Society for Neuroscience in Chicago in October. Cai is also in the process of combining two novel circuit labeling technologies being developed in his lab to define and map the complete neural circuit that involves visual signal processing and memory formation. That is due to be completed within two years. Mapping the entire normal brain will be years, even decades, of ongoing work, since it’s an extremely challenging science and engineering problem that requires the maturation of research in many different areas, he said.

Douglas H. Roossien, a research fellow in the Department of Cell and Developmental Biology, was hired by Cai to put the software to the test. “This will truly be useful for the field at large,” he said, moving from a situation where you can label only a couple of cells, to being able to label them all. He was attracted to the project because he wanted to do “cutting-edge microscopy technology, something new and exciting” and this fit the bill. “The images themselves are very stunning. They’re breathtaking structures. I was sold on the pictures and how they can further advance the field.” Since many neurodegenerative diseases are manifested in changes in the brain’s circuitry and how information is processed in the brain, Brainbow’s ability to look at large circuit structures in diseased vs. normal brains and see what’s causing the symptoms will be hugely significant, he said.

Cai will be using his software in a partnership with William Dauer, Einor

Levine Professor of Neurology and a professor of Cell and Developmental Biology, to explore the causes of pediatric dystonia. In this neurodevelopmental disease, children appear initially normal, but develop abnormal movements during adolescence. These movements are triggered, in part, by irregularities in a part of the brain called the striatum. The striatum is made up of several different types of nerve cells, but it is poorly understood which of these are affected in dystonia. Recent findings from Dauer’s lab have identified the degeneration of about half the population of one type of nerve cell in the striatum that may be important. “We want to look at why these cells are being lost and others which are also the same type of neurons are not being lost,” Dauer said. He plans to use Dawen’s technology to look at connections and morphology to test whether distinct connections predict

**Seven researchers in the University of Michigan Medical School’s Department of Cell and Developmental Biology are making significant progress. By closely studying the patterns of neurons in the brain and the way they connect to each other, they hope to better understand how a normally functioning brain works and compare it to a brain of an individual suffering from a neurodegenerative disease to determine what has gone awry. This could pave the way for new treatments.**

which cells are vulnerable. “Figuring out the pieces of the machine and where the wires go is one part of the equation,” he said. Identifying a class of cells that is different and connect to a different place would have implications for how the brain normally works. “One of the aims of the project is to understand what brain circuits go awry that cause this disease and then focus study on the region that is most implicated in causing the abnormal symptoms that afflict these children,” he explained.

#### \* BEN ALLEN: HEDGEHOG SIGNALING PATHWAY

Allen became interested in studying neurodegeneration based on collabo-

ration with a colleague, Jeffrey Martens, investigating the mechanisms that control the sense of smell. Together they are searching for clues to treat neurodegenerative diseases through a mechanism called the Hedgehog signaling pathway. Hedgehog is a universal signal-



Ben Allen

ing pathway that functions in every tissue and can do many different things in different tissues, but until now, had yet to be studied in the context of the sense of smell. It’s well established that Alzheimer’s and Parkinson’s patients lose their sense of smell before their disease is diagnosed, which can help predict whether someone will be at risk for developing these diseases, he said.

Every time a person smells, they activate a particular set of neurons inside their nose. The outermost tissue is an epithelial tissue inside the nostrils; embedded in that tissue are olfactory sensory neurons that connect the outside environment to the brain. The olfactory deficits are being

viewed as a possible way to provide an early diagnosis for potential neurodegenerative disorders. Olfactory sensory neurons are one of the few neuronal tissues that will regenerate; every month to three months, the old neurons in the nose die and will be replaced by new ones.

Allen explains that skin cancer patients who take a drug to block the growth of their cancer also lose their sense of taste and smell, but that these senses return when they go off the drug. Allen wonders, however, if there is a point of no return, where if they’re on the drug for many years, it’s not reversible. “We’re interested in studying what regulates the normal turnover and regeneration of both your sense of taste and smell following injury or insult and in the context of both neurodegenerative diseases and cancers.”

Allen’s new finding, published as part of a collaboration with Anj Dlugosz, Robert Bradley and Charlotte Mistretta in the February, 2015 *Journal of Neurophysiology*, is that the hedgehog pathway is critically important to maintain the sense of taste. Allen suspects that the hedgehog pathway also regulates the sense of smell by controlling the ability of stem cells to differentiate into those olfactory neurons that die and are not replaced. The expectation is that by manipulating Hedgehog signaling appropriately, you could prevent cancer patients from losing their sense of smell during treatment. “The long-term hope is if we can understand how Hedgehog signaling controls smell, this will lead to potential therapeutic approaches to treat patients with Parkinson’s and Alzheimer’s,” he said. Allen explains that there is a population of stem cells in the olfactory epithelium that expresses these hedgehog pathway components. If Hedgehog signaling is manipulated in that population of stem cells — either by deleting them genetically or expressing different versions of them — the ability of those olfactory neurons to regenerate and function is disrupted. Allen says this aspect of his research is still in the very early stages and won’t see publication until sometime next year. Until recently, he’s focused on the role of Hedgehog signaling in embryonic development;

this is his first foray into understanding the role of the hedgehog pathway in adult tissues and adult disease. “For us, it’s really exciting because it’s giving us a chance to have an impact on an adult population,” Allen said.

#### \* ROMAN GIGER: SPINAL CORD INJURY

One of the most vexing disorders of the nervous system is spinal cord injury. Roman Giger, a professor in the Department of Cell and Developmental Biology and Department of Neurology, has toiled endlessly in search of a cure, and his research could offer hope to the 250,000 people in the U.S. suffering from this injury. He is looking into why molecules important in building the brain during development are silenced during adulthood, and are incapable of repairing the brain following injury. In a spinal cord injury, cells survive, but just lose their connections, like a computer that cannot connect with a printer. “We’re trying to fix these cables,” Giger says. He is looking at ways to help injured neurons repair their cable-like structures, called axons. Currently, axonal growth and neural repair are very limited. Rehabilitation and physical training can help, but won’t completely fix the problem. “At the end of the day, what we want to create is functional connections,” reestablishing connections that have been lost or damaged by injury, he said.

In collaboration with Benjamin Segal in the Department of Neurology, he published a study this year that shows how activation of the immune system positively influences axonal regeneration following central nervous system injury. After injury, central nervous systems axons fail to regenerate spontaneously. They found that you can use intrinsic mechanisms of your body, the immune system, and tinker with it in a way that promotes regeneration of severed axons. “That’s very exciting. We found specific immune receptors that need to be activated to regenerate severed axons in the optic nerve,” looking at one eye as the control and the other as experimental. They showed that administering a compound called particulate beta-glucan engages an immune receptor that can

trigger enhanced axonal regeneration. Delaying administering it even by two days allows for the same regenerative response, indicating it doesn’t need to be used immediately to work effectively. What’s more, ongoing studies found that the same molecules are not just important for building the optic nerve, but also for spinal cord injury and possibly neurodegenerative disorders. The finding suggests a new way of repairing neurons: using the immune system, which could help reverse nervous tissue damage inflicted by trauma or disease. “If we find ways to strongly promote regenerative axonal growth in the adult mammalian central nervous system, this will be highly relevant for traumatic brain injury, stroke and neurodegenerative disorders,” he said.



Roman Giger

Giger says a cure for spinal cord injuries won’t be developed any time soon. “What I realistically want to accomplish is to make significant contributions toward a cure, providing stepping stones on which the cure could march.” His research breakthroughs could, in the interim, improve one’s quality of life, perhaps allowing a spinal cord injury patient to regain partial use of some limbs, or a stroke survivor to regain some speech. “These are realistic milestones which could be accomplished within a decade,” he said.

Research published in May by Bing Ye, associate professor of Cell and Developmental Biology and the Life Sciences Institute, holds hope for those with Down syndrome. He found a class



of chemical compounds that treated the developmental defects in animal models of Down syndrome. Ye studies the role that a Down syndrome Cell Adhesion Molecule (Dscam) plays in regulating the growth of axons. He found that when Dscam is too high, there is too large of an axon terminal. He discovered a link between a mutated Dscam gene and those with Down syndrome, with those patients having higher levels of Dscam than those without the disorder. “We came up with the idea that if we inhibit Dscam levels and reduce its function in Down Syndrome patients, we may provide a way of treating the patient,” Ye said.

