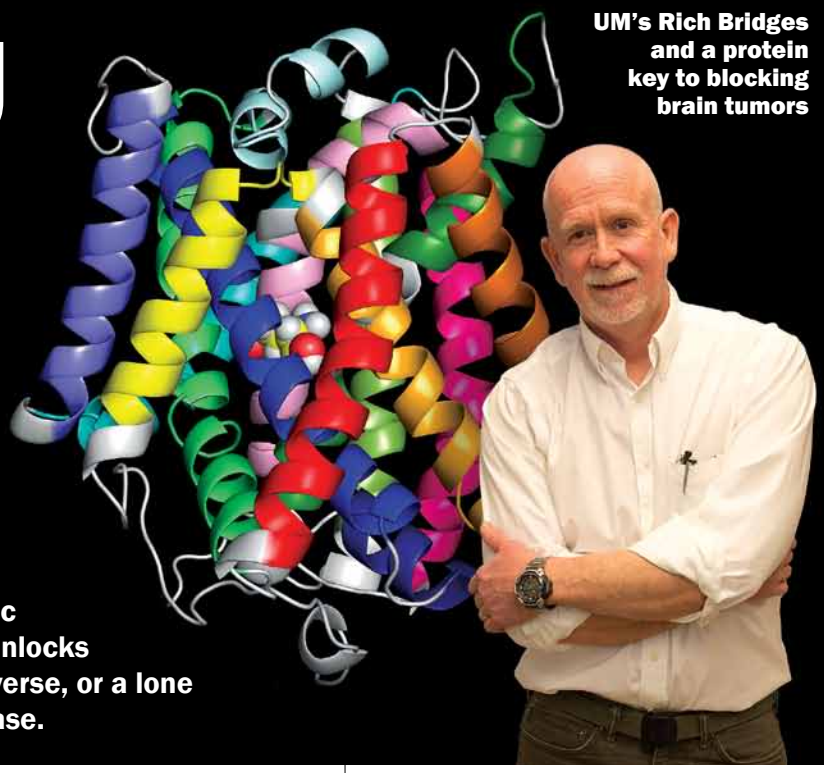
Spring 2015

Research View, Spring 2015

RESEARCH VIEW
Spring 2015
UNIVERSITY OF MONTANA Research, Innovation & Imagination

Attacking Tumors

UM center partners with pharmacy company to create new therapies



UM's Rich Bridges and a protein key to blocking brain tumors

Movies about scientific discoveries — "A Beautiful Mind," "The Theory of Everything" — usually involve dramatic revelations: A single mathematical equation unlocks the answer to a larger question about the universe, or a lone scientist's microscope reveals a cure for disease.

In real life, of course, scientific discoveries don't fit so neatly into one edited stroke of genius. But when they do emerge, their implications for the world of science and medicine are as intriguing as any big-picture biopic.

"You don't have many light-bulb moments," says Richard Bridges, Regents Professor of Pharmacology and Toxicology in the University of Montana Department of Biomedical and Pharmaceutical Sciences. "You have many moments spread out over time that lead to breakthroughs. It's like an actor becoming an overnight success, but really they've been working at it for years."

For Bridges and a research team at UM's Center for Structural and Functional Neuroscience, it took almost two decades of experimentation to arrive at two related breakthroughs. They offer a potential treatment for brain tumors, which is an area in dire need of new therapies. It's also great news because the now-patented research has led to an exclusive agreement with a drug company – and that kind of commercial development has resounding economic effects for the University and the Missoula community.

The discoveries in the group began with transporters – tiny proteins found on the surface of cells, which Bridges describes as turnstiles or revolving doors that move small molecules into and out of cells. Experimenting with those revolving doors has been a major focus for a number of groups in UM's neuroscience center since its inception in 2002.

In order to truly investigate the characteristics of the transporters, medicinal chemists, biochemists and neuroscientists in the department worked together using a collaborative approach that reflects the philosophy on which the center was founded.

There are all kind of transporters in the body, and the UM team had a family of transporters in the brain they were interested in studying. Naturally, they started looking for cells featuring that particular type, and in that quest they discovered something unexpected: The cells that expressed their particular transporters in the highest amounts were brain tumor cells.

"About the same time other scientists who were studying brain tumor cells also happened upon the presence of these transporters," Bridges says. "They looked at it from the cancer side, and we looked at it from the biochemistry side."

That discovery, which happened around 2004, changed the course of the team's work. They started looking specifically

Brain Tumors — continued page 6

UM's Own Renaissance Woman

Meradeth Snow leads a double life.

By day, she synthesizes ancient DNA to uncover lost histories of past populations while also teaching anthropology. By night, however, she assumes the persona of Meradeth Houston, author of young-adult fantasy literature.

Meradeth Snow

A UM assistant professor of anthropology, Snow specializes in molecular anthropology, which involves the study of DNA to more thoroughly understand populations.

"I have a focus in ancient DNA, so I tend to look at the DNA of past individuals, either through their skeletal remains or other things that they've had close contact with, like pipe stems or stone tools," Snow says. "For my dissertation I worked on populations from the desert Southwest, like the Ancestral Puebloans — more commonly known as the Anasazi — and how the populations are related to one another within the Southwest and bigger regional areas."

