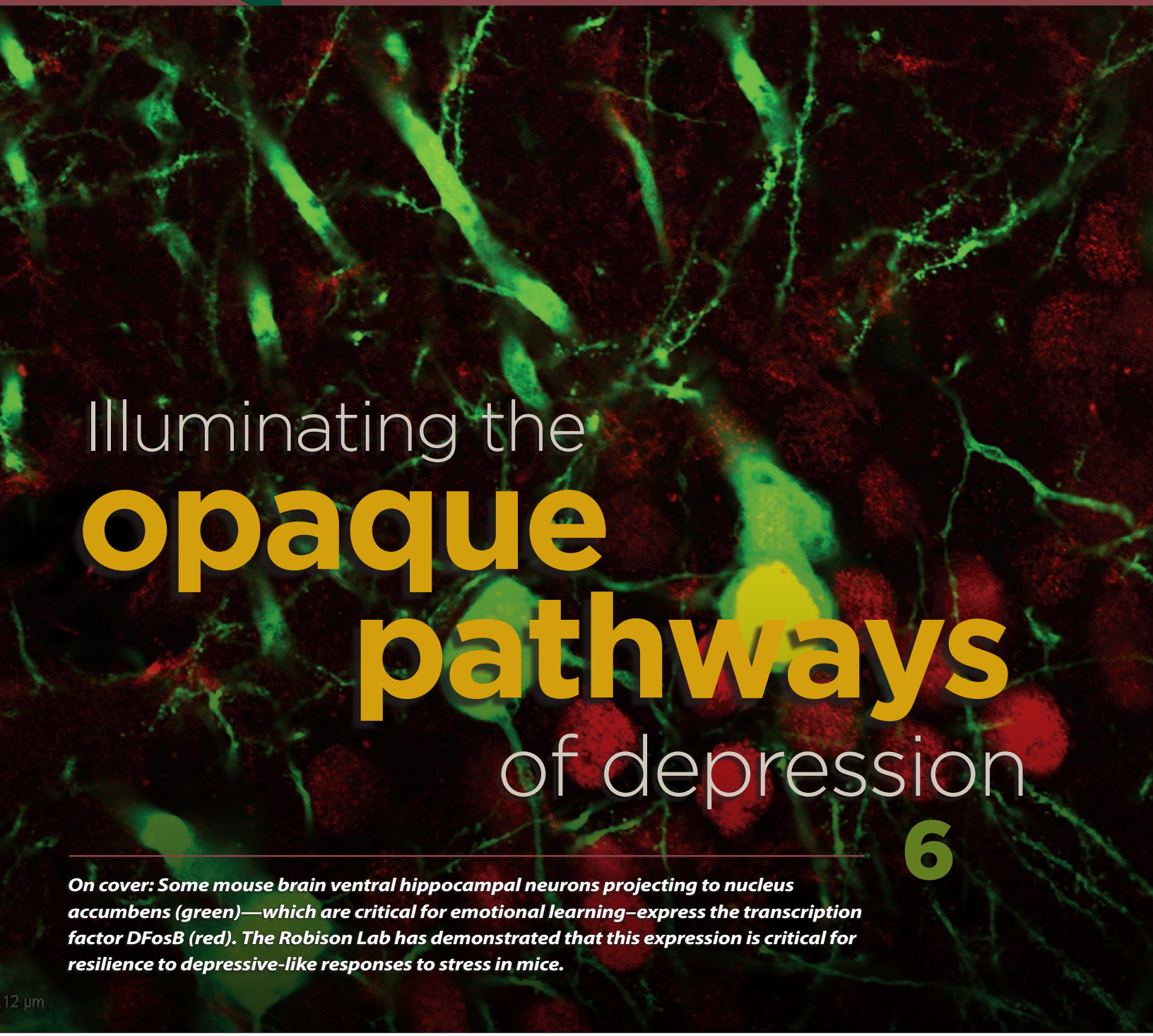
DEPARTMENT OF
Physiology
SUMMER 2021
MSU College of Natural Science | *Newsletter for Alumni and Friends*



Illuminating the opaque pathways of depression

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On cover: Some mouse brain ventral hippocampal neurons projecting to nucleus accumbens (green)—which are critical for emotional learning–express the transcription factor DFosB (red). The Robison Lab has demonstrated that this expression is critical for resilience to depressive-like responses to stress in mice.

INSIDE

From the Department Chair...

Hello fellow Spartans! The COVID-19 pandemic has been a challenge for us all, but it reinforces the importance of science and scientific discovery.

Over the past 15 months, we have all experienced unanticipated changes in our lives. I hope that our family and friends have managed to stay healthy despite the many challenges that the pandemic has posed. I am proud of our students, staff and faculty for their resilience as well as adapting to unique and unpredictable changes in our education and research efforts.