Dscam needs to interact with another signaling protein, Abelson tyrosine kinase (Abl), in order to influence the growth of presynaptic terminals. When Dscam activates too much Abl, it results in larger presynaptic terminals. So Ye turned to approved drugs that inhibit the activity of Abl. He found that a class of chemicals that already has received FDA approval for the treatment of leukemia. When used to treat fruit fly larvae, the drug reversed the defects caused by the increased Dscam. This showed that suppressing the abnormally high activity of the Abl protein could pave the way for treating brain disorders caused by excessive growth of Dscam. The treatment has yet to be tested on mammals, but Ye said the fruit flies offer hope, since their cellular and molecular mechanisms are similar to humans. The next step is to test it on mice. “It’s very exciting because Down syndrome is prevalent; it’s in one in 700 live births and there is no treatment at all and we found a drug target that seems to be safe for clinical use,” Ye said.

#### \* KATE BARALD: HEARING LOSS

Kate Barald, a Cell and Developmental Biology and Biomedical Engineering professor, and her research group have focused on deafness and the replacement or repair of inner ear neurons lost to various kinds of neurodegeneration: aging, injury often caused by loud noise exposure, including rock concerts and loud sound through ear buds, as well as genetic conditions such as Usher syndrome. She says that hearing loss can also be

caused by cancer drugs that contain heavy metals. “There are a lot of people who are in need of better hearing function, not just the aged,” she said. Barald is completely deaf in one ear and has a close friend with two children suffering from Usher syndrome, so she has personal connections to the research as well.

While birds and fish have the ability to regain hearing loss by regenerating sensory hair cells, the cells responsible for hearing, mammals can’t. “You can take your chicken or zebrafish to a rock concert with impunity; their hearing organs are capable

**A big strength of the Department of Cell and Developmental Biology is the faculty’s willingness to collaborate. “If you don’t know the answer, you can see if anyone is studying it in the world; if the person who studies it is down the hall, that’s the best. If they’re two blocks away, that’s pretty good too.”**

of regeneration, but you’d better wear ear plugs,” she says. Fish and birds regenerate their sensory hair cells by recruiting inner ear supporting cells to turn into hair cells. Supporting cells make an immune system inflammatory cytokine: macrophage migration inhibitory factor, or MIF. MIF guides the early development of the inner ear’s neurons and is made by both Schwann cells and supporting cells in the inner ear. Mice that have been engineered not to express MIF are deaf. Since adult neurons still have receptors for MIF, Barald thought it might be possible to use MIF or MIF-producing cells to help neurons regenerate.

In a study published in 2012, Barald and her colleagues found that MIF and other cytokines, which are known to be critical for immune system function, are also important for both nervous system development and for repair. She and her graduate students produced the first embryonic stem cell-derived Schwann cells, which, like all Schwann cells, make MIF. In the lab, this has allowed a way to enhance inner ear neuron contact with a cochlear implant, by “coating” the cochlear implant with hydrogels carrying the MIF-producing Schwann cells made



Kate Barald

from stem cells. Cochlear implants are presently the only cure for deafness when people have lost the sensory cells in their inner ears, but the quality of hearing with such an implant is substandard. Her group’s goal is to improve the chances that the remaining auditory neurons will hook up with the implant, eventually improving range and quality of sound perception. Barald has submitted a grant application to the National Institutes of Health to investigate the role that MIF might have in repairing the auditory nervous system in zebrafish whose inner ear neurons are poisoned by the cancer drug cisplatin, with the goal of discovering why and how auditory system regeneration occurs in zebrafish, but not in humans and other mammals.

In her 35 years at the University of Michigan, Barald said, this was one of the most significant discoveries her group has ever made. “You have serendipitous moments of discovery like this relatively infrequently.” She called the finding “startling and surprising and intriguing.” She is encouraged that MIF has also recently been implicated in ALS and multiple sclerosis, raising the possibility

that discovering MIFs’ role in neuronal development and regeneration will hold promise for new approaches to these diseases as well.

Barald has involved 360 undergraduates in her research during her tenure at the University of Michigan. Hannah Marcy, a 21-year-old senior majoring in Cellular and Molecular Biology, is one of them. She’s been looking at zebrafish hearing development to figure out the pathway in which they can regrow cells when they’re damaged. The research, she said “is incredibly inspirational,” due in large part to Barald’s enthusiasm and dedication to her work. Marcy’s interest in this area was twofold; her grandparents suffered hearing loss and, as a clarinetist, she thinks everyone should be able to experience the beauty of music. Marcy, who is planning to become a doctor, said being at the cutting edge of research that could lead to a cure in hearing loss is particularly exciting.



Lois Weisman

#### \* LOIS WEISMAN: LIPID SIGNALING PATHWAY

Lois Weisman, a professor in the Department of Cell and Developmental Biology and the Life Sciences Institute, is looking for clues on how to solve the puzzle of regenerative disease through the lens of yeast. She’s working with Baker’s yeast, the kind found in bread, and became attracted to this area since the single cell organism is far easier to study. “How a neuron behaves is a lot like how a yeast behaves,” she said. She thought, “if I could discover a pathway

that had been unknown, I might provide a new way to study how cells are regulated.” She accomplished that feat, and in parallel studies with three other labs, uncovered the existence of a new lipid signaling pathway in yeast. The Weisman lab then found that this same pathway is critical to mice and humans and is required in all tissues, especially the brain. Weisman first suspected that this lipid signaling pathway was important after watching its response when salt was applied to the yeast. The lipid levels increased 20 times higher, then within a few minutes, returned to their normal levels. “To me, that looked like adaptation,” Weisman said.

To understand if this pathway was important for animal physiology, Weisman engineered a mouse mutant missing one of the proteins required for the pathway and found that the mutant mice with it died and had severe neurodegeneration. The discovery of the pathway is the first step to finding out what causes this type of disease and fixing it. “If we know how a normal neuron works, we’re going to have more insight into how to treat a diseased one,” she said. Even though the mice had half the normal levels of the lipid, “the brain is so messed up,” she said, adding that deficiencies in the pathway can create other problems in the heart and lungs. Coincidentally, Miriam Meisler, a professor in the University of Michigan Medical School’s Department of Human Genetics, discovered another mouse mutant with defects in the same pathway and found that some patients with Charcot-Marie-Tooth disease, a hereditary neurological disorder, have mutations in this pathway. By mimicking this mutation in yeast, the Weisman lab found that the mutation was surprisingly minor, though it causes a serious disease. These discoveries raise questions about the role of the signaling lipid, and why having just the right amount is so important in the nervous system. “Just knowing how this lipid signaling pathway works in neurons will be important,” she said.

Michael Lang is a 27-year-old graduate student in the Department of Cell and Biology who has worked in Weisman’s lab since 2013. He was attracted to the study of lipid regulation in cells because it was a relatively new field that hasn’t yet been extensively studied. “I like to go left when everybody is going right,” he said. Though he said the lipids are difficult to study, very low in abundance and intractable to work with, they had their upsides. “It’s really cool that it works the same from yeast to humans.” He appreciates the chance to be a part of a discovery that not only holds potential for curing human diseases, but also contributes to a better understanding of basic research science, “a case study for how cells and proteins work as a whole.”

Weisman believes that these advancements in basic science could be particularly important in the search for cures. She’s currently in the process of preparing a study that provides more insight into how the levels of the lipid are regulated in yeast and will be submitting this for publication. These new yeast studies may also help in learning more about the regulation of this pathway in neurons. “The lipid signaling pathway is turning out to be very complicated,” she said. “It will require a cadre of scientists across the world studying it.” She said a big strength of the Department of Cell and Developmental Biology is the faculty’s willingness to collaborate. “If you don’t know the answer, you can see if anyone is studying it in the world; if the person who studies it is down the hall, that’s the best. If they’re two blocks away, that’s pretty good too.”