In addition to spending time in the lab, Snow teaches a number of undergraduate courses in anthropology. But once the lab work is done and classes are over, Snow throws herself into her writing. An author of four young-adult fantasy novels with several others in the works, she embraced her love of writing at a young age.

"I've always been a voracious reader, and at some point along the way, I realized that if I couldn't find more books to read about things I really enjoy, I could actually write them myself," Snow explains. "I wrote my first novel in junior high, and that was just for fun. It was something that gave me a good escape and also provided me with something entertaining to do."

When asked how she manages to juggle teaching, research and writing, Snow has one piece of advice. "Don't watch a lot of TV," she says. "That's my biggest tip, honestly. I don't have a whole lot of free time, I'll admit. I work crazy hours, and it's a lot of work. But if you want to do something, it has got to be your goal."

Snow has published four novels — "Colors Like Memories," "The Chemistry of Fate," "Surrender the Sky" and "An Absence of Light" — under the name Meradeth Houston — Houston being her maiden name. Her work may be purchased through Amazon, the UM Bookstore and various other booksellers. More information about her books can be found on her website, http://www.meradethhouston.com/ or on her blog, http://meradethhouston.blogspot.com/.

— By Ashlynn Andersen

UM Helps NASA Get the Dirt on Soil Moisture

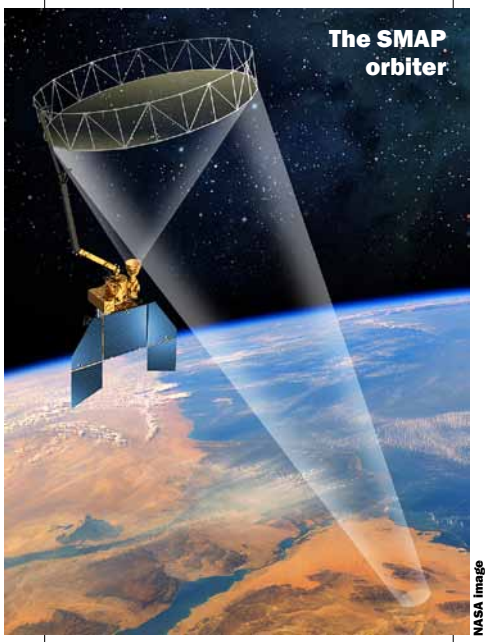
NASA launched a satellite on Jan. 29 to peer into the topmost layer of Earth's soils to measure the hidden waters that influence our ecosystems, weather and climate.

UM Professor John Kimball is among the team of researchers involved in the project. He developed algorithms that digest the vast amount of data collected by the satellite and spit them into a software platform that estimates and monitors global land-atmosphere carbon dioxide exchange, ecosystem productivity and underlying environmental controls.

"We've been working with NASA for almost a decade to develop methods for effective global monitoring of surface soil moisture and freeze-thaw status from satellites," Kimball says. "These parameters are very dynamic and strongly impact weather, climate and ecosystem processes, including vegetation growth."

The Soil Moisture Active Passive, or SMAP, mission can produce the most accurate, highest-resolution global maps ever obtained from space of the moisture present in the top 2 inches of Earth's soils. It also detects and maps whether the land surface is frozen or thawed.

Kimball and his team hope to reduce uncertainty regarding the status and potential vulnerability of the global carbon sink, and better understand relationships between global water, carbon and energy cycles. These new observations will benefit a variety of applications, including regional assessment and monitoring of vegetation productivity and health, as well as drought impacts to forests, rangelands and agricultural systems.



NASA image

Globally, the volume of soil moisture varies between 3 and 5 percent in desert and arid regions, to between 40 and 50 percent in saturated soils. In general, the amount depends on factors such as precipitation patterns, topography and more. From space, SMAP will produce global maps with 2- to 6-mile resolution every two to three days.

Faculty Help Launch Bhutan Ecological Journal

UM researchers and a doctoral student recently helped launch a scientific journal in Bhutan.

Proceedings of the Bhutan Ecological Society was created with assistance from UM's College of Forestry and Conservation. Faculty members Jill Belsky, Mark Hebblewhite and Steve Siebert, as well as doctoral student Tshering Tempa, are members of the editorial board for the journal. Former UM faculty member Scott Mills and former doctoral student Ellen Cheng also served on the board.

Belsky, Hebblewhite and Siebert all have worked in Bhutan on a variety of research projects – from studying Asian tigers to looking at historic livelihoods – for more than a decade. UM has had a formal memorandum of understanding with UWICE since 2012.

Proceedings will cover various ecological issues facing Bhutan in its next issue, including the challenges of hydroelectric power. The journal can be read online at http://www.bhutanecologicalsociety.org.bt/publications.php.

Research: Air Pollution Affects Short-Term Memory, IQ

City smog lowers children's IQ. This is among findings from a recent UM study that found children living in cities with significant air pollution are at an increased risk for detrimental impacts to the brain, including short-term memory loss and lower IQ.

Findings by UM Professor Dr. Lilian Calderón-Garcidueñas and her team of researchers reveal that children with lifetime exposures to concentrations of air pollutants above the current U.S. standards, including fine particulate matter, are at an increased risk for brain inflammation and neurodegenerative changes, including Alzheimer's and Parkinson's diseases.