With the rolling out of the vaccine, we anticipate this fall will be a chance for us to come back together within our Spartan community. On the bright side, most of our labs reopened during the summer/fall, and science keeps marching forward. We have also learned many positive aspects of virtual teaching and learning that will further strengthen our education endeavors in the future.

"The COVID-19 pandemic has been a challenge for us all, but it reinforces the importance of science and scientific discovery."

In this issue, we highlight the research of one of our newest faculty members, Geoffroy Laumet. Additional features include the impactful research by A.J. Robison, Bruce Uhal, Laura McCabe and Eran Andrechek. A major strength of our department is the broad diversity of research programs that can promote unique and highly productive collaborative efforts.

The makeup of our department is always changing, and this year we'd like to thank multiple retirees. After joining the MSU faculty in 1995, Richard Miksicek continued his research career in endocrinology. More recently, he served as the undergraduate director (2007-2018) and played a critical role in the Shared Discovery Curriculum in the College of Human Medicine (CHM). Adele Denison joined the MSU faculty in 1988 and has been a key professor developing and teaching two of our largest enrollment physiology courses since 2001. Over the years, Adele has been the face of physiology for tens of thousands of undergraduates in multiple pre-health majors. Bill Wonderlin joined the faculty in 2013 and retired in summer 2020; he played an important role in our physiology education at the Grand Rapids campus of CHM. After 26 years on campus, my right-hand person in the main office, Elvira Martinez-Jones, retired in January 2021. We are very thankful for these numerous contributions to the multiple missions of the department and wish these individuals the best for the future.

Given the uncertain funding climate for science, we hope that our alumni and friends will remain actively committed to physiology. Our department priorities remain the same: training graduate and undergraduate students in cutting-edge research laboratories, and recruiting and retaining outstanding faculty members. Maintaining research excellence requires the efforts of talented undergraduate students, graduate students and postdoctoral fellows. We continue to seek endowments to establish research and travel funds targeted to our students and would like to establish named chair positions for outstanding faculty that allow recognition and flexibility for higher-risk research that may lead to creative discoveries within biomedical sciences.

Our alumni are important to us, and we want to hear from you. I encourage all of our alumni and friends to keep in touch by visiting our website (physiology.natsci.msu.edu). Any questions can be directed to me.

I wish you all a safe and healthy 2021. GO GREEN!

C. Lee Cox, Ph.D., Chair
Department of Physiology
pslchair@msu.edu

ALUMNI CLASS NOTES

David Newhouse, physiology, '70, who received his MBA in 2018, recently retired after 38 years as a physician. He is now consulting on how to use analytics and root cause analysis to reduce health care inequity.

Daniel Harvey, M.D., physiology, '79, chief of family medicine at Torrance Memorial Medical Center in California, has been a coronavirus frontline responder in hospitals and nursing facilities. He discovered a formula of azithromycin, steroids and zinc that helped 90 COVID patients recover. He continues to teach at UCLA family medicine, and looks forward to resuming his medical work in Mexico at the migrant farm camp in San Telmo, and with the La Caravana refugees/Haitian refugees in Tijuana through his church.

Christopher Tracy, M.D., F.A.C.P., F.A.C.R., physiology, '98, was awarded the Legion of Merit by the Department of Defense in recognition of his significant career contributions to U.S. Army Medicine as part of his retirement recognition in December 2020. He has transitioned to civilian practice in Pinehurst, N.C., where he works as a clinical rheumatologist.

Roger Racine, physiology, '99, has been employed as an infectious disease epidemiologist for the State of Michigan since 2004. He has served as president of the Michigan Public Health Association for the past two years.

Ben Collins-Hamel, D.O., physiology, '07, received a degree from MSU's College of Osteopathic Medicine, joined the faculty at the internal medicine residency program where he trained (Ascension Macomb-Oakland Hospital, Warren Campus) and advanced to associate director of the internal medicine residency program at MSU.

Irving Salinas, M.S., physiology, '19, was accepted to the University of Texas Rio Grande Valley Master in Physician Assistant Studies Class of 2023. He will start the program in fall 2021. He recently published a first-author review article—"Androgen-induced Epigenetic Modulations in the Ovary"—with MSU master's thesis PI Aritro Sen.

Kayley Irwin, physiology, '20, was accepted to Ohio State University for medical school and will start pursuing her M.D. in the fall.

In Memoriam

Tai

Mei-Hui Tai, professor in the College of Osteopathic Medicine, died February 18, 2020. She was 55. Tai developed a passion for the sciences during her childhood in Pintong, Taiwan, and received her Ph.D. in physiology from National Taiwan University. Her research focused on the isolation of human pancreatic stem cells with the aim of further characterizing components of the genetic networks that regulate pancreatic development. She taught several courses, including pathophysiology and hematology, and was a much-loved teacher and well-respected colleague.