# the “Developing Future Biologists” Pilot Takes Off

University of Puerto Rico  
Ponce, Puerto Rico  
May 25–29, 2015

CDB graduate student Martha Echevarría-Andino (center) works with students on a lab during the Developing Future Biologists' first short course.

During the 2014–15 academic year, a U-M Department of Cell and Developmental Biology (CDB) postdoc, Andrea Ramos-Serrano, decided to establish Developing Future Biologists (DFB), a student-run program designed to lower the cultural barriers to graduate education and increase awareness of life science careers for undergraduate students currently underrepresented in the field of developmental biology. She soon recruited CDB graduate students Martha Echevarría-Andino, Brandon Carpenter, David Lorberbaum and Justine Pinsky to create a team to help her realize her vision.

Both Ramos-Serrano and Echevarría-Andino had come to Michigan from the University of Puerto Rico at Ponce. “We both have a passion for the life sciences but our options were limited in Puerto Rico due to a lack of courses, resources and hands-on experiences,” explains Echevarría-Andino. Once they discovered what was possible at U-M, they wanted to find a way to expose other undergraduates in Puerto Rico to these possibilities. “A program like DFB would not only raise awareness among students but could eventually increase the presence of underrepresented minorities in the sciences,” she explains.

## The Short Course

With the help of CDB graduate students, funding from several sources, support of CDB faculty and Edu Suarez (a faculty member at Ponce), DFB piloted its first short course at the University of Puerto Rico in Ponce, Puerto Rico from May 25–29, 2015. Developing Future Biologists provided students with personal mentoring, direct exposure to cutting-edge research and inspiration to pursue a career in the life sciences. A set of hands-on experiments accom-

panies short lectures to allow students to experience a topic of biology that is not currently offered at Ponce.

The goal of the course was to provide the next generation of biologists with basic knowledge in: developmental biology, commonly used model organisms, experimental tools and molecular mechanisms of disease.

The curriculum focused on fundamental aspects of embryogenesis, cell signaling and disease development. Lectures covered aspects of early development, tissue and organ formation and disease. The laboratories complemented the lectures and provided hands-on experience through the dissection and examination of several model organisms. Class participation and small group discussions were also encouraged throughout the course.

Lecturers included CDB faculty Scott Barolo, Ben Allen and Deneen Wellik.

The Laboratory Instructors included all members of the DFB graduate student team.

“We had 22 students total this year. We also made sure to have several informal social gatherings so they could get to know the faculty and the graduate students, ask us questions and get advice,” adds Echevarría-Andino. “There was a very enthusiastic response from the participants (see sidebar). The students were excited and inspired by the experience. Many of them left the course saying ‘I really want to do this!’”

## DFB Student Voices

“I just want it to say THANK YOU. This week was wonderful and it’s sad that it’s over. I learned a lot from all of you and not only about biology but also about many opportunities I never knew about. I’m really grateful for that!!! This course was the first of many and I’m glad I was part of its beginning.”

– Cristal Medina

“I want to say thanks for letting me be part of this amazing experience. Loved the organization of the course, the topics and laboratory activities. Personally this experience not only increased my knowledge in biology but also gave me the inspiration to continue pursuing my dreams!!! I hope to see you all in the future. So sad it is over!!!”

– Yesenia Rivera

“This experience opened doors for me! After DFB, I participated in an internship and now I work as a volunteer in a lab! Thanks!”

– Karina Matos

## Next Steps

After the successful pilot course, DFB plans to go back to University of Puerto Rico at Ponce again in Spring 2016. They hope to open the program up to students from all 10 of the University of Puerto Rico’s undergraduate campuses with the hopes of recruiting up to 25 participants. Weeklong programs are also currently planned for the Detroit area and Native American-serving universities and historically black schools and colleges as well.

DFB is currently seeking additional funding and recruiting more CDB graduate students to participate in the short course’s planning and implementation. “This is a great opportunity for graduate students to gain teaching experience — developing curriculum and labs,” says Echevarría-Andino. “And it’s really rewarding to share something you love with such a receptive audience. They are really engaged. These students are there because they really want to learn more about science.”

## Get Involved

**i** If you’d like to learn more about how to support or participate in the Developing Future Biologists Initiative, e-mail [DFB.coordinators@umich.edu](mailto:DFB.coordinators@umich.edu). You can also visit their website at [developingfuturebiologists.com](http://developingfuturebiologists.com).



# Celebrating 10 Years of Bioartography

A Bioartography image titled: *Intestinal Fortitude*

While you may have heard the saying “Discover your inner artist,” have you ever thought about discovering your “inner art”? Every day at the University of Michigan, scientists from many fields work together to study organism development, function and disease. While the goal of these studies is to design new and effective ways to treat disease and provide better understanding of ourselves as well as the world around us, many are also taking the time to share the beauty of their work with others through a program called BioArtography.

In the course of research, scientists use special stains to add color to the otherwise transparent tissues. Microscopes then allow detailed observation of the tiny, colorful biological structures from inside our bodies revealed in these images. This results in a fascinating combination of art and science that U-M researchers are capturing in pictures taken through microscopes and turning into artworks that would look beautiful on any wall.

## BRINGING THE MICROSCOPIC WORLD TO LIFE

Founded by Deborah Gumucio, Ph.D., Interim Chair of the Department of Cell and Developmental Biology and Professor Sue O’Shea, Ph.D., Director of the pluripotent stem cell laboratory, BioArtography has developed into a thriving program now entering its 10th year. Gumucio, who leads the project,



says the effort to turn science into art helps bring the microscopic world to life for the general public — and shows that researchers aren’t just about data and facts.

Each year the program sells prints and notecards featuring their artwork at Ann Arbor’s South University Art Fair. Proceeds from all sales are used to help young scientists launch their careers and do more research.

A jury of scientists, art professors and artists choose the 16 new

images for the collection that is featured at their booth each year. The weeks leading up to the fair are a frenzy of activity, as staff prepare the prints, and frame and package them.

In 2015, the team introduced images printed directly onto canvas, and images printed on metallic back-grounds, which give the cells and molecules extra shimmer and depth. They also offered several sizes of matted, framed prints and packs of notecards.

Past BioArtography sales have raised enough money to send more than 80 graduate students and postdoctoral fellows to scientific conferences, where they can present their work to other scientists and make connections that can help them launch their careers in research and industry.

The “Dance of the Neurons: The Art of Neuroscience” exhibit is currently on display at the University of Michigan Museum of Natural History (since Feb. 2015). The images were selected from the U-M BioArtography collection in support of the Museum of Natural History’s Winter term program on brain science.

## GET YOUR OWN BIOART

All of the BioArtography images featured at the Art Fair are available for order online at [bioartography.com](http://bioartography.com), along with prints and notecards of more than 200 images chosen in past years.



## REFLECTIONS ON 160 YEARS OF EXCELLENCE

On April 23 and 24, 2015, alumni, faculty, staff and trainees of Cell and Developmental Biology gathered to celebrate the department's long and illustrious history of teaching and research at the University of Michigan Medical School.

Departmental roots reach back to the first professorship in anatomy, held by Corydon L. Ford, M.D., from 1854 (four years after the Medical School's establishment) to 1890. From an original dual mission to teach human anatomy to medical students and to utilize comparative anatomy as a means to understand human form and function, departmental interests have evolved dramatically to encompass teaching and research in histology, embryology, cell biology, developmental biology, stem cell biology and advanced imaging.

**Fifteen department chairs and 94 faculty later, the department is a vibrant hub of collaborative researchers and dedicated teachers who are elucidating basic mechanisms that control the cellular behaviors that underlie human health and disease.**

Now, 15 department chairs and 94 faculty later, the department is a vibrant hub of collaborative researchers and dedicated teachers who are elucidating basic mechanisms that control the cellular behaviors that underlie human health and disease. A gold watch, given in 1885 by Dr. Ford to Charles Stowell, M.D., a departmental champion of histology, sits prominently in the office of the chair, as a constant reminder of the department's rich historical legacy as well as its future potential to fuel new discoveries in personalized and regenerative medicine.