Calderón-Garcidueñas' findings are detailed in a paper titled "Decreases in Short-Term Memory, IQ and Altered Brain Metabolic Rations in Urban Apolipoprotein ε4 Children Exposed to Air Pollution."

The study found that clinically healthy children who live in a polluted environment and who also carry a gene – the apolipoprotein ε4 allele, already known to increase a person's risk of developing Alzheimer's disease – demonstrated compromised cognitive responses when compared with children carrying a gene with apolipoprotein ε3 allele.

Mexico City is an example of extreme urban growth and environmental pollution, where 8 million children are involuntarily exposed to harmful concentrations of fine particulate matter in the air every day.

The study matched two groups of children living in Mexico City by multiple variables, including age, gender,

socioeconomic status and education. It then compared children carrying the ε4 allele to children carrying the ε3 allele and found that those with the ε4 allele had three significant alterations. They had short-term memory shortfalls, an IQ that, while within the normal limits, measured 10 points less, and changes in key metabolites in the brain that mirror those of people with Alzheimer's disease.

"The results add to growing data suggesting ε4 carriers could have a higher risk of developing early Alzheimer's disease if they reside in a polluted urban environment," Calderón-Garcidueñas says.

Study Finds High Impact From Montana's High-Tech Businesses

Montana's high-tech industry will grow 8 to 10 times the projected statewide growth rate, with average wages at about $50,000 – twice the median earnings per Montana worker, according to a recent study by the UM Bureau of Business and Economic Research.

BBER Director Patrick Barkey conducted the study, which was commissioned by the Montana High Tech Business Alliance. It found that high-tech jobs in Montana outpace other sectors and hold high growth potential.

"The result showed high-tech employers on average to be younger, higher-paying and more growth-focused than the economy as a whole and that Montana quality-of-life plays an important role in their competitiveness," Barkey says.

Some of the findings include:

- The Montana-based activities of MHTBA members were responsible for $632 million in gross sales in 2014.
- Alliance members expect to net more than 400 new jobs in 2015, a much stronger job growth than has occurred in the overall economy.
- High-tech businesses that are MHTBA members expect to make at least $35 million in capital expenditures at their Montana facilities in 2015.
- Montana's quality of life – its lifestyle, the work/life balance available here, the recreation opportunities and the beauty of the landscape – provide MHTBA members a significant advantage in business.

Professor Earns Caribbean Philosophical Association Outstanding Book Award

A UM professor's cross-cultural analysis received one of the top book awards from the Caribbean Philosophical Association.

Benedicte Boisseron, an associate professor of French and Francophone language and literature at UM, received the Nicolás Guillén Outstanding Book Award for "Creole Renegades: Rhetoric of Betrayal and Guilt in the Caribbean Diaspora."

"This book was important for me to write because it carries an autobiographical resonance," Boisseron says. Her father is from Guadeloupe, a French Caribbean island. He moved to France when he was 17 years old, where he met Boisseron's mother.

"Now back in Guadeloupe, my father is somehow seen as a 'Creole renegade,'" which is part of the book's title, Boisseron says. "Likewise for me as a half-Guadeloupean who was not taught Creole while growing up in France."

Boisseron

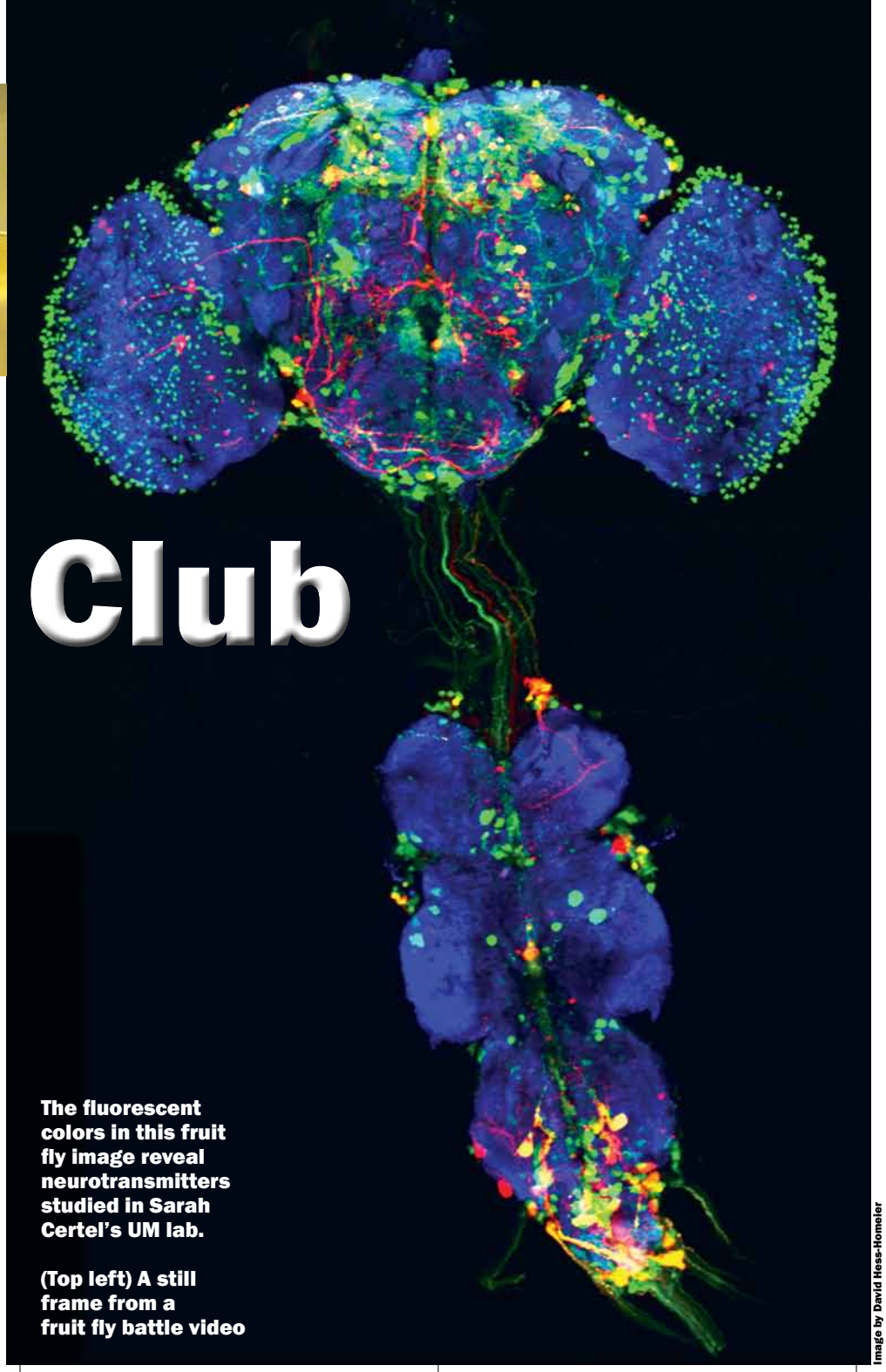
The award committee's evaluator called Boisseron's book "a brilliant text. Its original investigation into the problem of cultural affiliation, loyalty and betrayal in movement between the Caribbean, North America, Europe and beyond marks it as a major contribution to postcolonial studies, Caribbean studies, African-American studies and new-world studies," the evaluator wrote.