Departures

Hampton

Patricia Hampton, research administrator II, departed in March 2020 after being elected vice president of the MSU Administrative Professional Association (APA). During 37 years of service at MSU, she has gained extensive experience in management, grants and customer service and has built long-term relationships that have assisted her in her new role as a passionate advocate for the MSU-APA.

Ogrodzinski

Yvonne Ogrodzinski, instructional equipment and supplies technician for the Wehrwein and Zubek labs, is leaving the department in July to pursue her M.D. at the University of Toledo College of Medicine and Life Sciences.

New Faculty and Staff

Bennett

Spitzley

Jessica Bennett and **Jessica Spitzley** both joined MSU in October 2019 as full-time facility coordinators in the newly finished PSL and MMG Facilities Center located in the Biomedical Physical Sciences Building at MSU. Their responsibilities include shipping and receiving, health and safety, managing access and security, and capital asset management. Bennett and Spitzley successfully supported faculty and maintained the two biomedical units throughout the pandemic. Before managing the center, Bennett was a research assistant in PSL and MMG for 19 years, and Spitzley was assistant director for Rainbow Child Care Center in Howell, Mich.

Eynon

John Eynon, research administrator, joined the department in April 2020. He provides administrative support, including monitoring financial transactions and fielding questions from faculty regarding research grants. Before joining MSU, Eynon managed two federal grants for a statewide nonprofit organization in Michigan.

La

Becky La joined the department in June 2020 as the neuroscience undergraduate advisor. She advises more than 800 students on scheduling, career goals, campus resources, and personal and academic well-being. Before joining as a full-time staff member, La completed her M.A. in student affairs administration at MSU in 2020 and was an assistant resident director at the University of California, Los Angeles, from 2016-2018.

Williams

Erika Williams joined CHM as a fixed-term assistant professor in January 2020. She will be involved in the planning and teaching of early and middle clinical student sessions, including whole-class, large-group activities; integrative biomedical labs; weekly small-group problem-based learning activities; and several intersession courses. Williams received her Ph.D. in physiology and biophysics at the University of Mississippi Medical Center in 2019.

Retirements

Denison

Adele Denison, associate professor, will retire in August. During a total of 24 years at MSU, Denison taught more than 16,000 students and received a teaching award from medical students as well as two NatSci teaching awards. She taught both Introductory Physiology and Physiology for Pre-health Professionals, a course she created, which has grown to an enrollment of 500 students in both fall and spring semesters.

Martinez-Jones

Elvira Martinez-Jones, administrative assistant to the chair, retired in December 2020 after 26 years of service. Before joining physiology in 2013, she was assistant to two MSU presidents. As part of an admissions team, Martinez-Jones was awarded the University Minority Award for work with minority students on campus, including translation, scholarship opportunities and assistance with MSU's Día de la Familia. In 2019, she received NatSci's prestigious Support Staff Award for her extraordinary commitment to and excellence in administration.

Miksicek

Richard Miksicek, associate professor, retired in May 2021 after 25 years of research and teaching in CHM. Recruited to MSU in 1995 as part of the Great Lakes Cancer Initiative, his research focused on the molecular biology of steroid hormone action and its role in mammary gland development and breast cancer. Miksicek was director of the Undergraduate Physiology Program from 2010-2018 and was recently recognized with the 2021 CHM Outstanding Curriculum Contribution Award.

Wonderlin

Bill Wonderlin, fixed-term associate professor, retired from the department in June 2020 after six years of teaching cellular and systems physiology in CHM. Wonderlin was the inaugural director of the Early Clinical Experience in the Shared Discovery Curriculum that launched in 2016, and received two distinguished teaching awards during his career. He continues to develop software for teaching physiology.

Faculty Honors

McCabe

Laura McCabe, who explores the mechanisms regulating bone cell differentiation and formation for osteoporosis prevention and treatment, was named an MSU Foundation Professor. She holds several patents related to the treatment of osteoporosis, and her internationally recognized research program has been continuously funded for more than two decades through external funding agencies including NIH, NSF and DoD.

Mazei-Robison

Michelle Mazei-Robison, associate professor, received a 2019 American Society for Pharmacology and Experimental Therapeutics Neuropharmacology Early Career Award. She investigates the molecular mechanisms underlying changes in VTA dopamine neuron signaling, morphology and activity induced in neuropsychiatric disorders.

Wehrwein

Erica Wehrwein, associate professor, received the 2021 MSU Donald F. Koch Quality in Undergraduate Teaching Award for her commitment to quality undergraduate education. She is a model educator who significantly strengthens MSU's mission through her exemplary teaching and major contributions to curricular reform in physiology education as well as graduate and medical education.