*Deborah L. Gumucio (Ph.D. 1986)*

*James Douglas Engel Collegiate Professor and interim chair of the Department of Cell and Developmental Biology*



*Interim Chair Deb Gumucio shows off the CDB history book*



*Scott Barolo in character as Corydon L. Ford, the first chair of the department*



*Manu Prakash demonstrating the foldscope*



*Danielle Rux giving one of the great student presentations*

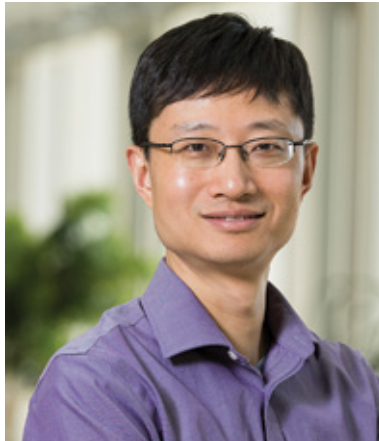


*Shahin Rafii, M.D. presenting during the day-long symposium*



## ENDOWED PROFESSORSHIPS

### The Burton L. Baker Collegiate Professorship of the Life Sciences



Bing Ye

Dr. Bing Ye was promoted to associate professor, with tenure, in the Department of Cell and Developmental Biology and research associate professor in the Life Sciences Institute on September 1, 2015. A member of the CDB faculty since 2008, Dr. Ye studies how neuronal development contributes to the assembly and function of nervous systems and how defects in this process lead

to diseases. He is particularly interested in how experience and neuronal activity interact with the genome to shape the development of nervous system.

Dr. Ye requested that his collegiate professorship be named the Burton L. Baker Collegiate Professorship of the Life Sciences.

**Dr. Ye studies how neuronal development contributes to the assembly and function of nervous systems and how defects in this process lead to diseases.**

#### About Burton L. Baker



Dr. Baker spent his entire academic career at The University of Michigan Medical School where he joined the faculty as an instructor of anatomy in 1941, becoming a full professor in 1952.

During his 37-year tenure, Dr. Baker became a highly respected researcher, teacher and administrator, publishing more than 110 scientific articles in his field of neuroendocrinology and reproductive biology. He was one of the first investigators to demonstrate, by the use of labeled antibodies, the presence of reproductive

hormones in the pituitary and hypothalamus and that this part of the brain controls pituitary functions. Dr. Baker was internationally known and recognized for his important scientific contributions.

Dr. Baker was the recipient of the Henry Russel Award in 1947, and in 1977 received the Distinguished Faculty Achievement Award. He was twice elected to the Executive Committee of the Medical School and served continually as Chairman of the Cancer Research Committee for almost 20 years. He served on the University of Michigan Senate Assembly, on the Executive Board of the H. H. Rackham School of Graduate Studies and on the Advisory Committee of the Dental Research Institute.

Nationally, Dr. Baker was managing editor and associate editor of the *American Journal of Anatomy* and served on the Editorial Committee of the Endocrine Society. His participation in professional societies included the American Physiologic Society, the Endocrine Society, the Society for Experimental Biology and Medicine, where he was on the Editorial and Publications Committee for over five years, and further served on the Michigan Section. Professor Baker passed away on October 14, 1978.

Dr. Ye has chosen to honor his career and contributions through the naming of the Burton L. Baker Collegiate Professorship of the Life Sciences.

**“He was one of the first investigators to demonstrate, by the use of labeled antibodies, the presence of reproductive hormones in the pituitary and hypothalamus and that this part of the brain controls pituitary functions.”**

### The George Linius Streeter Collegiate Professorship



Roman Giger

Dr. Roman Giger was recently installed as the first George Linius Streeter Collegiate Professor.

In 2001, Dr. Giger was appointed as an assistant professor of neurology at the Center for Aging and Developmental Biology, University of Rochester School of Medicine and Dentistry in Rochester, NY. He was promoted to associate professor in

2006. In 2008, he was actively recruited to the University of Michigan Medical School as an associate professor in the Department of Cell and Developmental Biology and promoted to professor in 2014; he also holds a joint appointment in the Department of Neurology.

**“Dr. Giger’s research focuses on proteins that regulate neuronal growth and synaptogenesis, including members of the semaphorin family and their cognate receptors (neuropilins and plexins), and myelin associated inhibitors/chondroitin sulfate proteoglycans and their receptors.”**

Dr. Giger’s research, which is extremely well funded, focuses on proteins that regulate neuronal growth and synaptogenesis, including members of the semaphorin family and their cognate receptors (neuropilins and plexins), and myelin associated inhibitors/chondroitin sulfate proteoglycans and their receptors. The goal of the research is to understand how enhancing

neuronal plasticity can improve functional outcomes after nervous system injury. Dr. Giger’s work is routinely published in top journals including *Nature*, *Neuroscience* and *Journal of Neuroscience*. Another line of investigation is focused on mechanisms of axon-glia interaction (a poorly studied aspect of neuronal disease) during nervous system development, adult homeostasis and disease. At this point, Dr. Giger is internationally known as an expert in these areas, has served on study section, is winning national awards (e.g., Dana Foundation) and is Associate Editor of the *Journal of Neuroscience*.

He is also an important senior leader and mentor for the neuroscience faculty in CDB and one of CDB’s most active and influential neuroscience faculty members in the growing, active neuroscience community at Michigan.

#### About George Linius Streeter



Dr. Streeter was a prominent and prolific embryologist who served as chair of the Department of Anatomy at the University of Michigan from 1907 to 1914. Though he was only at the University for seven years,

Dr. Streeter completely revitalized the Anatomy Department, increasing its research productivity significantly. His time as chair saw innovations such as the founding of a graduate training program and the institution of modern preservation techniques for cadavers. He was also a consummate teacher, introducing the “flipped classroom” decades before its time. Dr. Streeter believed that self-directed reading assignments, not lectures, would prepare students best.

Dr. Streeter also developed teaching aids that were invaluable for student success, including “bone boxes” for each student of gross anatomy. His personal preparations of neurological specimen slides are still used by neuroanatomists today. At the time of his departure from the University in 1914, to work for the Carnegie Institution Department of Embryology, the U-M Anatomy Department had grown to become an innovative, productive and thriving unit. Dr. Streeter was elected to the presidency of the American Association of Anatomists in 1926, was inducted into the National Academy of Sciences in 1931 and into the American Philosophical Society in 1943, capping an outstanding career as an educator and embryonic neuroscientist.

CDB honors his rich legacy through the George Linius Streeter Collegiate Professorship.

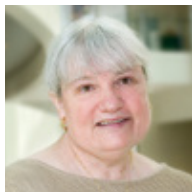




**Ben Allen**  
Assistant Professor

How do secreted proteins control the formation of various types of neuronal cells (e.g. motor neurons) in the embryonic brain and spinal cord? Also, how does deregulation of these proteins cause disease, such as pancreatic cancer (a collaboration with Marina Pasca di Magliano)?

We are pursuing the activity of a family of secreted proteins (known as Hedgehog) in embryonic development and disease.



**Kate Barald**  
Professor

Birds and fish can regenerate their hearing organs and inner ear neurons, but mammals can't. What crucial molecular and cellular differences in the way the inner ear forms and regenerates are responsible for these differences? What role does the immune system play in inner ear development

and its possible repair? Can these findings be used to enhance cochlear implant function?



**Scott Barolo**  
Associate Professor

Cells emit molecular signals to "talk" to their neighbors. Those signals are interpreted by special sequences called enhancers in the genomes of the receiving cells, which regulate the expression of nearby genes. How do enhancers respond to signals during development, stem cell

function, and disease, and how are those signals translated into precise changes in gene expression?



**Dawen Cai**  
Assistant Professor

How are our one billion neurons generated from stem cells? How do they physically connect during development? How are these connections modified during learning?



**Mara Duncan**  
Assistant Professor

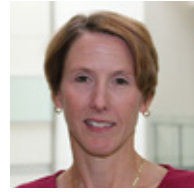
How do cells respond when they face a situation of low oxygen or low energy (such as in heart attack or stroke)? What cellular machinery gets activated to allow the cell to survive such dangerous situations?