"Specialists and general readers alike will appreciate its examination of fundamental aspects of our postcolonial and globalized experiences, including the enigmas of creoleness, and returning and leaving 'home,' as well as Boisseron's incisive literary analysis and theoretical approaches," the review continued.

French Professor Ione Crummy, Boisseron's colleague in UM's Department of Modern and Classical Languages and Literatures, read and edited the book. Boisseron published the book in 2014 and was informed of her award in early 2015. She will attend an awards ceremony June 18-21 in Riviera Maya, Quintana Roo, Mexico.

Fruit Fly Fight Club

Wired for aggression, fly brains may lead to improved drugs



The fluorescent colors in this fruit fly image reveal neurotransmitters studied in Sarah Certel's UM lab.

(Top left) A still frame from a fruit fly battle video

Image by David Hess-Homeier

People seem hard-wired for anger, joy and other human emotions. For UM neurobiology professor Sarah Certel, finding out how behavior is wired into the nervous system is the guiding question for her research.

The star of the Certel lab is the simple fruit fly, *Drosophila melanogaster*. With only about 100,000 neurons in its brain – compared to the human brain that dazzles with as many as 100 billion neurons – the fruit fly offers a surprisingly comparable brain to all vertebrates.

Neurons are the cells that process and transmit chemical and electrical signals in the brain. While the numbers of neurons in the fruit fly are far fewer than ours, their neurons transmit the same chemical signals and function in the same manner as our neurons.

