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Wisconsin's Magazine for the Life Sciences • SPRING 2018

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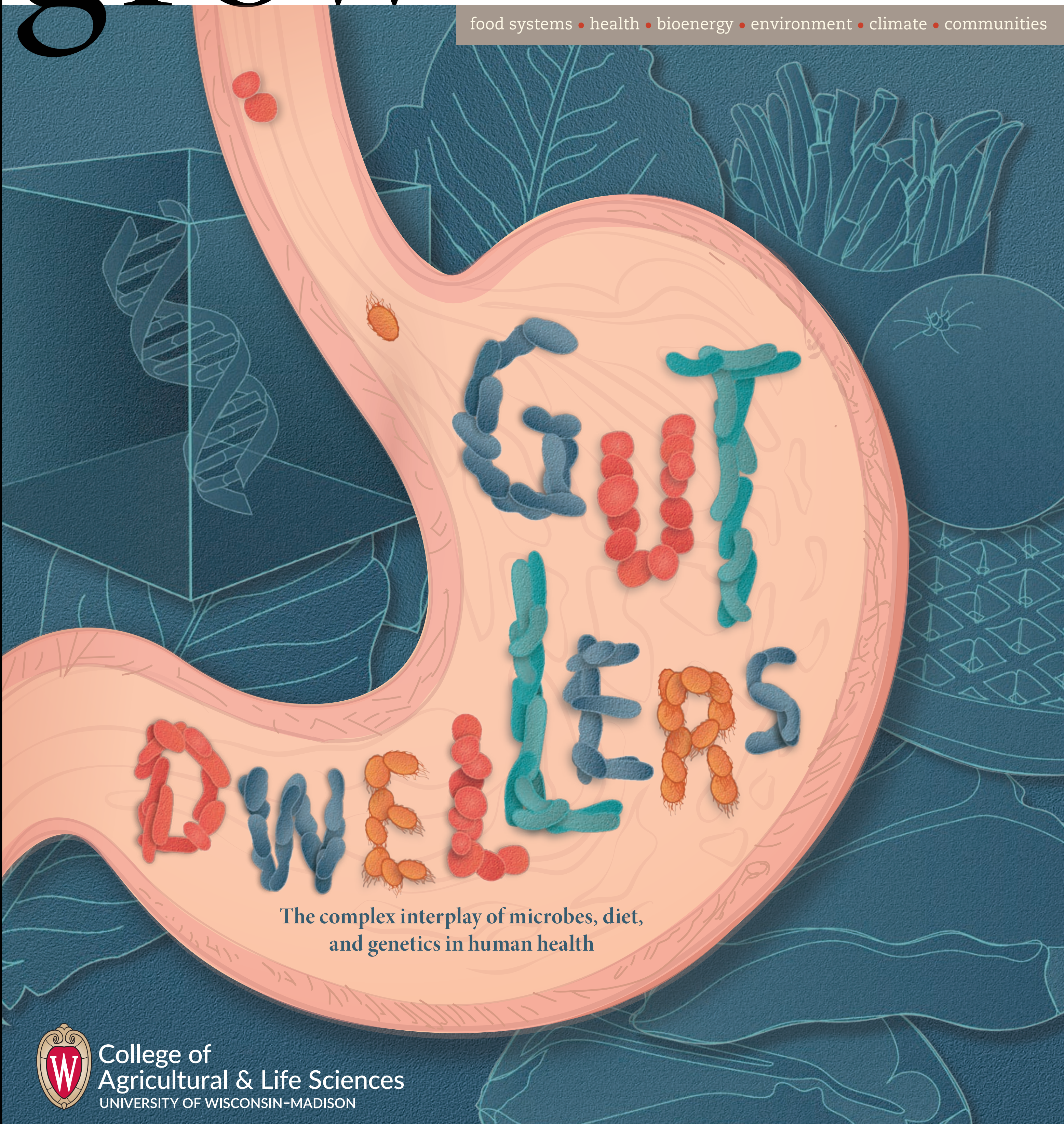

GUT DWELLERS

The complex interplay of microbes, diet, and genetics in human health

College of Agricultural & Life Sciences
UNIVERSITY OF WISCONSIN–MADISON

PIGS AND PRECISION MEDICINE • FARM INNOVATION THROUGH COLLABORATION • PLANTS IN SPACE!

Gelbvieh cattle, a gentle breed with Bavarian origins, are part of a rotational grazing system put in place by alumnus Gerry Weiss in collaboration with CALS faculty and staff. To learn about other innovations on the Weiss farm, see page 26.

Photo by Mark Hirsch

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Wisconsin's Magazine for the Life Sciences

FEATURES

DEPARTMENTS

Cover illustration by Danielle Lamberson Philipp

Dean Kate VandenBosch

New Resources for Discovery

The University of Wisconsin–Madison is a mighty force for research by many measures, from its life-changing discoveries to its global reputation for scientific excellence. Yet another measure is the extent to which the university sustains its research enterprise.

In recent years, successive cuts at the state level have reduced UW's overall budget, making the prioritization of core activities a major challenge. This hinders our ability to attract research funding, and the impact of this trend can be seen in national rankings. Between 1972 and 2014, the National Science Foundation (NSF) consistently ranked UW–Madison among the top five institutions in research expenditures. In 2015, following a steady four-year decline in those numbers, the university slipped to sixth place.

In response, Chancellor Rebecca Blank has called for a significant reinvestment in UW in a variety of ways. This means greater legislative and private support, but it also means the campus needs to find new, stable revenue streams. To boost our research endeavors, campus leadership has developed new seed funding mechanisms. These programs are designed to help our scientists do the arduous preliminary work that is necessary for securing major grants from large government agencies and nonprofits.

"To boost our research endeavors, campus leadership has developed new seed funding mechanisms."

Today, we seem to be on the right track. In 2016, UW–Madison's research expenditures rose, and the university's NSF ranking held steady. Another encouraging fact: faculty, staff, and students at CALS are making the most of these new opportunities.

For example, the UW2020 Initiative was established in 2015 to fund high-risk, high-impact projects. Selected proposals receive an average award of $300,000 for two years, and CALS projects have been among the winners in all three rounds. In fact, in 2017, one third of the awardees hailed from CALS, with projects in areas ranging from artificial intelligence in dairy farm management to the role of the human gut microbiome in health and disease.

Speaking of the microbiome, UW's Microbiome Initiative was established in 2017 with goals similar to that of UW2020. But it was also designed to encourage interdisciplinary work in an area where UW has a high concentration of expertise. Twelve of the 13 microbiome proposals selected for funding involve CALS faculty, many of them as principal investigators. These projects, covering topics such as how gut microbes might influence Alzheimer's disease and the role of the tomato's microbiome in pathogen resistance, have the potential to make transformative discoveries.

UW2020 and the Microbiome Initiative are both made possible by funding from the Wisconsin Alumni Research Foundation and other sources. But university funds will support yet another program to encourage interdisciplinary work that will make UW–Madison more competitive in garnering extramural research support. Over the next three to five years, around 70 faculty will be hired in 20 different strategic "clusters" — groups of scholars, chosen for their shared research interests and specialties, who can collaborate and pool resources from where they are situated in departments across campus. A campus committee is now reviewing proposals for these clusters, and many touch upon areas of expertise that can be found in abundance at CALS. I look forward to updating you on this initiative in the future.