**Doug Engel**  
G. Carl Huber Professor

Our laboratory currently focuses on three different areas of hematopoiesis. We are investigating how transcription factors GATA2 and GATA3 regulate hematopoietic stem cell function and maintenance, how T cells develop in the thymus, and how specific enzymatic inhibitors inactivate

epigenetic modifying enzymes in erythroid progenitors leading to induced synthesis of fetal hemoglobin as a treatment for sickle cell disease and beta-thalassemia, the world's most common inherited diseases.



**Diane Fingar**  
Associate Professor

We study an evolutionarily conserved cell signaling pathway centered on the protein kinase mTOR (the mechanistic target of rapamycin), which plays a central role in determining the cellular response to the environment (to grow in mass/size; proliferate; differentiate; or die). mTOR constitutes the

catalytic core of functionally distinct signaling complexes and regulates critical cellular process related to metabolism, tumorigenesis, and immune function. Not surprisingly, misregulated mTOR function contributes to diverse diseases including diabetes, cancer, and inflammatory disorders. Despite the clear physiologic importance of mTOR, fundamental gaps exist in our knowledge regarding cellular mTOR regulation and function. Improved understanding of the cellular mTOR signaling network may enable the future development of targeted therapeutic agents to treat human diseases linked to aberrant mTOR function.



**Roman Giger**

**George Linus Streeter Collegiate Professor**

Neurons have to grow and connect (or synapse) properly during development and they have to establish new connections during learning, and following injury (e.g. spinal cord injury, traumatic brain injury, stroke or multiple sclerosis). How is neuronal growth regulated at the cellular level?

How do synapses get established and what regulates the strength of these connections?



**Deborah Gumucio**

**James Douglas Engel Collegiate Professor and Interim Department Chair**

How does the intestine develop in the embryo? How does a soluble signaling protein called hedgehog control both intestinal lengthening and development of the absorptive surface area of the intestine? Additionally, in adults, how does

Hedgehog signaling modify the inflammatory response in the intestine, especially in the setting of inflammatory bowel disease?



**Michael Hortsch**

**Associate Professor**

Modern technologies play an important role in teaching the biomedical sciences to today's students. Our department is at the forefront of developing novel and exciting teaching resources. However, are these new technologies really effective in educating tomorrow's scientists and

health care providers? How can we use these new teaching modalities to help our students both learn better and gain a deeper understanding of the expanding range of scientific knowledge?

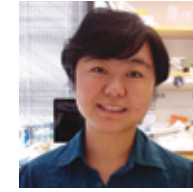


**Ajit Joglekar**

**Assistant Professor**

Cells build multi-protein "machines" that insure that every time the cell divides, its recently duplicated chromosomal DNA gets properly distributed to each daughter cell; cancer results when this machine doesn't function properly. How does this machine work on a physical/chemical

and molecular level? Can we build our own machines to distribute artificial chromosomes to cells for gene therapy?



**Lei Lei**  
Assistant Professor

The mature oocyte has the remarkable ability to both support early embryogenesis and to reprogram terminally differentiated somatic cells to totipotency. What are the key molecular components that determine egg quality and the developmental potential of early embryos?

Another lingering mystery of mammalian oogenesis is continuous germ cell loss. What determines why less than 1% of germ cells develop into mature oocytes, whereas the majority undergoes apoptosis during oogenesis? How do germ cells interact with ovarian somatic cells to maintain the ovarian reserve and normal ovarian function?



**Jiandie Lin**

**Associate Professor, Bradley M. Patten Collegiate Professor in the Life Sciences**

How does the body's network of nutrient and energy control (the metabolome) go awry in the context of type 2 diabetes, cardiovascular disease and non-alcoholic fatty liver disease? Can we develop therapies that prevent or correct the malfunction of this metabolic network?



**Daniel Lucas-Alcaraz**

**Assistant Professor**

The levels of the different cell types in the blood are exquisitely regulated. Blood cells are produced by hematopoietic stem cells in the bone marrow. After hemorrhage, inflammation or injury stem cells proliferate to restore tissue homeostasis. How do stem cells sense the changes in the blood? How

does inflammation regulate hematopoiesis? Can we manipulate these signals to increase blood cell production?

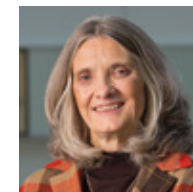


**Kentaro Nabeshima**

**Assistant Professor**

What controls chromosome dynamics during meiosis (cell divisions for generation of eggs and sperms)? How do chromosomes move around in a nucleus in search for their homologous partner? How do they recognize and pair specifically with their partner? Mistakes in any of these steps can

lead to reproductive problems, such as miscarriage and birth defects. We are addressing these fundamental questions by exploiting a simple model organism: the nematode *C. elegans* and by applying a wide variety of techniques including functional genomics, genetics, molecular biology, cell biology and high-resolution 3-D microscopy.



**Sue O'Shea**

**Crosby-Kahn Collegiate Professor**

Human induced pluripotent stem cells (iPSC) and human embryonic stem cells (hESC) can be grown in culture and coaxed to yield a variety of human cell types that are difficult or impossible to study in the human body, including various types of brain cells (neurons). Thus, for the first time,

we can ask fundamental questions such as: what genes are involved in neuronal differentiation? In differentiation of glial cells? Which neurons are damaged in the context of bipolar disease or depression? What is the nature of such alterations?



**Billy Tsai**

**Corydon Ford Collegiate Professor**

DNA tumor viruses such as polyomavirus (which cause cancer) and bacterial cholera toxin (which causes life-threatening diarrhea) have a feature in common: they both use molecular trickery to hijack the host cell machinery to enable their entry and trafficking to specific sites inside the cell.

What features of these proteins allow them to disguise themselves and avoid the quality control mechanisms of the cell? What parts of the cellular machinery participate in this molecular scheme?



**Kristen Verhey**

**A. Kent Christensen Collegiate Professor**

Inside of every cell, motor proteins move diverse cargos over a set of highly connected "railroad tracks" composed of microtubules. How do motors choose their cargos? How do chemical modifications of the microtubules act as biochemical road signs to direct motor protein

transport to specific cellular destinations?



**Lois Weisman**

**Sarah Winans Newman Collegiate Professor in the Life Sciences**

Basic cell biological functions can be readily studied in yeast. Many yeast genes are conserved in humans. For example, Fig4, which is important for lysosomes in yeast, is also critical in humans. Minor mutations in Fig4 can

cause neurodegenerative disease! Yeast can be used to decipher the mechanisms underlying Fig4 function. Understanding Fig4 function may provide insights into how to treat some neurological diseases.

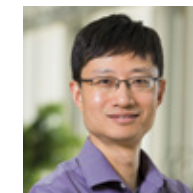


**Yukiko Yamashita**

**Associate Professor, James Playfair McMurrich Collegiate Professor of the Life Sciences**

We are all derived from a single fertilized egg, but our bodies contain hundreds of different types of cells, each of which performs a specific function (a skin cell is not the same as a brain cell). What

processes control asymmetric cell divisions in which one cell can give rise to two daughters with different identities and functions?



**Bing Ye**

**Associate Professor, Burton L. Baker Collegiate Professor of the Life Sciences**

How do neurons in the brain grow their processes (dendrites and axons) to form functional neural circuits and how do defects in this process lead to human diseases (e.g. Down syndrome and autism)?



## CELL AND DEVELOPMENTAL BIOLOGY JOINT FACULTY



### **Richard Altschuler**

**Professor, Otolaryngology**

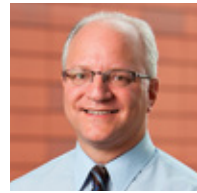
Tinnitus (ringing in the ears) and age-related hearing loss are important medical problems affecting quality of life. What insults are damaging auditory neurons in the context of these diseases? How can we enhance the survival and growth of the nerves that control hearing?



### **Maria Castro**

**Professor, Neurosurgery**

The microenvironment of brain tumors affects tumor progression and metastasis. How do tumor cells signal to immune cells and cause them to invade the tumor microenvironment? What signals do immune cells provide that modulate tumor cell behavior? How can these signals be used therapeutically to inhibit tumor growth?