Staff Honors

O'Reilly

Pavangadkar

Martinez-Jones

Seischab

Sandra O'Reilly received a Support Staff Award at the 2020 NatSci Annual Awards for her exceptional support of the department in contributing to its ongoing effectiveness in advancing teaching and research.

Kanchan Pavangadkar received the 2020 MSU Outstanding Established Advisor Award for her ability to work proactively and effectively in connecting students to success through her advising.

Elvira Martinez-Jones received a NatSci Support Staff Award at the 2019 NatSci Annual Awards ceremony for her long-term service to the department. Her work supports faculty as individuals worthy of respect, and advances MSU's core value that people matter.

Lori Seischab received the 2019 NatSci Undergraduate Academic Advisor Award in recognition of her contributions and expertise in advising undergraduate students in the college.

Student Honors

Zayn Al-Zahid, a graduate student in the Leinninger Lab, received a NatSci Excellence-in-Teaching Citation at the 2020 NatSci Annual Awards ceremony.

Isabella Green, a senior majoring in neuroscience and anthropology, won a 2021 Fulbright Scholarship. The Fulbright Program provides grants for individually designed study/research projects. Students meet, work, live with and learn from the people of their host country sharing daily experiences.

Ayo Ifaturoti, a junior Drew Science Scholar, is among five MSU students to receive a 2021 Dr. Martin Luther King, Jr. Scholarship from the MSU Office for Inclusion and Intercultural Initiatives.

Brent Strong, an Honors College 2020 graduate, was named MSU's 20th Marshall Scholar. He plans to pursue an M.Sc. in statistics at the University of Glasgow his first year and an M.Sc. in population health sciences at the University of Edinburgh during his second.

Meenakshi Sudhakaran, a doctoral candidate in Andrea Doseff's lab, received a 2021 Keystone eSymposia Scholarship and attended the April Keystone conference on "Innate Immunity: Mechanisms and Modulation." Accepted into the MSU Plant Biotechnology for Health and Sustainability Training Program, she receives fellowship support from NIH.

Nguyen Truong, a doctoral candidate in the Olson Lab, received a 2020 MSU Excellence-in-Teaching Citation.

Jennifer Watts, a doctoral candidate in the Amy Ralston lab, was inducted into the National Edward Alexander Bouchet Graduate Honor Society in April 2021; she also received first prize in the Oral Presentation Award category at the 2019 Alliance of Graduate Education and Professoriate Student Success Conference at MSU.

Illuminating the opaque pathways of depression

Depression is a dark horse.

The disease often goes unnoticed, but affects work performance, social interaction and the ability to take pleasure in everyday life. According to the National Center for Biotechnology Information, antidepressants help only around 50 percent of those struggling with depression and anxiety, and even when they are effective, scientists have yet to understand how they work in the brain.

But groundbreaking research in the lab of geneticist A.J. Robison, associate professor, has directed new rays of light onto the molecular, cellular and circuit-level mechanisms underlying depression-like diseases.

"We performed the first ever CRISPR-based gene editing in a single circuit between two areas of the mouse brain," explained Robison about the culmination of five years of research funded by the National Institutes of Mental Health. "We can reach into the mouse brain and manipulate specific genes in a circuit involved in depression and anxiety-like behaviors, a critical advance on the road to genetic medicine for psychiatric diseases."

A.J. Robison (pictured above) and members of his lab use a combination of transgenic mice, viral gene transfer and fluorescence microscopy to measure and manipulate gene expression in discreet circuits of the mouse brain.

Scientists estimate there are roughly 80-100 billion neurons connecting regions of the brain. Locating and manipulating a single gene in a small subset of neurons among billions required new and sophisticated viral vector technology specifically designed and packaged by Rachael Neve, director of the Gene Transfer Core at Massachusetts General Hospital.

"The key advance is that we designed a dual-vector CRISPR system to manipulate a specific gene in the connections between two brain areas," Robison said.

The team split the CRISPR system in half. One half, inert on its own, was an enzyme sent to mutate DNA in the ventral hippocampus (vHPC). The other half, a guide RNA, was sent to all cells that project to the nucleus accumbens (NAc). Only those cells specific to the vHPC to NAc circuit got both halves of the system, triggering the enzyme to bind with and turn off a single gene: that encoding the transcription factor ΔFosB.

"When the FosB gene was turned off in the neurons, we were able to get a circuit-specific behavioral effect relevant to a disease like depression," Robison said. "When we put it back, or rescued it within the circuit, the effect was erased."

But removing ΔFosB permanently altered the expression of a suite of genes, in effect removing the conductor from the orchestra. So, members of the Robison lab, including co-first authors Claire Manning, now a postdoc at Stanford University, and Andrew Eagle, now assistant professor in PSL, conducted in-depth experiments on one of the most exciting findings—the role of ΔFosB in conferring resilience to stress.