I know that our exceptional researchers will continue to experience great success with these programs. Their efforts will keep CALS in the vanguard of the agricultural and life sciences while helping UW–Madison retain its traditional place as a premier research university. I am excited for what the future holds.

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Five things everyone should know about . . .

Switchel

By Hong Jiang and Bekah McBride

1. **Switchel is an apple cider vinegar-based beverage.** It also contains water and other ingredients such as ginger or honey. Maple syrup, molasses, and fruit juice are common additions.

2. **The drink has been around for centuries.** Many historians believe that switchel originated in the Caribbean before making its way to North America in the 18th century. According to the book *Forgotten Drinks of Colonial New England* by Corin Hirsch, many colonists blended the beverage at home and enjoyed the tangy flavor of a refreshing and energizing alternative to water.

3. **Apple cider vinegar-based drinks like switchel are associated with certain health benefits.** They contain high levels of polyphenols (micronutrients found in certain plant-based foods), which may inhibit DNA damage and have a positive impact on cardiovascular health. Some anecdotal evidence suggests that apple cider vinegar may aid in gastrointestinal health.

4. **As innovative beverages surge in popularity, new versions of switchel are hitting the market.** The UW–Madison Center for Dairy Research (CDR) and the United States Dairy Export Council recently teamed up to create a protein-rich, cherry-flavored variety. The drink combines dairy-based whey protein with tart cherry juice produced in Wisconsin. By adding natural ginger flavor and just a touch of cane sugar, CDR food scientists created a product that contains only 120 calories and a whopping 11 grams of protein per eight fluid ounces. This new take on an old tradition adds to the list of the beverage's benefits. For one, cherry juice is known to have anti-inflammatory compounds that may help with muscle pain. Whey protein isolate, a filtered and dried by-product of cheesemaking, contains all nine of the essential amino acids. Often referred to as "the building blocks of life," amino acids are the catalysts for many important bodily functions, including muscle growth and repair. It's no surprise, then, that the Babcock Hall Dairy Plant is producing this whey protein cherry switchel as a sports recovery drink for UW's student-athletes.

5. **Dairy-based switchels require a few tricks to make them look and taste just right.** For the CDR's cherry switchel, all of the ingredients are mixed together and given about 30 minutes for the whey protein to be fully hydrated prior to pasteurization. This step, along with the right level of acidity (i.e., a low pH), provides the best conditions for a safe and good-quality whey protein drink. The beverage can be pasteurized (heated to 175°F for 16 seconds), bottled, and stored cold for three to four months. It also can be hot-filled (heated to 180°F for two minutes) into bottles for storage at ambient temperature for up to a year.

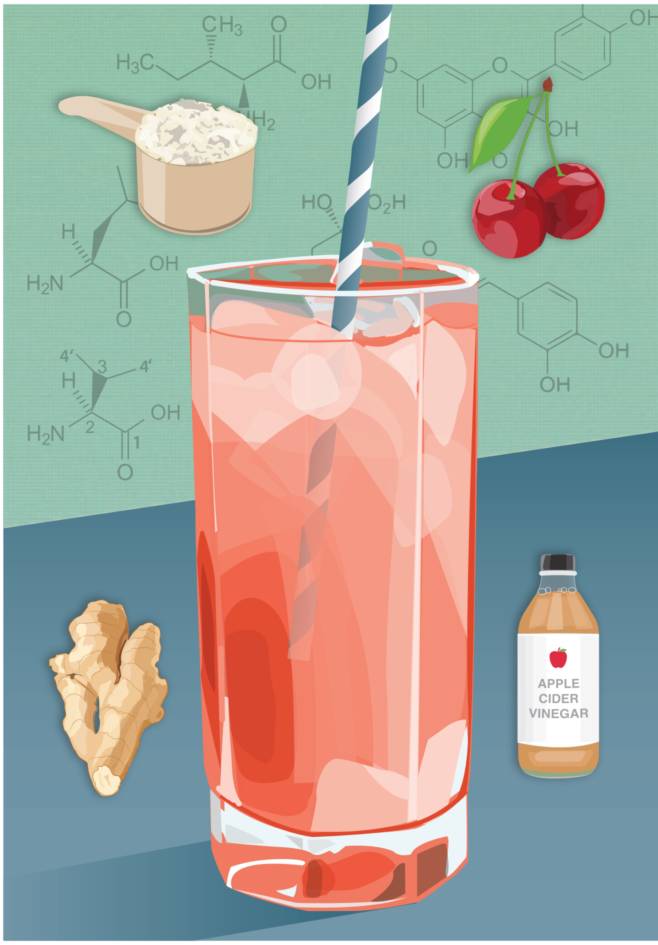

Illustration by Danielle Lamberson Philipp

Hong Jiang is a research specialist at the UW–Madison Center for Dairy Research (CDR). **Bekah McBride** is the CDR's communications specialist. Helping U.S. food companies create functional, nutritious, and flavorful dairy-based products is a major goal of the center. Learn more at **cdr.wisc.edu**.

Fermentation Education

A new certificate program offers hands-on production experience and classroom instruction in the fermentation sciences to give students a competitive edge in one of Wisconsin's burgeoning markets

Photos by Ben Vincent (3)

A harvester collects grapes of the hybrid French red wine variety called Maréchal Foch at Wollersheim Winery in Prairie du Sac, Wisconsin.

As the one and only enologist, or wine scientist, on the UW–Madison campus, a large part of **Nick Smith**'s job is guiding a group of hopeful undergraduates through Food Science 552 — and toward their futures in winemaking and other jobs in the fermented food and beverage industries.

Students who took Smith's fall 2017 course, "The Science of Wine," emerged with a solid understanding of the chemistry and microbiology behind the winemaking process. But they also went beyond lecture-style learning to get a real taste for the process of fermentation.

"A key element of the class is to teach the production process," Smith says. "How does the chemistry impact the final product?"

During the semester, students took two trips to Wollersheim Winery in Prairie du Sac, Wisconsin, where they learned about production procedures and bottling. Back on campus, students broke into small groups, each tasked with creating one of three different wine styles — sparkling, red, or white.

"[The course gave] me a greater appreciation for winemaking, and I found it very interesting to compare the winemaking and beer-making processes, as they have a lot in common," says **Miles Gillette** BSx'18, a senior majoring in food science. He was first inspired to select his major after dabbling in homebrewing of beer, a process he calls "hands-on microbiology."

Food Science 552 is just one component of the UW–Madison's new Science of Fermented Food and Beverages certificate program, which was made available to undergraduate students for the first time in the 2017-18 academic year.

The certificate is an option for students pursuing various science majors — food science, microbiology, biochemistry, and others — who want to delve deeper into fermentation. As they progress through the program, students learn about the various scientific aspects involved in fermentation.

Food Science 410, for example, teaches them about the chemical components of food constituents like proteins, lipids, carbohydrates, and enzymes. They also learn about the latest techniques and technology used to produce fermented beverages such as wine, beer, and cider, as well as fermented foods like cheese, bread, and pickles. The hope is that such a comprehensive suite of courses will give graduates a competitive edge in the field.

"The dream is to make UW–Madison the top college when it comes to the fermentation sciences," says **David Ryder**, former vice president of brewing and research at MillerCoors and an expert on fermentation and yeast physiology. Ryder was instrumental in coordinating the donation of pilot-scale beer brewing equipment from MillerCoors to UW–Madison in 2008, and he has been a steadfast advocate for the development of the university's fermentation sciences program, including the new certificate.