### **William Dauer**

**Professor, Neurology**

Diseases such as Parkinson's disease and dystonia disrupt motor function and cause uncontrolled movements. What single gene mutations cause these diseases and how do the mutations affect neuronal circuits? Which particular neuronal circuits are damaged in these

diseases and how might we diagnose and treat such damage more readily?



### **Andrzej Dlugosz**

**Professor, Dermatology**

How do alterations in the Hedgehog signaling pathway contribute to cancer initiation, progression, and maintenance in organs such as skin or stomach? Could targeting the hedgehog pathway, and/or interacting pathways, provide a useful approach for the treatment of certain types of cancer?



### **Xing Fan**

**Associate Professor, Neurosurgery**

Malignant brain tumors are thought to be maintained by "cancer stem cells." Can we develop novel therapies for malignant brain tumors based on depletion of these important progenitor cells?



### **Philip Gage**

**Associate Professor, Ophthalmology & Visual Sciences**

What molecular mechanisms and developmental signals control normal mammalian eye development? Which of these is misregulated in the context of eye diseases that result in blindness and how might we design molecular therapies to correct these abnormalities?



### **Gary Hammer**

**Millie Schembechler Professor of Adrenal Cancer, Molecular & Integrative Physiology/ Internal Medicine (MEND)**

Understanding the signaling and gene regulatory networks that dictate development and homeostasis of the adrenal gland is the focus of our work. Lineage and differentiation of adrenocortical stem cells in health and disease (adrenal aplasia, hypoplasia, hyperplasia and cancer). Basic translational and clinical research (genomic/genetic, molecular, cellular, developmental, cancer, mouse models, human/patient samples and database clinical trials).



### **Peter Hitchcock**

**Professor, Ophthalmology and Visual Sciences**

Research in my laboratory seeks to identify the cellular and molecular mechanisms that control neurogenesis in the central nervous system. We study neurogenesis in two contexts, during embryonic development and, in adults, during regeneration induced by an injury. We use the retina as the model brain tissue and employ a small freshwater fish, zebrafish, as the animal model. Our broad goal is to understand the molecular mechanisms that regulate regenerative neurogenesis. This work relates directly to understanding injuries to the human central nervous system and gaining insights into therapeutic approaches envisioned for treating these injuries.



### **Patrick Hu**

**Associate Professor, Internal Medicine/ Institute of Gerontology**

In the roundworm *C. elegans*, a conserved insulin-like signaling pathway controls development, metabolism, and life span. How is this pathway regulated, and by what means does it influence longevity? Can insights into the regulation and function of this pathway in *C. elegans* improve our understanding of the molecular basis for aging and aging-related diseases in humans?



### **Cheng-Yu Lee**

**Assistant Professor, Internal Medicine/Life Sciences Institute**

Stem cells in the fruit fly brain divide to produce a steady stream of additional stem cells while simultaneously producing hundreds of differentiated daughter neurons. What genes control this balance between stem cells and differentiating cells? Which of these genes have orthologs that function in mammalian brain development? Misregulation of such genes may cause birth defects or brain cancer.



### **Qing Li**

**Assistant Professor, Internal Medicine**

We work on the signaling of leukemic stem cells (LSC) with the goal of developing novel therapies to target LSCs. We use mouse models and human leukemia samples to identify the intrinsic and extrinsic mechanisms by which oncogenes and tumor suppressor genes transform normal hematopoietic stem cells and progenitors into LSCs. We are developing and testing novel targeted therapies in these models to eliminate LSCs.



### **Pedro Lowenstein**

**Professor, Neurosurgery**

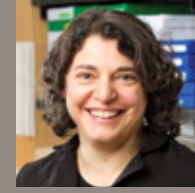
What is the molecular and cellular basis of malignant brain tumor invasion and growth? What are the essential mechanisms used by tumor cells to grow and to destroy normal brain tissue, thus killing the host? What are the first steps in the invasive process? Knowing this information, can we inhibit tumor growth?



### **Ivan Maillard**

**Associate Professor, Internal Medicine/Life Sciences Institute**

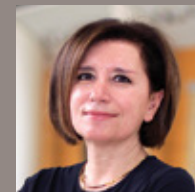
After a stem cell or bone marrow transplant, the implanted cells can attack the host in a reaction called graft vs. host disease. How does this reaction initiate? What signaling pathways are involved? Can the underlying mechanisms of this reaction reveal new strategies to prevent graft vs. host disease?



### **Marina Pasca di Magliano**

**Associate Professor, General Surgery**

Pancreatic cancer is one of the most lethal human malignancies; we know that pancreatic cancers often show activation of embryonic signaling molecules like hedgehog. What direct role does Hedgehog signaling play in pancreatic cancer initiation and progression and how can we use this information to design better therapeutic weapons against pancreatic cancer?



### **Ernestina Schipani**

**Professor, Orthopaedic Surgery; Professor, Internal Medicine**

Dr. Ernestina Schipani's laboratory has a long-standing interest in the study of bone development. Over the years, her laboratory has used cartilage and bone tissues as models to establish important principles in the broader fields of receptor and hypoxia biology.



### **Jason Spence**

**Assistant Professor, Internal Medicine**

Human pluripotent stem cells, grown in a culture dish, can allow study of human development and disease. Organoid-like structures grown from such cells recapitulate several tissues, including colon, small intestine, esophagus and lung. Using these, we can ask: How do organs assemble into functional units? What are the genes and signaling programs necessary to form proper organs and which of these are functioning improperly in disease?



### **Deneen Wellik**

**Associate Professor, Internal Medicine**

Hox genes encode a large family of DNA binding proteins that function in the development of multiple organs. These genes are expressed in mesenchymal stem and precursor cells and instruct the development, maintenance and repair of organs and tissues. The laboratory investigates the mechanisms by which these genes function.



### **Sunny Wong**

**Assistant Professor, Dermatology**

My lab's general interests involve understanding how hair follicles develop and how basal cell carcinoma arises in the skin. In terms of development, we are specifically focused on the biology of the hair follicle infundibulum, a poorly characterized domain that constitutes the hair follicle opening, or the pores visible on the surface of the skin. We are interested in the cellular events that generate this opening, the genes that maintain its normal function, as well as events associated with hair canal disruption, as occurs in acne patients. In terms of basal cell carcinoma, we are interested in studying the stem cells in the skin which give rise to these tumors, as well as their interactions with neighboring stromal cells. We are also currently investigating how these tumors regress in response to therapy, as well as how they potentially develop drug resistance.

## Research Faculty

Shuaiying Cui, Ph.D., Research Investigator  
Tomonori Hosoya, Ph.D., Research Assistant Professor  
Takamasa Inoue, Ph.D., Research Investigator  
Shiyong Jin, Ph.D., Research Investigator  
Kim-Chew Lim, Ph.D., Associate Research Scientist  
Kentaro Nabeshima, Ph.D., Research Assistant Professor  
Yu-Chi Shen, Ph.D., Assistant Research Scientist  
Katherine D. Walton, Ph.D., Research Investigator  
Xiaofeng Zhao, Ph.D., Research Investigator

## Supplemental Appointments

Allan R. Beaudoin, Ph.D., Professor Emeritus  
Susan S. Brown, Ph.D., Professor Emerita  
William E. Burkel, Ph.D., Professor Emeritus  
Bruce M. Carlson, Ph.D., Professor Emeritus  
Walter A. Castelli, D.D.S., Professor Emeritus  
Albert Kent Christensen, Ph.D., Professor Emeritus  
Peter Coyle, Ph.D., Professor Emeritus  
Stephen A. Ernst, Ph.D., Professor Emeritus  
Theodore V. Fischer, Ph.D., Associate Professor Emeritus  
Roy A. Glover, Ph.D., Associate Professor Emeritus  
Donald F. Huelke, Ph.D., Professor Emeritus  
Pentti T. Jokelainen, Ph.D., Associate Professor Emeritus  
Sun-Kee Kim, Ph.D., Associate Professor Emeritus  
John H. Lillie, Ph.D., Professor Emeritus  
Margaret I. Lomax, Ph.D., Research Professor Emerita  
Sarah Winans Newman, Ph.D., Professor Emerita  
Muriel D.K. Ross, Ph.D., Professor Emerita  
Donald S. Strachan, Ph.D., Professor Emeritus  
Osamu Tanabe, M.D., Ph.D., Adjunct Research Assistant Professor  
John Matthew Velkey, Ph.D., Adjunct Lecturer  
Masayuki Yamamoto, M.D., Ph.D., Adjunct Professor



## FACULTY HONORS & AWARDS



Sue O'Shea

Congratulations to Sue O'Shea, a 2014 EBS Teaching Award Recipient. O'Shea was recognized for her consistently outstanding work in Medical Embryology, which she has been teaching for over a decade. Numerous shifts in the Medical School curriculum have meant that O'Shea has had to totally revise the course format and rearrange the content many times over the years, most recently introducing flipped classroom and case studies into a previously lecture-driven course. Students uniformly praise the course (and O'Shea), noting that it plays a central and critical role in their medical education.