"This is only the beginning of years of work for our lab," Robison said. "Which genes are important in depression-like diseases and what are they doing in the brain? This is the challenge of a lifetime for me and my lab."

CHALLENGE

"Which genes are important to depression-like diseases, and what are they doing in the brain? This is the challenge of a lifetime for me and my lab."

Insightful alum gives back to NatSci students

"Better one, or better two? Is this clearer, or about the same?"

These words are familiar to anyone who has ever sat in an optometrist's chair. They also helped steer Mark R. Hanson, O.D., into his career. At five years old, he was diagnosed with nearsightedness and color deficiency and was fitted for his first pair of eyeglasses. At age 17, he began wearing hard contact lenses. By age 19, he knew he wanted to be an optometrist.

Connie and Mark Hanson

After receiving his bachelor's degree in physiology (with honors) from MSU in 1978, he earned a bachelor's degree in physiological optics and his doctor of optometry degree from Pennsylvania College of Optometry in 1982.

"The quality of the courses I took at MSU allowed me to exempt out of several courses in optometry school, which made my four years of optometry school easier," said Hanson, who opened his private practice—Insight Vision—in Arlington, Texas, in 1986.

"At MSU, I began to realize the importance of basic research," added Hanson, who relates an example he learned from eye care.

"Hard contact lenses were invented after WWII. Soft contact lenses did not come on the scene until the early '70s—but the real soft lens research goes back to the 1960s," he said. At that time, a chemist in Prague, Czechoslovakia, was trying to find a rubber-like material that would work for artificial joints.

"He found a bio-compatible material that didn't work so well for artificial joints, but had a brainstorm about using this new material for the manufacture of contact lenses," Hanson said. The first soft contact lens was developed in 1972. "This is an example of how basic research leads to applications in many other—often unexpected—directions."

He notes the many MSU connections he has experienced throughout his career. Hanson was mentored by an MSU alumnus during one of his first optometry jobs; hired an MSU graduate as an associate optometrist in his practice in the 1990s; and mentored an MSU graduate who is now an optometrist in Colorado Springs. He is a past president of the Dallas-Ft. Worth MSU alumni club. Now, he and his wife, Connie, are planning to establish an endowed scholarship "to help people like me—kids who are first in their family to go to college—kids who go to learn with passion and could use some support."

OPPORTUNITY

"...in NatSci, there are so many opportunities... to find something you have a passion for, and to become successful after graduation."

Hanson, who sold his practice last August, remains active in the Texas Optometric Association, serving on their political action committee. In 2014, he received their prestigious William D. Pittman Leadership Award.

During his retirement, he has become more active in politics—which he developed a passion for while at MSU. Texas recently passed a new scope of practice law for optometry with some help on the grassroots level from Hanson.

He also has some advice for new students coming into the College of Natural Science (NatSci). "Many freshmen and sophomores haven't decided on a major; but in NatSci, there are so many opportunities that it's easy to find something you're interested in and have a passion for, and to become successful after graduation."

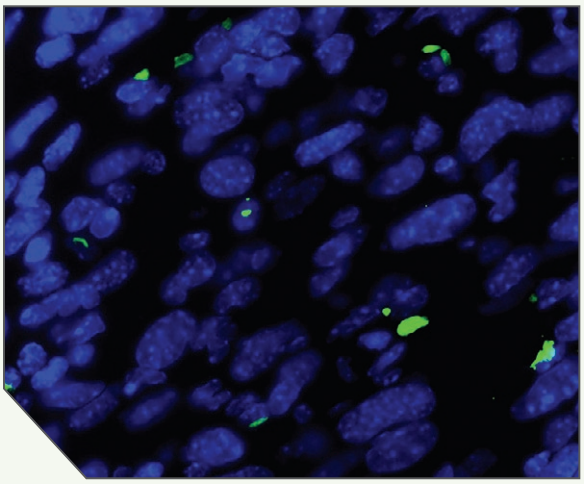
Diet and sunscreen: A potentially cancerous combination

In the United States, one in eight women will develop breast cancer, and many may be unwittingly taking a serious risk whenever they apply sunscreen.

Research by Sandra Haslam, professor emeritus of physiology, and Richard Schwartz, professor of microbiology and molecular genetics, showed a common sunscreen ingredient, benzophenone-3 (BP-3), combined with diet, can adversely affect the development of mammary gland tumors.

Using a mouse model where mammary glands lacked a gene often mutationally inactivated in human breast cancer as a proxy for susceptible women growing from puberty into adulthood, the researchers put the mice on three distinct diets: a lifelong low-fat diet, a high-fat diet during puberty and a high-fat diet during adulthood. These mice were split into two groups; one was fed BP-3 daily at a dose equivalent to a heavy application of sunscreen and the other not receiving BP-3.