Long viewed as a major national center for the beer and cheese industries, Wisconsin is also home to other major manufacturers of fermented goods. The state boasts a growing wine industry, with around a dozen new wineries opening each year. Every bottle of Kikkoman Soy Sauce sold in North America is brewed and bottled at the company's factory in Walworth. GLK Foods, headquartered in Appleton, is the largest producer of sauerkraut in the world. The scope of the industry in the state is only likely to expand. And that requires trained workers, specialists, and experts in the field.

"With the prominence of all the fermented food and beverage industries we have, we [aim to] start filling the niches and educational needs," says Smith.

Smith arrived at UW–Madison in March 2015 after spending eight years as an experimental winemaker at the University of Minnesota. The initial funding for his position was secured through a Specialty Crop Block Grant from the Wisconsin Department of Agriculture, Trade and Consumer Protection with the support of the state's key wine organizations. Beyond his teaching duties on campus, Smith works directly with winemakers to assess and improve their wines, helping to troubleshoot problems, as needed.

This hands-on experience is also a boon for Smith's students, who participate in the development of various fermented products while earning their certificates. Students in Food Science 551 participate in a beer design and brewing competition offered in collaboration with the Wisconsin Brewing Company (WBC) of Verona, Wisconsin. This partnership has yielded a new WBC beer in each of the last three years. The collaboration's 2017 brew, Red Arrow, proved so popular that the initial batch sold out in a matter of weeks.

Wollersheim Winery is also a partner in the fermentation sciences program. The company sends grapes to campus for students to make into small-batch wines and hosts students so they can observe what's involved in full-scale wine production.

With the new certificate program, UW–Madison is better positioned to be a wellspring of talent, research, and creativity to support the state's fermentation-related companies, according to program coordinator **Monica Theis** MS'88.

"Our vision is that Wisconsin is the place to go to learn about the science of fermentation and that our graduates leave here with a competitive edge," she says.

—BEN VINCENT

(Above left) Philippe Coquard, who owns Wollersheim Winery with his wife, Julie, displays a bottle of the freshly pressed grape juice that will become the next small-batch wine, called Campus Craft, to be developed with involvement from students in the Science of Fermented Food and Beverages certificate program.

(Above right) Students observe as red grapes harvested from the Wollersheim Winery vineyard are sorted prior to crushing and destemming.

Corn Conundrum

Highly productive corn varieties have more trouble adapting to changing environmental conditions, so more balanced breeding may be needed

When in place, plants have no choice but to adapt to their environments, responding to stresses like drought or pests by changing how they grow. On a broader scale, crop breeders need to be able to develop new varieties that are adapted to a new location or changing growing conditions in the same area.

Both types of adaptation rely on a pool of possibilities, the combinations from which one can choose. For the individual plant, those possibilities depend on the genome it was born with. For breeders, that pool of possibilities is the whole range of genomes of cultivated crops, which they can blend together to create new varieties.

CALS researchers wanted to know whether the last 100 years of selecting for corn that is acclimated to particular locations has changed its ability to adapt to new or stressful environments. By measuring populations of corn plants sown across North America, they could test how the corn genomes responded to different growing conditions. What they found is that artificial selection by crop breeders has constricted the pool of possibilities for North American corn varieties.

In a recent issue of *Nature Communications*, agronomy professor **Natalia de Leon** MS'00 PhD'02, her student **Joe Gage** PhDx'19, and colleagues at several institutions concluded that the existing corn varieties are strong and stable, but they are less flexible in their ability to respond to various stresses. At the same time, these corn populations might have a reduced ability to contribute to breeding programs that seek to create new varieties adapted to novel environments.

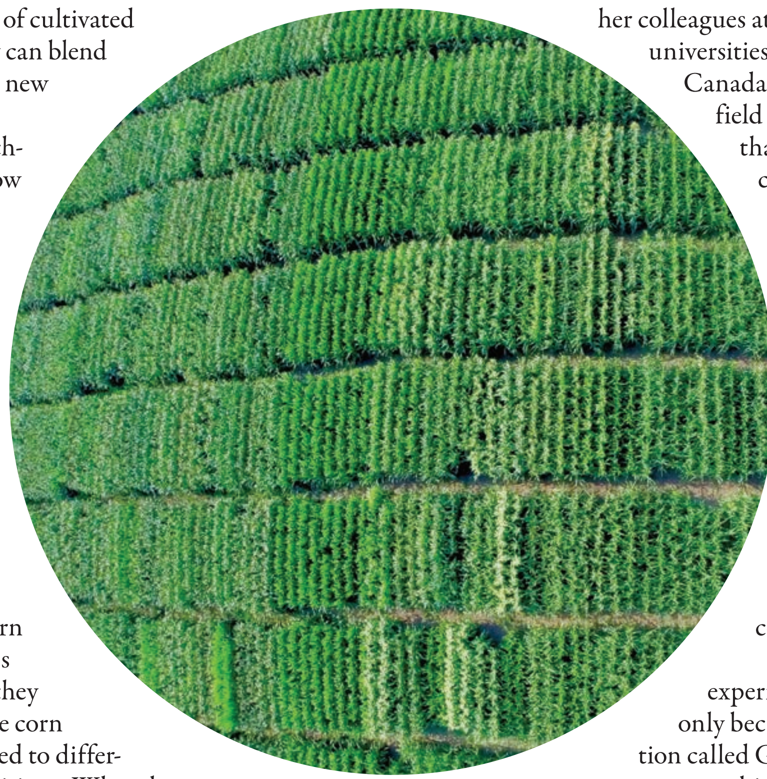

Photo by Dustin Eilert

A drone's-eye view of research plots for an experimental field maize hybrid grain trial at UW–Madison's West Madison Agricultural Research Station.

"Over the last 100 years, people have definitely improved cultivars," explains de Leon, the senior author of the report. "What we were trying to do in this study is to measure whether by doing that we have also limited the ability of the genotypes to respond to environments when they change."

By intensively breeding for high yield — in Wisconsin, for example — those plants might lose the flexibility to respond to environments that are very different from Wisconsin growing conditions. To test this idea, de Leon and her colleagues at 12 agricultural universities in the U.S. and Canada devised a large field trial with more than 850 unique corn varieties growing in 21 locations across North America. There were more than 12,000 total field plots where researchers measured traits like yield and plant height while recording weather conditions.

The massive experiment is possible only because of a collaboration called Genomes to Fields, which is led by de Leon, UW–Madison agronomy professor **Shawn Kaeppler** BS'87, and others. The project stretches across 20 states and parts of Canada. This provides precisely the range of various field conditions required to tease apart the different contributions of the genomes and of the environments to the final traits of the corn.

De Leon and her collaborators found that the regions of the corn genome that have undergone a

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high degree of selection — for example, gene regions that contribute to high yield in a particular location — were associated with a reduced capacity of corn to respond to variable environments compared to genomic regions that weren't directly acted on by breeders. The upshot is that the modern corn varieties are very productive in the environments they are grown in, but they might have a harder time handling changes in those environments.

"The data seem to point to the idea that by selecting genotypes that are better suited to be more productive, we are eroding variability that might be important as we move into a world where climate might be more erratic and where we might need to move cultivars into places where they haven't been grown before," de Leon says.

Yet this loss of flexibility is an inherent trade-off for highly productive cultivars of corn, she says.