The League of Research Excellence was established in 2011 to recognize faculty who have made significant contributions to the Medical School's research enterprise. Membership in the League is testimony to the quality of the inductees' research and scholarship, and is a reflection of the high regard we have for their service to the Medical School's research mission. Congratulations to those faculty members inducted this year into the League of Research Excellence, including Kristen Verhey, Andrzej Dlugosz, Peter Hitchcock and Ivan Maillard.



Kristen Verhey



Andrzej Dlugosz



Peter Hitchcock



Ivan P. Maillard

## SOCIETY FOR DEVELOPMENTAL BIOLOGY MEETING October 18–20, 2015

The 2015 Midwest Regional Society for Developmental Biology meeting was held October 18–20, 2015 at the University of Michigan in the Michigan League conference facility. Department of Cell and Developmental Biology students, postdocs and PIs networked and learned about the exciting research being performed in a wide range of organisms and a wide range of topics of interest to developmental biologists. Many took advantage of this unique gathering to interact with other developmental and regenerative medicine biologists from across the Midwest.

### Alex Holtz

Medical Science Training Program Fellow (2009–2017)

### Putting the Pieces Together



Alex Holtz

While growing up in Fairfield, CT, Alex Holtz became interested in science and research through a great biology teacher in high school. When he attended Cornell University, he continued to follow this path and earned a bachelor's degree in biochemistry. After graduation, he spent a year as a fellow at the National Institutes of Health. When Alex heard about the option to pursue a dual M.D.-Ph.D. degree, he was intrigued by the possibilities. He applied to the Medical Science Training Program (MSTP) at U-M, a program where students earn their doctor of medicine and doctor of philosophy degrees concurrently (typically in eight years). The MSTP is designed primarily for students who are interested in a future career in academic medicine with a focus in research related to medicine.

While some MSTP fellows enter the program with a firm idea of their research interests, Alex was open to exploring his options for fields of specialization. "What I love about this program is that I am able to explore all of my options: academia, research, teaching and clinical care," he explains. Fellows are encouraged to talk to investigators at U-M whose work is of interest. Laboratory rotations after the first and second years of medical school provide guidance in the selection of a thesis mentor and Ph.D. program.

After finishing his first two years of pre-clinical work in the medical school, Alex decided to pursue his Ph.D. in the Department of Cell and Developmental Biology. He worked in the lab of Ben Allen where he studied cell surface regulation of Sonic Hedgehog signaling, focusing on the interaction of pathway antagonists in mouse neural tube development. He

graduated from CDB in Spring 2015 and is currently doing clinical rotations as he finishes his last two years of medical school.

Since jumping back into medicine after focusing on research for several years, Alex has had to get up to speed on what he learned during his first two years of medical school. But he is also finding that his rigorous research training is giving him many advantages in medical school. "Through my Ph.D. program, I had to learn how to clearly and effectively explain and present my research. In medicine, communication is huge. You need to be able to communicate well with many audiences: patients and families from different backgrounds, your colleagues and hospital staff. My experience in research also reminds me to keep a broad differential when approaching patients so I don't jump to a diagnosis too quickly. I think about the data, come up with alternative hypotheses and then put all of the pieces together to come up with a plan. This is a huge asset during clinical rotations."

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Given the pressing need for medical scholars who are well trained in research, there are many opportunities for physician-scientists, like Alex, to teach and conduct research not only in medical schools but also in foundations, government and private industry. He hopes to continue in academia after finishing medical school, but has not settled on an area, yet. He is still exploring all of the fields of specialization.



## H. Lynn Kee

Visiting Assistant Professor of Biology, Stetson University

### Opening Doors to Biology



H. Lynn Kee

Throughout her life, H. Lynn Kee has been inspired by great science teachers and mentors, and is now sharing her passion and knowledge about biology and research with students. As a high school student in Malaysia, she was exposed to hands-on lab experiences that initially introduced her to the field. This inspired her to come to U-M to pursue a

B.S. in Cell and Molecular

Biology where she took part in the Undergraduate Research Opportunity Program and worked with U-M scientists conducting research at the Kellogg Eye Center and at the U-M Medical School. This exposure led her to pursue her doctorate in Cell and Developmental Biology where she worked with mentor Kristen Verhey until graduating in 2012 with expertise in intracellular trafficking, cell signaling and microscopy.

Since graduation, Kee has been teaching courses including Cancer Biology, Cell and Molecular Biology, and Molecular Genetics at Vassar College, the University of Richmond and the Broad Institute of MIT and Harvard. She is currently a visiting assistant professor of biology at Stetson University.

Kee has been developing inquiry-based laboratory coursework for undergraduates that actively engages students in current biomedical investigations. In addition, she has also been developing tools that integrate digital media and biology to enhance students' scientific communication skills.

"I'm really enjoying the opportunity to gain more teaching experience. I love being able to develop my own curriculum from the ground up. To try new and different things," she explains. At Richmond, Kee brought digital

media into the classroom by having students create whiteboard animations that explained how new cancer drugs worked. For another class, the lab investigative project involved creating a lab video report where students found effective ways to communicate their ideas and experiments visually — to view communication

as an important skill for scientists and researchers. "The experience and skills I gained at U-M have been critical to developing innovative curricula. You need to be able to think on your feet, to design and troubleshoot labs. I also still receive support and feedback from my mentor and other faculty at Michigan," she adds.

This past summer Kee had the opportunity to teach a genomics course for the Minority Introduction to Engineering and Science (MITES) program at MIT, a rigorous six-week residential academic enrichment program for promising high school seniors — many of whom come from underrepresented or underserved communities — who have a strong academic record and are interested in studying and exploring careers in science and engineering.

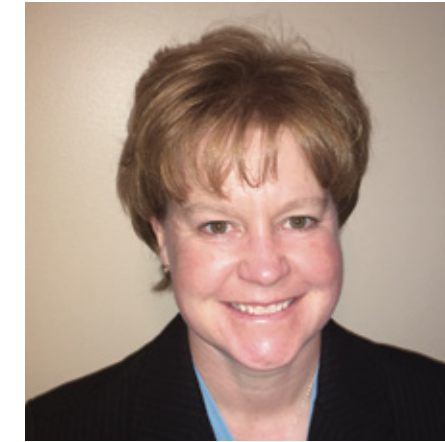
"It was a hands-on lab course. Many of these kids had never been exposed to this kind of lab experience," she explains. "It was rewarding to see them discover new possibilities for themselves. One of the students even said that it had 'changed her life.' She is now considering careers in biomedical science. It was great to be able to open that door for her and the other students, to open their eyes to a whole new world."

**The experience and skills I gained at U-M have been critical to developing innovative curriculum. You need to be able to think on your feet, to design and troubleshoot labs. I also still receive support and feedback from my mentor and other faculty at Michigan.**

## Nicole Slawny

Medical Science Liaison at Luitpold Pharmaceuticals

### Think Outside the Lab



Nicole Slawny

While at the Department of Cell & Developmental Biology, Nicole Slawny worked with mentor Sue O'Shea investigating using embryonic stem cells as a model system to study embryo development. After receiving her Ph.D. in 2010, Slawny remained at U-M as a Postdoctoral Research Fellow in the lab of Gary Smith in the Department of Obstetrics and Gynecology researching, designing and executing novel research projects focused on the role of the Tribbles family of proteins during mammalian oocyte maturation.