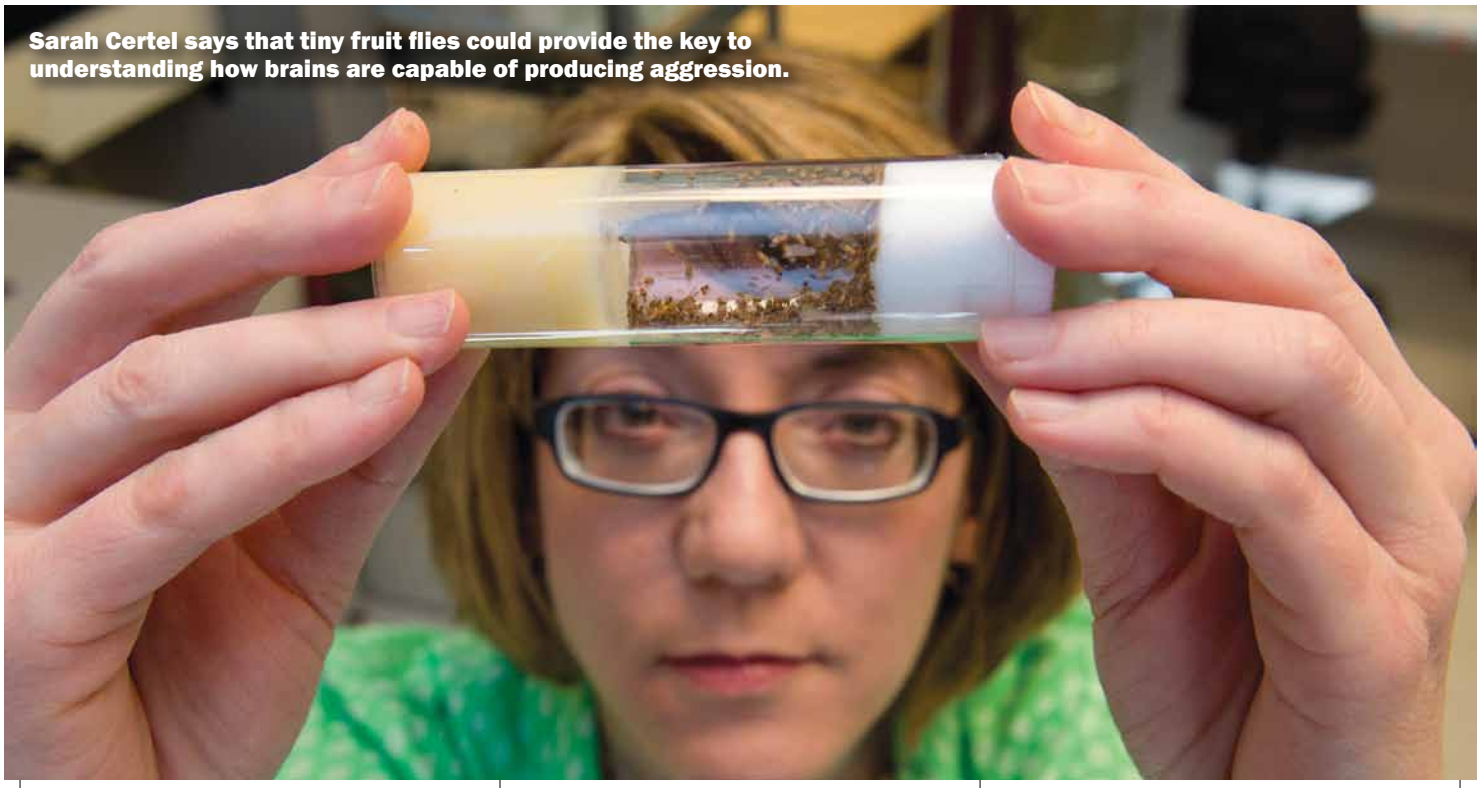
Certel and her team combine watching the behavior of fruit flies with sophisticated manipulation of genes or neurons to visualize how circuits function. The flies multiply rapidly. The behavioral patterns are reproducible. The data is prodigious.

"There are two lessons we hope to learn from our work," Certel says. "We want to understand the fundamental process by which environmental information gets transferred to the brain, and how we can target second-order neurons to alter one behavior and not another."

Results from the team's research will contribute to future studies focused on improving therapeutic drugs for conditions in which aggression is manifested, including schizophrenia, Alzheimer's disease, attention-deficit disorder, post-traumatic stress disorder, Parkinson's disease and depression. Currently, drugs affect an entire category of neurons that regulate many behaviors, including sleep, appetite, mood, movement and aggression. While these drugs may help quell aggressive behavior, they also have side effects like sleepiness or weight gain.

However, if drugs can be designed that only target the neurons within this category that are responsible for aggression, therapies could avoid undesirable side effects.

Certel, who is soft-spoken, serious and measured in her choice of words, is passionate about genetics linked to human behavior. After completing a genetics doctorate at the University of Iowa in 1999, she worked a postdoctoral position at Harvard Medical School in the laboratory of Dr. Edward Kravitz.



Sarah Certel says that tiny fruit flies could provide the key to understanding how brains are capable of producing aggression.

The Kravitz lab had turned to analyzing the genetic control of aggression in *Drosophila* at that time. Certel joined the UM faculty in 2010.

Aggression evolved for a purpose in males and females – fighting over turf, mates, food or defending progeny. While that concept is easy to understand, what triggers the behavioral response is difficult to pinpoint, especially if neurobiologists could only study the complex human brain.

The Certel lab's recent findings, published in the journal PLOS Genetics (May 2014), demonstrate that a specific type of neuron located in the leg of a male fruit fly receives a pheromonal (chemical) signal from another male and sends it to a second group of neurons in the brain called octopamine neurons. The neurons on a fly are critical, as the insect explores its world first with its legs, capturing minute and delicate signals to transmit to the brain. The male identification chemicals signal the circuits to produce aggression.

The role of octopamine neurons is significant. Neurons responsible for aggression reside in this group, along with other neurons that affect other behaviors, from sleep to hunger. Fruit flies have just 100 octopamine neurons. Studying the smaller number of neurons in fruit flies allows the Certel lab to differentiate their behavioral roles more easily.

In the fly lab, Certel and her graduate students, undergraduates and research assistants perform sophisticated, high-tech manipulations of genes and neurons on thousands of flies. The lab brims with boxes of labeled vials of genetically modified flies and bottles of live flies. Incubators keep live flies at the right temperatures and humidity for survival, with a light and dark cycle as well. Fruit flies grow from egg to larvae to pupae and then to adult in about two weeks. An adult fly can live for several weeks.

Members of the lab study videos of daily boxing matches held in a fly-sized arena. The action takes place in a closet-sized "behavior" room, where two video cameras point down at two shallow cups covered with a favorite fruit fly food, which looks like white chocolate but is a yeast substance. In each cup, two males compete over a larger female, as well as for food and space.