"When you try to adapt cultivars to many different environments, you end up with plants that are not great anywhere," de Leon says. "The cost of maintaining this plasticity is to the detriment of maximum productivity."

"So we have to strike the right balance in the long term," she says.

—ERIC HAMILTON

Natalia de Leon points out an experimental corn plant at UW–Madison's West Madison Agricultural Research Station. By measuring populations of corn plants across North America, de Leon and her colleagues tested how the corn genomes responded to different growing conditions.

This project was supported by the Agriculture and Food Research Initiative competitive grants program (grant number 2012-67013-19460) from the USDA National Institute of Food and Agriculture (NIFA), USDA NIFA Hatch program funds to multiple researchers in this project, National Science Foundation plant genome research project #1238014, the USDA Agricultural Research Service, the Ontario Ministry of Agriculture, Food and Rural Affairs, the Iowa Corn Promotion Board, the Nebraska Corn Board, the Minnesota Corn Research and Promotion Council, the Illinois Corn Marketing Board, and the National Corn Growers Association.

classAct

Kai Rasmussen

'Let's Grow Plants in Space'

Photo by Ben Vincent

Kai Rasmussen BSx'18 spends much of his time studying how plants react to being in outer space. For many of his friends, this calls to mind Mark Watney, the protagonist in the novel-turned-movie *The Martian*, who devised a way to grow potatoes in a failing space station on the Red Planet's surface. And Rasmussen agrees. So he wrote a song about it.

Visit Rasmussen's SoundCloud web page (**soundcloud.com/kainakano**) and you'll find "Young Mark Watney," an original composition filled with references to the emerging (but still relatively obscure) field of astrobotany. It's punctuated by a simple chorus that underscores his mission: "Let's grow plants in space." For Rasmussen, a junior majoring in biology, this musical venture is just one way he hopes to engage the public in his passion.

Rasmussen's interest in astrobotany was ignited after taking a class with UW–Madison botany professor **Simon Gilroy** and learning about his research in the field. Rasmussen soon began working in Gilroy's lab, where he was offered funding by literal rocket scientists.

"There was just no way I could pass up the opportunity to work on something funded by NASA," Rasmussen says.

The lab's research involves mimicking spaceflight using an in-house test structure, but it also integrates the real thing. In 2014 and late 2017, the Gilroy lab sent plants to the International Space Station, and the genetic data beamed back to Earth revealed how enzymes in the plants were affected by the journey.

Scientists have knocked down numerous long-standing barriers to sustainable spaceflight, but many remain. Botany and horticulture systems are critical components of life on Earth, but they evolved over billions of years. Creating similar systems from scratch in space requires some creative solutions.

Cue forward thinkers like Rasmussen.

"We don't want to send supplies from Earth every time our astronauts need to eat," he says. "We want them to have self-sustaining systems that provide them with food [and] water."

But that's a long-term project. Meanwhile, Rasmussen has created a website (**astrobotany.com**) and a T-shirt — all in an effort to bring the science of space plants back down to Earth.

—Ben Vincent

OUTSTANDING INVESTIGATOR

Xuehua Zhong, assistant professor of genetics, received an Outstanding Investigator Award from the National Institutes of Health for her work in epigenetics, a growing area of research focused on how chemical tags on DNA can change the expression of genes.

FELLOW FELLOWS

Francisco Arriaga PhD'00, assistant professor of soil science, received the Fellow Award from the Soil and Water Conservation Society for his exceptional advocacy of soil, water, and natural resource conservation, and **Richard Lindroth**, professor of entomology, was elected Fellow of the Entomological Society of America in recognition of his outstanding contributions to the field.

HALL OF FAMERS

Scott Craven MS'76 PhD'78, professor emeritus of forest and wildlife ecology, was inducted into the Wisconsin 4-H Youth Development Hall of Fame, and **Marilyn Scholl** MS'96, former staffer at the University of Wisconsin Center for Cooperatives, was inducted into the Cooperative Hall of Fame.

NEW LEADERSHIP

Courtney Berner MS'11 has been named executive director of the University of Wisconsin Center for Cooperatives (UWCC). She was previously a cooperative development specialist at UWCC and was responsible for creating a nationally recognized program that focuses on cooperative business development.

Number Crunching | 6:1

THAT'S THE RATIO OF COWS TO PEOPLE in southwestern Wisconsin's Lafayette County. The Applied Population Laboratory at UW–Madison has examined the many ways in which rurality is defined demographically. They proposed this as one approach for Wisconsin given the state's strong dairy culture and industry.

Photo by Sevie Kenyon BS'80 MS'06

PUERTO RICO

Mongoose Tracker

Photo courtesy Diana Guzmàn-Colón

Diana Guzmán-Colón searches through Río Abajo State Forest in Utuado, Puerto Rico, for the right spot to set a live trap for mongoose.

Imagine if squirrels were fearless and rabid and preyed upon your pets rather than the acorns in your yard. In Puerto Rico, this is quite common. The small Indian mongoose — a sleek, fierce, weasel-like critter — has been troubling the island for decades, yet little is known about this invasive species and how to control it.

Diana Guzmán-Colón PhDx'18, a doctoral student in the Department of Forest and Wildlife Ecology and a Puerto Rican native, is no stranger to these animals. Through her work at UW–Madison's SILVIS Lab, she has chased her childhood curiosity and dedicated the last five years of her life to making sense of these mysterious carnivores.

They may be modest in size, typically measuring about two feet from snout to tail, but small Indian mongooses have a large impact on Puerto Rico. Native to India, they were first introduced to the island in the 1890s by sugar plantation owners to hunt rats. Since then, the mongoose population has exploded while expanding its menu to include native birds, amphibians, and domestic animals like cats, chickens, and small dogs. These attacks frighten and infuriate citizens. Today, the mongoose is so common in Puerto Rico that locals often refer to them as squirrels.

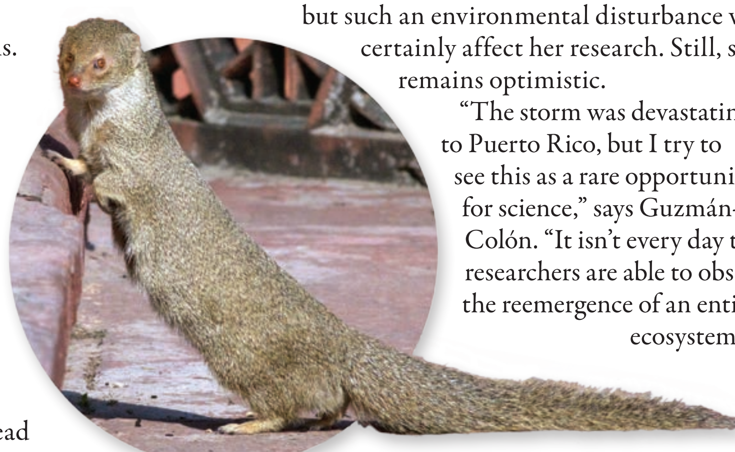
Local and federal agencies have tried to keep the mongoose population in check, but because they are aggressive and often rabid, most strategies have failed. "Mongooses are an extremely resilient invasive species and seem to be unaffected by past control measures," says Guzmán-Colón.

By tracking the mongoose population, Guzmán-Colón hopes to uncover how the species has spread throughout Puerto Rico, where they thrive, and where they may go next. But how do you keep tabs on an entire community of such elusive little creatures? Guzmán-Colón believes the answer lies in their DNA.