In 2012, she decided to explore her career options and ended up landing an industry position as the Applications Director with a U-M startup called 3D Biomatrix, a company that develops a line of 3D cell culture disposables. "A lot of the research I did at U-M had to do with 3D tissue culture models. This company was marketing 3D tissue culture tools. With my scientific background, I could clearly communicate the value of these tools to researchers. I could also help our clients troubleshoot when something was not working in the lab because I understood exactly what they were doing," she explains. Slawny's science knowledge became a real asset

in helping them grow the business. "Because it was a startup, I had both a lot of freedom and a lot of responsibility. This allowed me to gain experience in business development, customer support and new product design. I even created and developed educational webinars to build trust and be used as a key resource for clients trying to establish a 3D culture model in their research program," she adds.

Just this past July, Slawny moved to Chicago, IL, to take her skills to the next level as a Medical Science Liaison with a larger company, Luitpold Pharmaceuticals. In this new role, she talks with healthcare providers about clinical trial opportunities using the company's intravenous iron product. "In addition to educating providers about the possibilities, I'm also learning about their needs and finding out how they would actually use a product like this," she explains. Since it's only been a few months and she is just recently completed her training, Slawny is still in the process of getting settled into her position. She hopes to incorporate some of the elements she established at 3D Biomatrix — such as education webinars — once she is more established.

When asked what advice she would give current CDB students and graduates considering working in industry. She added, "Don't be afraid to go out and meet new people and network. Talk to people, ask them about their work. I put myself out there. That's how I got into a job at 3D Biomatrix that allowed me to learn and grow and start a professional path that I'm really excited about. I never would have discovered how much I enjoy this unless I allowed myself to 'think outside the lab.'"

## ALUMNI

Cell & Developmental Biology alumni are leading the way as teachers, scientists, doctors. Through formal collaboration or informal knowledge sharing our community continues to help each other innovate. However, the group of alumni is only as vibrant as the people who participate, so regardless of where you live or whether you are working in an entirely different field, we encourage you to stay involved! Here are just a few ways to stay connected:

### Send us an Alumni Update

Let us know what you are up to now. Fill out our online alumni update form or send us a message to [cdb-alumni-update@umich.edu](mailto:cdb-alumni-update@umich.edu). We would love to hear what you have been doing since your time in CDB.

### Online Social Networks

Do you use social media? Find us on Twitter, Facebook and LinkedIn.

### Host a Regional Event

Are you interested in hosting an event for fellow alumni in your area? Contact Greg Witbeck at [germaine@med.umich.edu](mailto:germaine@med.umich.edu) or 734-232-6017 to discuss opportunities.

### Scholarship Support

You can make a difference in the lives of today's students. Find out how at [cdb.med.umich.edu/giving](http://cdb.med.umich.edu/giving)



## GRADUATE STUDENT AWARDS



**Martha Echevarria Andino**  
(Allen Lab)  
NSF GRFP Fellowship; Rackham Pre-Candidate Graduate Student Research Award; 2015-2016 Bradley Merrill Patten Fellowship



**Alex Holtz**  
(Allen Lab)  
Defended his Ph.D. Thesis; Rackham Conference Travel Grant



**Justine Pinskey**  
(Allen Lab)  
2015 PIBS Graduate Student Award for Excellence in Teaching and Service; Rackham Conference Travel Grant; Predoctoral Fellowship Award from the Center for Organogenesis; Sarah Winans Newman Graduate Student Service and Teaching Award; NIH Predoctoral NRSA Fellowship



**Ariell Joiner**  
(Allen Lab)  
Defended her Ph.D. Thesis; NIH Predoctoral NRSA Fellowship; ASPET Graduate Student Travel Award; AChemS Travel Fellowship for Diversity; Rackham Conference Travel Grant; Rackham Candidate Graduate Student Research Award



**Brandon Carpenter**  
(Allen Lab)  
Defended his Ph.D. Thesis; Rackham Graduate Student Research Award; Endowment for the Basic Sciences EDGE Award; NIH Teaching Postdoctoral Fellowship at Emory University starting in 2016



**Katarina Fabre**  
(Allen Lab)  
Received her Master of Science Degree in Cancer Chemical Biology



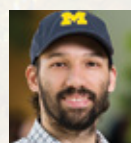
**Ye Li**  
(Cai Lab)  
2014–2015 Bradley Merrill Patten Fellowship



**Flor Mendez**  
(Castro Lab)  
2014–2015 Bradley Merrill Patten Fellowship



**Corinne Weisheit**  
(Dauer Lab)  
Defended her Ph.D. Thesis



**Jorge Martinez-Marquez**  
(Duncan Lab)  
NIH Predoctoral NRSA fellowship



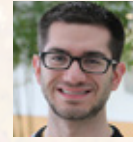
**Katie Baldwin**  
(Giger Lab)  
Defended her Ph.D. Thesis



**Ryan Passino**  
(Giger Lab)  
2015–2016 Bradley Merrill Patten Fellowship



**Titan Shih**  
(Hu Lab)  
2015–2016 Bradley Merrill Patten Fellowship



**Andrew Freddo**  
(Gumucio Lab)  
Travel Award to attend EMBO Workshop; NIH Predoctoral NRSA fellowship



**Pavi Aravamudhan**  
(Joglekar Lab)  
Defended her Ph.D. Thesis; 2015 PIBS Graduate Student Award for Excellence in Research; ASCB Kaluza Prize for Outstanding Research by a Graduate Student; Bradley Merrill Patten Award for Excellence in Graduate Research



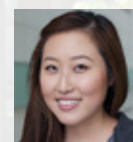
**Emily Bowers**  
(Lucas Lab)  
Predoctoral Fellowship Award from the Center for Organogenesis; 2014–2015 Bradley Merrill Patten Fellowship



**Jianrui Song**  
(Mortensen Lab)  
2014–2015 Bradley Merrill Patten Fellowship



**Brianna Dye**  
(Spence Lab)  
2015 PIBS Graduate Student Award for Excellence in Research



**Jane Song**  
(Wellik Lab)  
Warner-Lambert Fellowship



**Noah Steinfeld**  
(Weisman Lab)  
Bernard Maas Fellowship



**Michael Lang**  
(Weisman Lab)  
MAAS Professional Development Fellowship



**Shelby Peterson**  
(Wong Lab)  
NIH Predoctoral NRSA fellowship



**Hao Liu**  
(Ye Lab)  
2015–2016 Bradley Merrill Patten Fellowship

## POSTDOCTORAL AWARDS



**Choya Yoon**  
(Giger Lab)  
Wings-for-life Postdoctoral fellowship



**Sha Wang**  
(Gumucio Lab)  
Best poster award at the Gi FASEB conference



**Daisuke Takao**  
(Verhey Lab)  
Bradley Merrill Patten Award for Excellence in Postdoctoral Research

## STAFF AWARDS



**Lori Longeway**  
UMHS Shining Star award





**47%**  
STUDENTS FUNDED  
THROUGH  
FELLOWSHIPS

Kristen Verhey and students in CDB 530

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We appreciate the generosity from all of those who contributed this past year. Our students, programs and research have benefited because of your thoughtful donations. Gifts large and small can make a huge impact.

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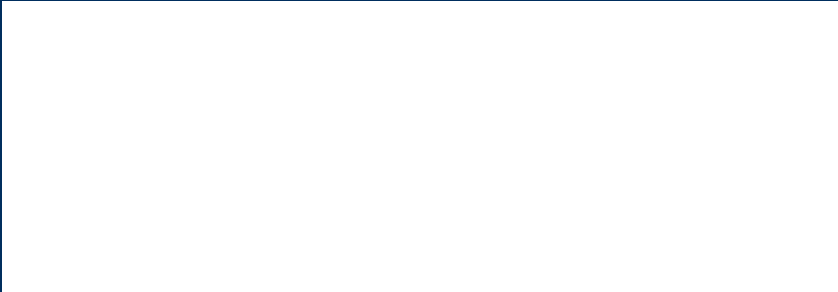
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