The resulting 30-minute videos are analyzed for aggressive and courtship actions. When a male identifies another male, he uses several aggressive behavioral patterns to respond. One such pattern is a lunge, where a male rises up on its back legs, lunges and snaps down on the competitor. He also can raise or elevate his wings to look menacing. Pairs will box, wrestle and strike each other until ones pushes the other off the edge of the cup.

To find out which neurons are important for aggression, "We genetically remove the neurons or silence the neurons we want to test and then analyze the aggression behavior of these male flies by placing the flies in the chamber," Certel explains. "For each experiment, there are two sets of controls with unaltered flies. The results tell us if the specific neurons we changed are indeed important for male behavior."

To examine specific neurons and neuronal circuits, members of the Certel lab dissect the tiny fly brains and identify individual or small sets of neurons by illuminating them with a green, florescent jellyfish protein that enables visualization of a neuron's cell body and elaborate branches. The resulting images show beautiful cobalt-blue colored fly brains with the neurons of interest highlighted in green. Lab members spend hours analyzing images of the brain to determine how neurons in an aggression circuit develop and connect with each other.

To share the remarkable complexity of these tiny insects, Certel helped UM's spectrUM Discovery Area set up an interactive demonstration area where kids can see what happens when, say, a blind male fruit fly meets a seeing male. They don't fight, because every cue is important, from visual to touch, taste and sound.

Fruit flies, it turns out, are more than annoying insects that magically appear around rotting fruit in your kitchen, or ho-hum subjects of science classes on basic genetics. Certel hopes that once people appreciate that a fruit fly's behavior is far from simple, random or boring, they will appreciate that every species – no matter how inconspicuous – is marvelous in its own right and just may contain the answer to big questions.

In this case, the fruit fly may hold the secret to more peace and less fighting in the world. V

— By Deborah Richie

Brain Tumors – continued from front

for compounds that would inhibit the transporter.

"You have a protein on the outside of the cell whose job it is to move molecules from the outside to the inside, and it's found on tumor cells," Bridges says. "So a good guess would be that it is really important to helping that tumor cell survive. We thought inhibiting that transporter might compromise the ability of tumor cells to grow – and it turns out that's the case."

Nicholas Natale, a chemist working at the University of Idaho at the time, went to a seminar by UM chemist Charles Thompson and heard about the center's experiments. He was working on designing molecules isolated from the *Amanita muscaria*, which resemble the Super Mario mushroom, that served as inhibitors. At their request, he sent a box of the compounds to the center at UM to see if they'd work, and they did.

"We got a hit for that particular transporter," Natale says. "And in 2007 I was invited to move to Missoula to work at UM." He joined the core team of professors, which along with Bridges and Thompson includes Sarjubhai Patel and Philippe Diaz.

The other major breakthrough for the group happened fewer than two years ago. While modifying the inhibitors to make them more potent, the group discovered these compounds were working at a new site on the transporter that was different from where the other inhibitors acted. It wasn't a "transporter site" but a "regulatory site" that no one else knew about.

"The transporter is like a lock on a door," Bridges says, "with the inhibitors acting like keys that block the lock and prevent it from working. Finding the regulatory site was like discovering the dead bolt and having an entirely new set of keys. Now we are focused on developing new drugs that only hit that regulatory site. Those drugs will probably be much more specific at inhibiting just our desired transporter, as well as more potent."

For the past few years, the team at UM's neuroscience center also has consulted for Promentis Pharmaceuticals Inc., a company developing drugs that work on the same family of transporters, but for other neurological disorders and not cancer. When Promentis caught wind of the group's investigations on brain tumor cells and new lead compounds, they were intrigued. With an already solid background of collaboration under their belts, the center and the company formed a partnership that includes licensing and research agreements.

UM faculty member Sarjubhai "Sarj" Patel (third from left) works with undergraduate researchers (left to right) Maxx Nehser, Daithi Martin and Dillon Schweitzer.

Research at UM's biomedical and pharmaceutical sciences department also matters on an economic development level. Over the years, the Montana Board of Research and Commercialization Technology – an organization within the Montana Department of Commerce that works to facilitate commercialization of research discoveries – has awarded the center grant money. This helps turn their basic neuroscience discoveries funded by federal grants into potential products to diagnose or treat neurological diseases.

Total federal funding in just the neuroscience center amounted to about $13 million in the past five years. About 60 to 70 percent of that money goes to salaries, which help support more than 40 people. So even without a commercial component, the department's basic research creates jobs. And because students, especially undergraduate students, are so involved with this basic research, the economic impact on them also is great. They can earn good wages in the labs and valuable experience for future careers.

"That's really important to appreciate," Bridges says. "When faculty researchers at UM get a multimillion-dollar research grant, that shouldn't be viewed economically as any different than if a Montana company receives a multimillion-dollar defense contract. Unfortunately, people don't think of those as the same. But these are real jobs, and they're high-tech jobs. And because they are funded by grants it is actually money from outside the state coming in. So it's new dollars with an even greater economic impact."