By live-trapping and collecting samples from local mongooses, she will be able to piece together a web of genetic relations similar to a family tree. These relationships can shed light on their population structure and movement patterns throughout the island and indicate where the species is successful. From there, Guzmán-Colón can help identify which mongoose populations should be priorities for management measures.

Since Hurricane Maria ravaged the island in September 2017, Guzmán-Colón has faced a new set of challenges in both her professional and personal life. Thankfully, her family was unharmed, but such an environmental disturbance will certainly affect her research. Still, she remains optimistic.

"The storm was devastating to Puerto Rico, but I try to see this as a rare opportunity for science," says Guzmán-Colón. "It isn't every day that researchers are able to observe the reemergence of an entire ecosystem."



The small Indian mongoose, first introduced to Puerto Rico by sugar plantation owners, has been plaguing the island for decades.

As for the mongooses, Guzmán-Colón sees a possible boom in their population. "Mongooses live in burrows underground, are efficient scavengers, and reproduce quickly. My prediction is that they'll be unaffected by or benefit from the hurricane."

All the more reason for further research.

—Gilliane Davison

Winter Awakens Spring Flowering

To avoid the dangers of frost, many plants have evolved a knack for waiting for winter to pass before flowering. But the season's cold weather is key to making it happen. **Rick Amasino** investigates this process — and the genes behind it — to reveal invaluable insights for farmers and plant breeders.

Interview by Kaine Korzekwa MS'16

IT'S SPRINGTIME IN WISCONSIN AGAIN. Home gardeners and farmers are busy tending to their beds and fields, relishing the fresh sprouts of flowers, vegetables, and crops. It begs the question: What happens in the inner workings of plants as they prepare for spring? What's the science that governs the growing season for different flora?

Rick Amasino, a plant biochemist and professor in the Department of Biochemistry, may have the answers — or at least some of them. He studies plant development and, specifically, how and when plants produce flowers. In 2016, his expertise earned him a place on a National Academies of Sciences, Engineering, and Medicine committee tasked with investigating the impacts of genetically engineered crops.

Many plants have effectively evolved a way to avoid flowering prior to winter. Instead, they use the cold season to help activate flowering when the weather warms. Amasino's research sheds light on what conditions a plant must experience in order to flower. In particular, he focuses on unraveling the genetic basis of the effects these conditions have on plants as they stimulate or repress flowering. His findings may allow other scientists and plant breeders to develop crops that are more efficient and have higher yields of food or energy.

g HOW DO PLANTS RESPOND TO SPRING?

There are a wide range of responses. For example, some plants need to be exposed to winter cold to flower in the spring, whereas others form spring flowers as a result of being exposed to the decreasing hours of sunlight during the fall season. Apple and cherry trees are in this latter category — their flowers are actually formed in the previous fall in buds that become dormant. Then, when it gets warm the following spring, everything that was crammed into those buds in the fall just unfolds.

Other plants like lilies, for example, require exposure to cold in order to flower. When they are growing in the fall, flowering is blocked. But over winter, the block is removed and they flower in the spring. The underlying processes for this involve a lot of biochemistry, and that's what we've studied in my lab. Specifically, we study how flowering is blocked in the fall and how exposure to cold results in the removal of this block. The block removal process is known as vernalization; this word is derived from vernal, which means "relating to spring."

g ARE THERE ANY MORE EXAMPLES OF PLANTS THAT NEED WINTER TO FLOWER?

Some common examples include many of the vegetables we plant in the spring, such as cabbage, carrots, and beets. We don't usually see these particular vegetables flowering because they will not flower until they experience winter, and we harvest them before they have a chance to flower. Many grasses go through this process as well.

g WHY SHOULD WE BE INTERESTED IN THIS PROCESS?

This requirement to go through winter in order to flower is important agriculturally; food plants keep growing without flowering all summer long and, therefore, the part which we consume can get very large. However, if you left a carrot in the ground after the summer, it would flower the next spring, and the underground part of the carrot we eat would become shriveled as it provides the nutrients for flowers to form.

g IF IT GETS WARMER EARLIER, IS THAT A PROBLEM?

An early warming trend in itself isn't problematic if it continues into spring, but our climate is likely to be more variable than that. So, if we have unusually high temperatures late in the winter and cherry blossoms in Door County open, but then we get a blast of cold afterward, the flowers will be destroyed and fruit cannot form.

WHAT'S GOING ON INSIDE THE PLANT THAT DETERMINES WHETHER OR NOT IT FLOWERS?

In the plants we study that require winter, there is a gene encoding a repressor protein that is expressed in the fall that prevents the plant from flowering. Then, over the winter, control of the repressor gene is altered in a way that the repressor is no longer expressed. Consequently, plants can flower when it gets warm, and they resume growth in the spring in the absence of the repressor protein.

We've recently published research specifically on the small Mediterranean grass called *Brachypodium*. Previous work has shown that a gene called VRN1 is responsible for activating flowering in these grasses after the winter. But what's the repressor gene keeping VRN1 in check in the fall? That was previously unclear. We did genetic screens and found several of the genes that repress the VRN1 gene prior to winter. We just published a scientific paper on one of these, calling it RVR1, for its role in repressing VRN1.

WHY ARE GENE DISCOVERIES LIKE THIS IMPORTANT FOR THIS AREA OF RESEARCH?

Scientists that breed cereal grains may find this newly identified gene interesting. However, we think it could also impact biofuels research. I am part of the U.S. Department of Energy's Great Lakes Bioenergy Research Center (GLBRC) here on campus. Although switchgrass, which can be used to make biofuels, doesn't go through the vernalization process, there's a good chance that taking the RVR1 gene from *Brachypodium* and putting it in switchgrass will delay switchgrass flowering. Delaying switchgrass flowering to various extents may improve yield.

WHY IS UNDERSTANDING THIS PROCESS IMPORTANT?

In basic research like ours, we often don't know where exactly it's going, but it often ends up having practical relevance. Our goal is to understand the biochemical pathways that plants have evolved to flower at certain times of the year. But in crops, in which the timing of flowering is important, this research can be applicable. For example, we share our unpublished work with wheat breeders who can translate some of the knowledge into increased efficiency in a breeding program.

Rick Amasino

Photo by Frederic Bouche

Also, our work has revealed basic principles of how genes are regulated, which has implications for many areas.

Another example of applicability, although not directly from our research, was useful for sugar beet farmers, who plant in the spring. A spring cold spell will trigger some of the sugar beets to flower, and flowering plants do not produce the part of the beet the farmers harvest. Scientists in Europe modified genes involved in the flowering response to cold and came up with a sugar beet variety that doesn't flower if it is exposed to cold. Now farmers can plant their beets in the fall rather than the spring to allow them to have a much longer growing season and to grow bigger — and they don't have to worry about the beets flowering. This has significantly increased the yield per acre of sugar beets.

WHAT'S YOUR NEXT STEP IN THIS RESEARCH?

We are going to continue to work with other GLBRC researchers to study *Brachypodium* and how different varieties of the plant live and persist in winters that have varying temperatures and lengths. How did one variety evolve a system tweaked to require 16 weeks of cold? Why does another one require just two weeks of cold? In other words, what's the genetic and biochemical difference between the requirement for a short winter versus a long winter? Grasses are really important crops, and this model for studying flowering can tell us a lot about how they work.