Over 18 months, the researchers collected tumors from the mice and found robust evidence for the adverse effects of diet and BP-3 on breast cancer development. While nearly all mice developed breast cancer tumors, those exposed to BP-3 developed more aggressive tumors, particularly those fed high-fat diets as adults. They also found that BP-3 increased the growth of normal breast cells on all diets, perhaps an early indication of aggressive tumor outcomes.

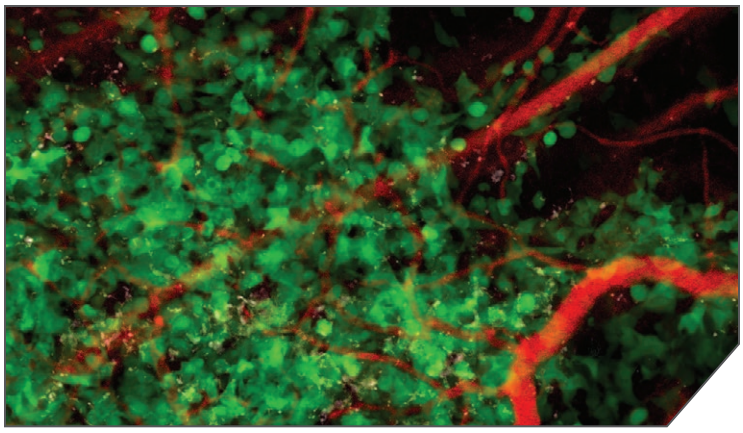


A fluorescent image of apoptotic cells (green) undergoing programmed cell death within a mammary gland tumor.

"When there are alternatives, stay away from BP-3," Haslam and Schwartz recommend, noting that zinc oxide and titanium dioxide creams are good candidates.

Building a "Trojan Horse" to fight breast cancer

A team of researchers, including co-investigator Eran Andrechek, are using nanoscopic particles to turn the body's own cells into weapons that cancer won't see coming—a precision, Trojan Horse nanotherapy that treats breast cancer without the typical side effects.



The small gray specks, which are monocytes and macrophages, are advancing on the red blood vessels and green cancer cells inside a living mouse.

The research team is working to overcome cancer's devious defenses and help the body's immune system infiltrate tumors. The NIH-funded project focuses on macrophages, cells that are part of the immune system that normally ingest—and digest—pathogens and other malignant intruders. Many cancer cells, however, have developed a defense; they coat themselves with a protein known as CD47—often called the "don't eat me" molecule. As breast cancer grows, the body recognizes something is wrong and sends macrophages to gobble up the perpetrators. But the cancer cells' CD47 holds the immune cells at bay.

The team is developing a nanoscopic solution: ultra-thin carbon tubes that seek out macrophages and monocytes, carrying a chemical cargo that orders immune cells to disregard CD47, which the tubes release only after they've made it inside macrophages or monocytes that are drawn to tumors. The drug-loaded tubes arm immune cells, helping launch a covert attack targeting breast cancer cells.

This strategy could also potentially work on other types of cancer that use a CD47 defense.

"This research, using nanoparticles as a selective therapy, has the potential to revolutionize therapy," Andrechek said.

Exploring the mechanisms of pain remission and relapse

One of the forces driving opioid abuse in the United States is chronic pain, which affects 50 to 100 million U.S. adults. Geoffroy Laumet, assistant professor, is exploring the cellular and molecular mechanisms underlying the remission and relapse of pain to decipher how and why it occurs, with the goal of developing ways to mitigate chronic pain among sufferers.

Chronic pain does not necessarily develop as a continuation of acute pain following an injury, but often begins after healing of the injury and remission of the acute pain has occurred. The pain then recurs without cause, becoming chronic.

Exacerbating the problem, chronic pain is often resistant to treatment, leading physicians to prescribe increasing doses of opiates to ease patient suffering, despite opiates being ineffective against most chronic pain conditions.

Laumet aims to understand the physiological mechanisms that normally prevent pain from re-emerging after acute pain has resolved. He and his lab have developed a novel mouse model to study the mechanism they believe prevents pain from recurring.

His earlier research found that the molecule Interleukin-10 (IL-10), which normally functions to inhibit inflammation at an injury site, is one of the mechanisms that regulates the balance between remission and relapse of pain. He is also investigating IL-10 as part of the mechanism that activates the endogenous opioid system, which acts as an analgesic without the side effects of synthetic opioids and occurs when the body is injured. Laumet suspects IL-10 achieves this effect by increasing the number of active opioid receptors at the point of injury, which then suppresses the pain of injury.

To further understand IL-10's functions, Laumet's lab induced short, acute pain in the mouse models through a small surgical incision to mimic injury or injection of chemotherapy, both of which induce pain for about two weeks. They then allow the model to remain pain-free for an additional two weeks before introducing a stressor or blocking IL-10 in the spinal column to reinstate pain to test their theory that IL-10 functions to prevent pain relapse after injury recovery.