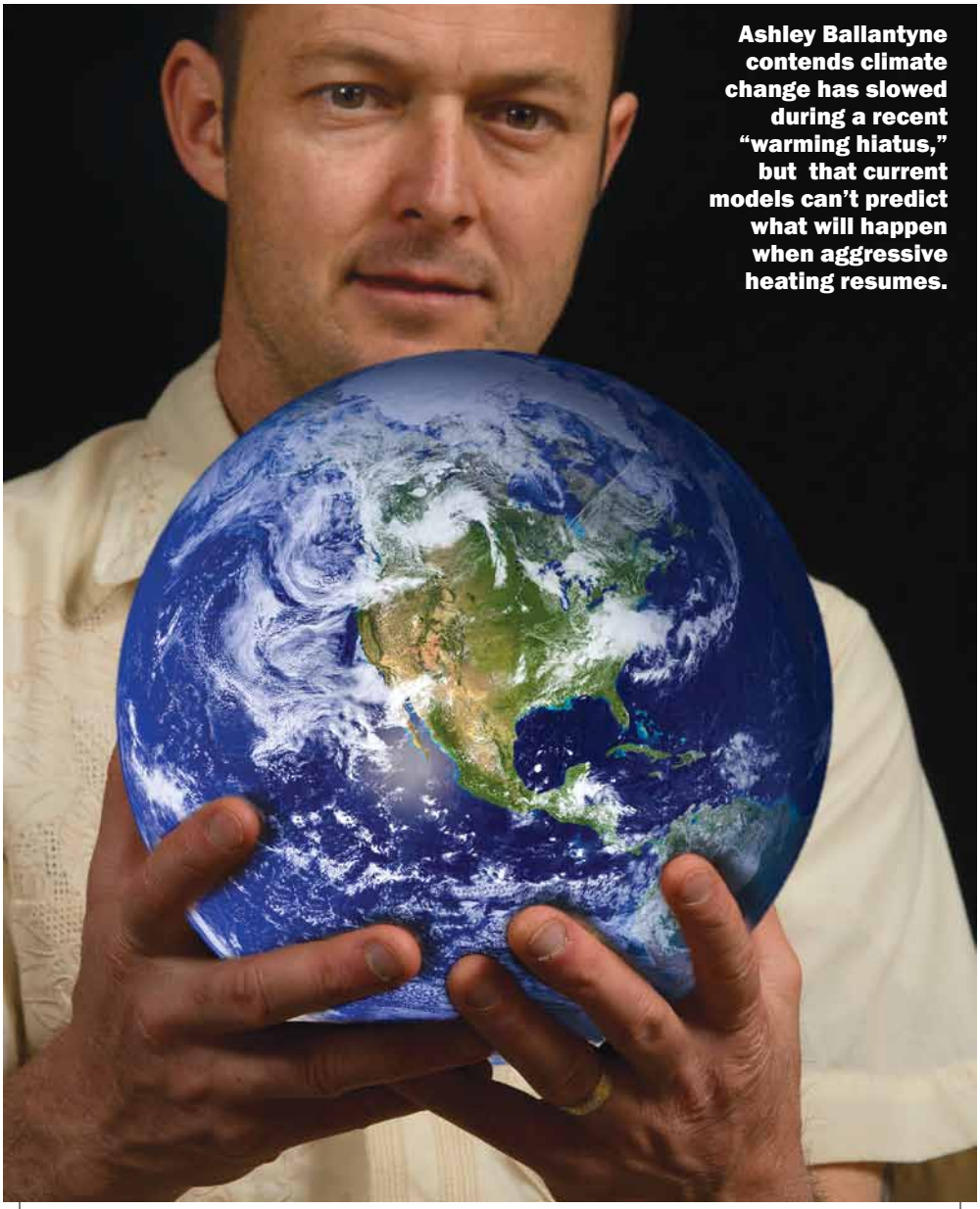
The Promentis agreement adds one more layer of potential economic development. If all goes well, the partnership with UM could create more jobs and continue putting money back into the local economy. It will take some time. As with all real-life discoveries, the road to clinical testing involves myriad tests.

"We still don't know if our inhibitor can be developed into drugs," Bridges says. "We haven't looked at delivery into the brain; we haven't looked at toxicity. But that's the type of work these days that you have to do in collaboration with a pharmaceutical company because they have the funding and expertise to do it."

It's the deliberate collaboration between UM's chemists, neuroscientists, biochemists and pharmacologists that makes it possible for the University to carry the project to this point. Never mind that UM doesn't have a medical school: The fact that the neuroscience center's team discovered a way into cancer research is part of the magic of a university that does basic research.

"If I was to tell you the work I was doing before it was related to cancer, you might say 'How relevant is that?'" Bridges says. "We didn't know where it was going to go. But if you do good basic science, it almost always lays the foundation for important work. Six years ago I would not have called my lab a cancer lab, and now we're not really a cancer lab – we're doing the same chemistry we've always done – but now we have a target that's related to cancer."

— By Erika Fredrickson



Ashley Ballantyne contends climate change has slowed during a recent "warming hiatus," but that current models can't predict what will happen when aggressive heating resumes.

The Earth Experiment

UM bioclimatologist tracks carbon in quest to improve climate change models

When not teaching and free from meetings, Ashley Ballantyne can be found on his computer, scrolling through carbon readings from around the globe. He searches for patterns, ones that will illuminate the carbon dioxide cycle between Earth's surface and atmosphere.

This cycle is complex, evolving and difficult to grasp. The closer bioclimatologists like Ballantyne can get, however, the more precisely they can make predictions for a warming world.