A PRECISE HOPE

by Kelly April Tyrrell

Photos by Jeff Miller

With gene editing — and pigs — CALS scientists are developing a model for "precision medicine," the possibility of highly individualized treatments for patients living with the rare disease called NF1

MASON KONSITZKE IS 7. He loves food (especially when he can share it with others) and anything military (both of his grandfathers served). He likes to fly kites and play with his 5-year-old sister, Alexandra. But Mason was born with a disease called neurofibromatosis type 1, or NF1, and each day can present new challenges for him and his family.

NF1 is a genetic disease caused by changes, or mutations, to a single gene in the human DNA library. Roughly one out of 3,000 babies born in the United States has it. That's more than three times the incidence of cystic fibrosis, a much better-known condition. Yet few people have heard of NF1.

Mutations in the NF1 gene cause defects in the neurofibromin 1 protein, which acts as a tumor suppressor. Children with NF1 can develop painful tumors along their nerve tracts, sometimes in their skin and in their eyes, which can render them blind. They are often diagnosed with autism spectrum disorder, though not all children with NF1 also have autism, and they are sometimes diagnosed with attention deficit hyperactivity disorder. They may have soft bones that bend and break easily. They are at a higher risk for cancer. And there is no cure.

It was not a disease Mason's parents, **Charles** and **Malia Konsitzke**, had ever heard of. As a newborn, he was healthy, but when Mason was 6 months old, the couple began to suspect something was wrong. Mason developed coffee-and-cream-colored spots all over his body, which his father later learned are a hallmark of NF1. Mason received a genetic diagnosis of the disorder just before his first birthday.

"We were like deer in the headlights," Malia says. "We were in shock, wondering, what does this mean for us? What does it mean for Mason?"

At 18 months, Mason began to lose his ability to speak. He was falling over, screaming constantly, and deliberately banging his head. That's when an MRI revealed a tumor called a plexiform neurofibroma in a mesh of nerves in the left side of his face. It was growing fast.

A FATHER AND SCIENCE FACILITATOR

Charles (who goes by Chuck) is a research administrator and the associate director of UW–Madison's Biotechnology Center, a sort of one-stop shop for scientists in need of DNA sequencing, genome editing, and other services.

Upon Mason's diagnosis, he began to delve into published NF1 research. He wanted to know where it was happening, who was doing it, and how he might be able to help. He sought opinions from experts, wondering how the field could be improved. Many identified the same bottleneck: the lack of a good research model.

In biology, research models are animals, cells, plants, microbes, and other living things that allow scientists to study biological processes and re-create diseases in order to better understand them. Good models yield information relevant to humans, but the right model can sometimes be difficult to find.

NF1 is especially complex, affects many systems of the body, and touches many areas of scientific inquiry, from cancer research to neurobiology. Chuck began to search for a better model and, in 2013, when Mason was 3, he settled on pigs. Pigs are similar to humans in many ways that other common research animals, such as mice and fruit flies, are not. That includes their size, which means drugs and devices that work on humans can also be tested on pigs. They have a robust immune system, which rodents lack. And they're intelligent, so scientists can study changes in their cognition.

Knowing all of this, Chuck went on the hunt for researchers who studied swine.

BRAVING THE RISKS

Dhanansayan (Dhanu) Shanmuganayagam BS'97 PhD'06, assistant professor of nutrition and animal sciences at CALS, has spent most of his career using swine to study human diseases, particularly heart disease. In fact, he and colleagues in the animal sciences department created the Wisconsin Miniature Swine, a pig that, like people, can develop heart disease under the right conditions.

Dhanu's office was a few blocks from Chuck's, but they'd never met until a few years ago, when they bumped into each other while helping to campaign for the new UW Meat Science Laboratory. They got to know each other, and Chuck asked Dhanu whether he had ever heard of NF1. He hadn't. Chuck told him about Mason, about the need for a better model, and about the promise that pigs offered to help understand and treat the disease. Then he asked Dhanu if he would join forces to help create that model.

Taking some time to think about it, Dhanu consulted the members of his laboratory who would all be helping to forge this new path. His risks would be their risks. A pig model could fail, leading them all down a blind alley.

Dhanu told Chuck he was in.

The risks remain significant, Dhanu says, "but I've come to terms with it, and it's fine. I've been lucky in my career to work on things that have gone to clinic. If it works, it's going to be impactful."

There aren't many places in the world where this kind of work — melding basic science with clinical research and a large animal model like swine — is possible. UW–Madison has large biomedical research centers, the capacity for high-powered basic science, and a 1,500-pig research facility called the Swine Research and Teaching Center (SRTC) in Arlington, a 35-minute drive from campus.

"It's a brave new frontier, to move into swine," says **David H. Gutmann**, a physician and researcher at the Washington University School of Medicine in St. Louis, who is considered one of the foremost NF1 experts in the world. "I'm glad they're doing this work at UW–Madison because the combination of specialized resources and expertise are found in very few places worldwide."

LIKE SCISSORS FOR GENES

Dhanu and Chuck determined that the course they wanted to chart included gene editing using a powerful new tool known as CRISPR, which stands for Clustered Regularly Interspaced Short Palindromic Repeats. The genetic technology is reshaping basic biological research. Like a pair of molecular scissors, CRISPR enables scientists to target a stretch of cellular DNA for alteration. They can cut out pieces of DNA or swap out letters in the genome, changing the message it encodes or shutting off genes entirely.

The two set their sights on creating pigs that carry the NF1 mutations they and other researchers are most interested in studying. "But we had to figure out where to start," Dhanu says. "It's like learning to fly a space shuttle."

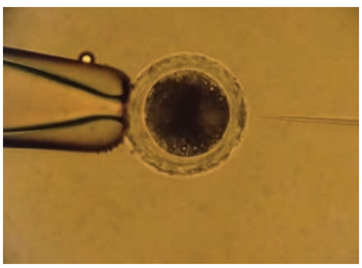
With Dhanu's lab manager and lead scientist **Jen Meudt** at the helm, the team dove in. But the challenges were many. They had to learn about swine reproduction, about CRISPR and gene editing, how to perform the necessary surgeries on pigs, how to time events so no step of the process failed and ruined all the efforts before it. Again and again, they hit roadblocks.

It took more than a year, but finally, they came up with a plan: The researchers would use artificial insemination to impregnate a female pig carefully primed to produce more eggs than she naturally would. Shortly after fertilization, they would remove the embryos, whisk them to the Biotechnology Center, and inject them with a solution containing the gene-editing CRISPR. This would have to be done quickly, while the embryos were still a single cell. This way, when the single cell divided, all the subsequent cells would contain the NF1 mutation. (Inject too late and the pig would develop into a mosaic of cells that contain the mutation and those that do not.) Then it would be off to the surrogate mother, a pig chosen to reproductively match the embryo-donating pig. The researchers would perform surgery to implant the CRISPR embryos into her womb. If all went well, months later she would give birth to piglets, at least some of which would carry the desired NF1 mutations.

A few months passed. On Nov. 7, 2016, Chuck and Dhanu were meeting in Madison with a group from the Neurofibromatosis (NF) Network, which supports NF1 research and clinical care. They were sipping coffee when a text came in from Jen: "The mom carrying NF piglets is delivering right now."