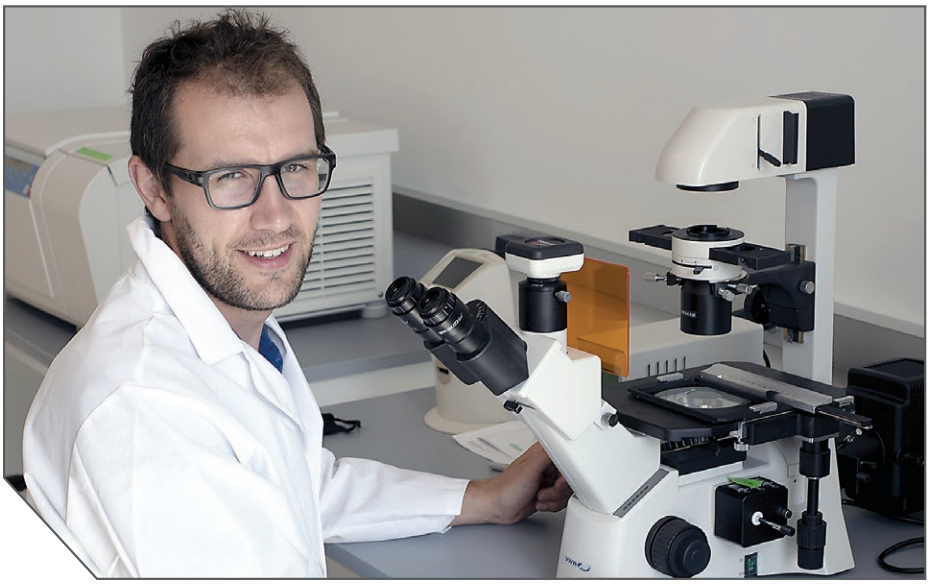
Laumet found that blocking IL-10 in mice that have never experienced pain has no effect on the mouse's state; pain neither appears nor increases. This suggests that remission from pain after recovery is not a return to the body's baseline state before acute pain occurred, but rather a long-term change in the pain-sensing system following a pain-inducing injury that makes IL-10 necessary to prevent pain relapse.

"If we understand more precisely how IL-10 exists as a mechanism to prevent the relapse of pain and discover why it is more active in some people versus others," explained Laumet, "we might be able to predict who might be more vulnerable to chronic pain in the event of acute injury—and work to prevent that outcome after treatment.

"It also means we might be able to treat those in chronic pain through medication that stimulates IL-10, which then might be used to stimulate the endogenous opioid system."

THERAPEUTICS

"...we might be able to treat those in chronic pain through medication that stimulates [the molecule] IL-10..."



Geoffroy Laumet works at an inverted microscope to look at living pain-sensing neurons.

Using probiotics to treat bone loss

Laura McCabe, MSU Foundation Professor, has a better solution than drinking milk to get strong bones.

McCabe's lab investigates the effects of probiotics in patients with osteoporosis, or bone loss. She and her team identified that probiotics benefit bone health and prevent bone loss under a variety of conditions including menopause, type 1 diabetes and following antibiotic treatment.

Her recent work with Narayanan Parameswaran, physiology professor, and Robert Quinn, assistant professor in the Department of Biochemistry and Molecular Biology, found a common link between these conditions—an imbalance of gut microbiota, or dysbiosis—that causes inflammation and ultimately osteoporosis.

"Recently, we identified that bone loss caused by chronic steroid use, an important therapy for managing autoimmune diseases like inflammatory bowel disease and rheumatoid arthritis, is prevented in our mouse model by providing mice with a probiotic," McCabe said. "This suggests that this terrible side effect, glucocorticoid-induced osteoporosis, may be easily preventable by manipulating the gut microbes."

Fifty-four million Americans have low bone density or osteoporosis, according to the National Osteoporosis Foundation. About one in two women and up to one in four men over the age of 50 will break a bone due to osteoporosis, and the disease causes an estimated two million broken bones every year.

MSU's Laura McCabe and members of her lab have shown that probiotics benefit bone health and can prevent bone loss under a variety of conditions.

"Preventing bone loss is important because low bone density is a risk factor for bone breaks," McCabe said. "Despite the many medications available, the number of patients with osteoporosis and its associated fractures is increasing. Our lab team's goal is to help the body build bone, prevent bone loss and decrease bone breaks in patients."

With the help of the MSU Innovation Center and the Swedish healthcare company BioGaia, McCabe and Robert Britton, former associate professor in the MSU Department of Microbiology and Molecular Genetics, patented the use of a probiotic as a preventative measure against the development of osteoporosis. BioGaia sells the probiotic as part of its lineup of dietary supplements, and it is now purchased by people around the world.