Despite the time spent analyzing atmospheric data, or perhaps because of it, Ballantyne will be the first to tell you that while Earth's temperatures will continue to rise with increasing CO_2, just how much remains anyone's guess. His hope is to make it as educated a guess as possible.

Ballantyne grew up near Lake Tahoe, California, which you can sometimes tell from his unkempt hair and relaxed voice. But when he explains his research, it is with focus and intensity and no small amount of gesticulation.

His career at times finds him looking back millions of years, but today he's mostly interested in the past 15. Since roughly 1998 – about when Ballantyne graduated as a biology major from the University of California, Davis – global warming appears to have slowed down in what is commonly called the "warming hiatus."

This slowdown is not unprecedented, Ballantyne says, and matches historical temperature data. When put on a graph, the rise in Earth's temperature makes a stair-step pattern, the top of each step being a decade or two pause in warming similar to what we're experiencing now.

Meanwhile, humanity continues to rapidly increase the amount of CO_2 in the atmosphere. There has been no hiatus there.

This rapid rise of human-generated CO_2 worries Ballantyne, who knows more than most how uncertain the consequences are for the planet. Yet he's a scientist first and frequently refers to Earth as "a sample size of one."

While other climatologists have published on the causes of the hiatus and skeptics have clung to it for support, Ballantyne wants to use it as an experiment. He sees a chance to examine how the carbon cycle has reacted to steadier temperatures but increasing CO_2.

The Earth naturally cycles CO_2 from the atmosphere into oceans and the land, and vice versa. It does so using methods ranging from plant respiration to complicated processes lasting anywhere from decades to centuries.

The land's ability to continue absorbing carbon despite forest loss, agricultural practices and spreading cities impresses Ballantyne. "The biosphere is remarkably resilient, even though humans are taxing it," he says.

In what he calls "a novel conclusion," he's finding that while the same amount of CO_2 is being taken up by Earth's biosphere, less is leaving. Plant photosynthesis has sped up, which draws carbon into the soil, but soil respiration, which expels it just like the exhalation of a human breath, has slowed down. Ballantyne says this is a result of respiration responding to the recent slowdown in warming.

But what will happen when temperatures begin to rise again? Soil respiration, like a dog panting in the heat, could begin to speed up as things get warmer. It's a big question. As Ballantyne puts it, the Earth has been holding its breath for the past 15 years, and at some point we expect it to exhale all that CO_2.

Ballantyne earned his doctorate at Duke University, where he studied iconic Lake Titicaca and its response to climate. He was based out of La Paz, Bolivia,

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and worked high in the Andes. He finished in 2007, the year the fourth Intergovernmental Panel on Climate Change report was published with one chapter written by Steve Running, UM Regents Professor of Ecology and Ballantyne's future boss.

Ballantyne also was cited in the report for work he and his team did on past climate in the tropics. By measuring traces of carbon and oxygen in the growth rings of trees, they reconstructed climate and estimated temperature and precipitation from tens of thousands of years ago.

Many scientists tend to drill down, looking ever deeper into a single subject over the course of their career. Not Ballantyne. "You're pulling on all these threads, and you never know which one's going to lead you somewhere," he says.

In 2012, he became an assistant professor in UM's Department of Ecosystem and Conservation Sciences. Along with his work on the warming hiatus, he's hired a postdoc to help him continue research on Elsmere Island off Greenland's northwestern coast.

According to Ballantyne, 4 million years ago the island's arctic tundra was a lush forest, home to beavers, camels and larch trees much like the modern Yukon. Its average annual temperature also was almost thirty degrees warmer than today.

"The other interesting thing about this time in Earth's history," Ballantyne says, "is it's the last time that CO_2 levels were 400 parts per million in the atmosphere." In January of this year, it averaged out at 400.14 ppm, according to the National Oceanic and Atmospheric Administration.

On its website NOAA suggests "Further Reading," and topping the list is a 2012 paper in the prestigious journal Nature by one A.P. Ballantyne.

That paper played a large role in bringing Ballantyne to Montana's attention, says Running. He chaired the department at the time, and Ballantyne's record of publication impressed.

"I didn't have a paper in Nature at that age," Running says, recalling the decision with a grin.

In that paper, Ballantyne and his fellow co-authors explored how the Earth's natural carbon cycle is reacting to unprecedented increases in CO_2.

As the paper notes, "since 1959, approximately 350 million tons of carbon have been emitted by humans to the atmosphere," and just over half of that was then absorbed by land and sea. Despite predictions, through that 50-year period Earth continued to absorb CO_2 from the atmosphere. Far from slowing, the amount of CO_2 being taken into oceans and the land has increased.

Focused on the natural carbon cycle, this was like his current work on the warming hiatus, but the scale of time was much longer, and the findings less specified as a result.

"As a human I'm terrified of what's happening," he says, "but as a scientist, I think it's a pretty cool experiment." He laughs and adds: "And it's a pretty challenging problem to work on, and a very worthy one."

For now Ballantyne sticks to the science, and has not taken an advocacy role, though he feels certain that humanity needs to move past fossil fuels. He believes that you need credibility and accomplishment as a scientist before you can consider speaking as an advocate.

Running, who often does take an advocacy role, agrees that it's better to build credentials as a scientist than speak out as a citizen too early.

"Hopefully 10 years from now he can," says Running, "and he's on a good start."

— By Andrew Graham