The piglets — eight in all, and four with the NF1 mutation — were a living embodiment of the team's hard work. They

Dhanansayan "Dhanu" Shanmuganayagam describes his research during a Neurofibromatosis Type 1 (NF1) symposium for patients and families held at the UW–Madison Health Sciences Learning Center in May 2017.



A breed of pigs called Wisconsin Miniature Swine (top) were created by a team of UW–Madison scientists to help better model and understand human diseases, including NF1.

Seen through a microscope, researcher Kathy Krentz guides a micro-needle (bottom) to inject DNA into one of several pig embryos at UW–Madison's Biotechnology Center.

had proved that they could create pigs genetically engineered to carry the disease. It was an emotional experience for the scientists, involving tears and prayers. They immediately went out to celebrate.

Then they set to work building on that success. One of the four piglets with the mutation is a male. Mason named him Tank. His job is to sire more piglets with the mutation since the changes conferred by CRISPR were designed to be passed on from generation to generation.

The team took the process they'd developed and applied it to other NF1 mutations, including some related to cancer. And they set an even more ambitious goal: precision medicine. In other words, a pig personalized for every child with NF1.

With CRISPR, the researchers believe they can take the genetic fingerprint of an individual child's NF1 mutation and create a pig with that same mutation. They can then test potential medications and treatments and see if they'll work. Can tumors, like the one that afflicts Mason, be shrunk?

THE PROMISE OF PRECISION

By the time Mason reached prekindergarten, the tumor in his face had grown into his cranial sinus. His parents were told he could lose his sight and his ability to taste. Surgery wasn't an option. It was too risky and could leave Mason in even greater pain, permanently. "He's literally been in pain his whole life," Malia says.

Then, for reasons doctors couldn't explain, the tumor stopped progressing. He regained his speech and no longer screamed or struggled to stay upright. His doctors keep a close watch on the tumor with MRI scans. They continue to work to determine the best medication regimen for the other symptoms that come with his particular variant of NF1. His treatment must be continuously modified.

Mason still exhibits some of the behavioral challenges often associated with NF1, which for him began at age 3. At age 5, he was diagnosed with autism. His parents say that, although it's relatively late to get such a diagnosis, it opened up more therapeutic doors. Most doctors and insurance companies are unfamiliar with the social and behavioral implications of a NF1 diagnosis, but autism is well recognized and the need for early intervention well studied. Mason now sees an occupational therapist and speech-language pathologist in and out of school and a psychiatrist several times each year.

The therapy helps, but managing Mason's disease has also taken a toll on the family. In 2016, with "everything fraying at the edges," Malia says, the couple decided she would take time off from work to help refocus and slow down. She prepared to resign from her job working for a school district; instead, they offered her a one-year leave of absence. It provided the family the respite they needed, but it also presented a significant financial strain. "We laugh a lot because you have to," Chuck says.

Laughter is just one way to cope with a disease with so many different faces. NF1's unique manifestations make each child and each child's treatment plan experiments unto themselves. But pigs develop faster than children do, so they offer the possibility of helping to predict how NF1 might affect a particular child, enabling parents, doctors, teachers, and others to prepare. Earlier intervention for a child who develops autism could lead to better outcomes. Doctors could start working to find drugs to treat tumors before they grow too large.

"Precision medicine is more than matching the right drug to the right gene. With NF1, it's more complicated and involves searching for the factors that make each individual with NF1 unique," says Washington University's David Gutmann.

"This is an amazing opportunity to find the risk factors that put an affected child at risk for developing a brain tumor, a bone defect, or another serious complication of NF1."

Dhanu, Chuck, and Jen are not doing this work on their own. The team now includes many talented individuals like Biotechnology Center scientists **C. Dustin Rubinstein**, **Kathy Krentz**, and **Michael Sussman**, along with **Jamie Reichert**, manager of the Swine Research and Teaching Center, and his team. And there's now a broader research group, the UW NF1 Translational Research team, which includes **Thomas Crenshaw**, an animal sciences professor and department chair, and **Marc Wolman**, a professor of integrative biology.

They have also enlisted the skill and knowledge of **Neha Patel**, a pediatrician at the UW–Madison School of Medicine and Public Health who treats about 150 children with NF1 in Wisconsin and surrounding regions.

Dhanu hopes to make the NF1 pigs accessible to other researchers around the country, charging only what it costs to produce them. And the team plans to use the pigs to help identify metabolic and cellular pathways common to the variety of NF1 mutations to help target and develop better drugs.

But to accomplish all of this requires funding.

"We're at a critical moment," Dhanu says. "We have to turn our successes into funding opportunities."

The UW NF1 Translational Research team has bootstrapped most of its work so far, relying primarily on funding and donations from the NF Network.

Literature about Neurofibromatosis Type 1 (NF1) is displayed (top) at a NF1 symposium for patients and families held at the UW–Madison Health Sciences Learning Center in May 2017.

Larry Britzman and his 11-year-old daughter, Mackenzie (bottom), who has NF1, talk to health advocate Lindsay Geier during the NF1 symposium.

Most of that comes from an annual charity golf tournament the Konsitzkes and four other families help organize and run. Called Links for Lauren, the tournament honors **Lauren Geier**, an 8-year-old girl in Madison with NF1.

Finding funding for rare diseases through federal agencies like the National Institutes of Health can be challenging. However, families can play a surprisingly influential role in the fight against rare diseases.

"They often provide critical resources and financial support at the earliest stages of a high-risk project, when funding from federal agencies is not possible," David Guttman says. "Our families, they inspire us because they ask us to do things that are really meaningful and take risks by taking the roads not frequently traveled. Through their involvement, they can move the field forward in ways that no one else can."

'WHERE THERE'S RESEARCH, THERE'S HOPE'

Larry Britzman had no idea there were pigs at UW–Madison that might one day help children like his 12-year-old daughter, Mackenzie. He learned that, and much more, in May when he traveled to campus from La Valle, Wisconsin, for a symposium for NF1 patients and their families.

"I didn't realize each child is specific," he says. "I didn't realize UW has swine research and there aren't too many facilities in the country researching NF1."

The NF1 team hopes to host the symposium each year, to invite families to learn more about the science of NF1, to give them a chance to meet researchers and clinicians, and to ask questions and meet other families living with the disease.

"We've gone very far in two years because it hasn't been just about building a model, it's also been about creating a community around it," Dhanu says.

The opportunity to work so closely with and on behalf of the people who may ultimately benefit from his work is not something he'd ever experienced. And he has found it profoundly rewarding.

Not long ago, he invited a family into his lab whose college-aged daughter has NF1. They'd been donors to NF1 causes for years but had never talked to a researcher. "It meant a lot to them, and my first thought was: 'How can we do more of this?'"

He and his lab members now participate in running events like the Madison Half Marathon, often with the NF Team organization, to raise money for NF1 research and to increase awareness. The runners sport neon yellow performance shirts with bold, black lettering. They also participate in the annual charity golf tournament.

"As scientists, we don't often see the payoff of what we're working on," Dhanu says. "It redefines our research priorities, and it also aids discovery. The best people to note observations are the people who live with it."

Alexandra and Mason Konsitzke play with their parents, Chuck and Malia Konsitzke, at the family's home in Stoughton, Wis. To help the family face the challenges of living with NF1, Chuck says, "We laugh a lot, because you have to."

To him, success can be measured by individuals. "Even if our research just raises awareness and someone gets treated because of what we do, that alone is big," he says.