McCabe said she feels fortunate to have such a valuable resource on campus with dedicated staff who helped bring her research to the market, including Anne Di Sante, associate director of MSU Technologies, and Charles Hasemann, assistant vice president for Innovation and Economic Development.

"I am so lucky to work with so many great colleagues at MSU who make research fun," she continued. "How can I not get excited about the idea of our lab's research having an impact on how we think about clinically treating and preventing low bone density."

Contact Us

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Send correspondence to:
MSU College of Natural Science
Advancement Office
288 Farm Lane, Room 5
East Lansing, MI 48824

(517) 432-4561 | natsci4u@msu.edu

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CONNECT WITH NATSCI

The enzyme that changed the world, and a professor's career

When Bruce Uhal, professor, began investigating the role of angiotensin-converting enzyme-2 (ACE-2) in lung injury and repair 16 years ago, he never imagined it would bring the world to a halt. ACE-2 is the main docking molecule for the SARS-CoV-2 virus responsible for more than half a million deaths in the United States.

"Last February, I got a lot of calls from people all over the world wanting to know how ACE-2 is controlled in the lungs and other organs," Uhal said. "I never imagined that I would end up studying a virus, but it became clear that what I've learned about ACE-2 is critical to helping the world figure out how to deal with SARS-CoV-2."

After joining MSU in 2000, Uhal's lab was the first to describe how ACE-2, which degrades angiotensin II, protects the lungs from the injurious effects of this peptide. Unchecked angiotensin can cause increased blood pressure, organ fibrosis and epithelial cell death.

Then SARS-CoV-2 began surging in 2020, and ACE-2, the enzyme that serves as an essential protective protein in the lungs, was quickly confirmed to be the coronavirus's preferred entry point for infection.

Uhal was on the brink of retirement, but with so many lives at stake he switched to COVID-19 research soon after the virus hit the United States, working first with Yong-Hui Zheng, professor in the Department of Microbiology and Molecular Genetics. Soon afterward, Uhal joined an international group of scientists from India, Europe and the United States—the Self-Assembled Covid Research and Education Directive, or SACRED consortium.

The group of computational biologists, mathematicians, vaccine experts, clinicians and basic scientists like Uhal published a flurry of papers in 2020.

MSU physiologist Bruce Uhal, whose two decades of enzyme research uniquely prepared him to help during the pandemic, explains we had better be prepared for the next one.

COLLABORATION

"It's a... fascinating and critical task for scientists all over the world to keep up with this virus."

They analyzed publicly available genetic sequences of SARS-CoV-2 and ACE-2 and used protein simulations to generate computational models that predicted future mutations of the virus. Their work is helping to establish the origin of SARS-CoV-2 and how it may have infected humans.

"We predicted a possible transmission flow from animals to humans and are concerned that some animals might be reservoirs of the virus, including some household pets, based on their ACE-2 sequence," Uhal said. Early in the pandemic, for example, Spain was forced to cull almost its entire mink industry due to coronavirus infections.

The binding affinity of SARS-CoV-2 with ACE-2 devastated the world but is also key to Uhal's collaborations with drug companies on the cutting-edge of COVID-19 therapeutics.

"ACE-2 expression is concentrated in the upper nose and becomes less expressed further down into the respiratory passages," Uhal explained. "Because ACE-2 is the main molecule that the virus uses to gain entry, it should be theoretically possible to design decoy molecules based on ACE-2 structure, apply it as a nasal spray and 'mop up' the virus to prevent it from getting into the body.

"It's a crazy, fascinating and critical task for scientists all over the world to keep up with this virus," Uhal added. "If we learn only one thing from this pandemic, it should be that we had better be prepared."

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c/o College of Natural Science
288 Farm Lane, Room 103
East Lansing, MI 48824-1115

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P-MIG special collection of 14 physiology manuscripts

Under the direction of Erica Wehrwein, the Physiology Majors Interest Group (P-MIG) published 14 manuscripts in a special collection of papers featured in *Advances in Physiology Education*, representing the culmination of recent efforts to capture the breadth of the group's work, including its history and purpose. P-MIG focuses on creating program-level guidelines for undergraduate physiology and related programs.

"Despite the history and popularity of the physiology major, there is no coordinated plan for the design, administration or assessment of degree programs at the undergraduate level," Wehrwein said. "Guidelines can help educators make informed decisions about their courses, provide for a more uniform student experience among different schools, serve as a basis for assessment and improve student achievement."

Topics include key missions to improve undergraduate programs, including core concepts, professional skills and advising. A snapshot of the coursework in existing degree programs, student perceptions, career trends and the rollout of a new curricular mapping database is also included.

Twenty-five physiologists contributed to the collection, six with ties to MSU.

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