Chuck believes the disease is underdiagnosed because very few people are genetically tested for it, and most physicians are not familiar with it. So they may diagnose patients with autism or a behavioral disorder and miss the broader picture.

That has frustrated **Danielle Wood**, a teacher and mother of two who lives in Reedsburg, Wisconsin. Her daughter, Bernadette, is 2 and was diagnosed with NF1 as an infant. Along with springy blonde curls and an arresting smile, Bernadette has a weak abdominal wall, which causes her pain and may require surgery. She wears braces to support her frail ankles.

Danielle, too, has NF1. Her mother had it and so did her grandmother. Though her condition is mild — she simply wears glasses for poor vision caused by a tumor on her optic nerve — deciding whether to have children was hard. Because it is a dominant mutation, Danielle and her husband had at least a 50 percent chance of giving birth to a baby with the disease. Having grown up with NF1, Danielle felt she had a good idea of what to expect. She now sees herself as an advocate for Bernadette.

"While things never move as fast as we want them to, there's a tremendous amount of exciting progress in this field, and where there's research, there's hope," David Gutmann says. UW–Madison is "in a really great position because (it has) young faculty who are excited and a patient community that is challenging them to improve the lives of people with NF1 through research."

This is what drives Chuck, Dhanu, and the rest of the UW NF1 Translational Research team, which is working to establish a NF1 Center for Excellence at UW–Madison. Not only is this possible, David says, it is necessary. "There is no established therapy for NF1 and no magic bullet that works for all kids or adults. The challenge for us is to learn more about this disorder so that personalized and effective treatments emerge."

Moreover, he says, what NF1 teaches researchers will inform their approaches to other conditions, like some types of cancer. And he's excited to see what the future holds.

"All of us in the NF field get up every morning and are excited to get to work. What we learn from our colleagues and our families each day brings us one step closer to that better future for children and adults with NF," he says. "I can imagine getting up every morning and running to work to see what's happening with those pigs."

For Mason, pigs — including Tank — don't play much of a role in his daily life today. Instead, he continues regular visits to therapists and other professionals to help him manage his symptoms. He also benefits from the support of his family, from Chuck and Malia to aunts and uncles who have learned all they can about NF1. And the family dog, Donatella, is his packmate, Malia says. But at 7, Mason can still take all of that for granted and focus on what he loves best. Like sharing the tastiest mini pizzas he can make. He would absolutely love it if you tried one.

VIDEO

LIFE WITH NF1

Two families describe how NF1 affects them.

The Britzman family
go.wisc.edu/nf1-britzman

The Wood family
go.wisc.edu/nf1-wood

GUT DWELLERS.

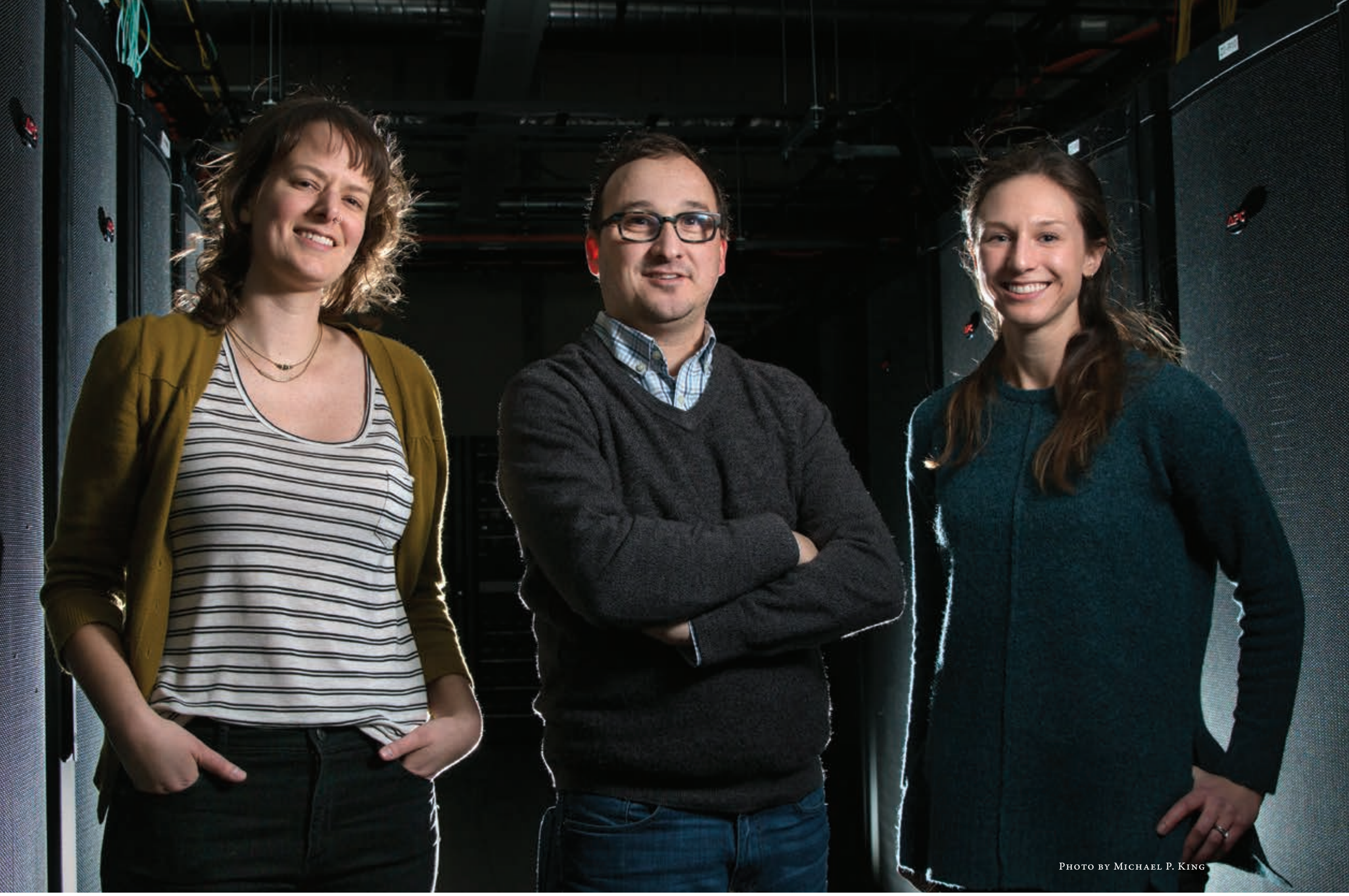
CALS scientists delve into the microbial communities in our digestive tracts — and their implications for our health

BY ERIK NESS

The second floor gallery of the Wormfarm Institute in Reedsburg, Wisconsin, is a far cry from the funky glassware and biosafety protocols of a working microbiology lab. One corner contains an improv kitchenette, circa 1987. Sprout — the mascot offspring of the Jolly Green Giant — waves improbably from behind a cubicle wall across the room; the child-size plastic statue is missing a hand. A cool draft of autumn rain and small-town traffic noise flows through an open window.

Assistant professor of bacteriology **Federico Rey** chats with his Wormfarm hosts as more than three dozen attendees of the annual Fermentation Fest assemble into a casual arc of folding chairs and a couple of vintage couches. These are people who already understand the idea of microbes as friends. Makers of coleslaw and kimchi, kombucha and beer — they are motivated by microbes and have paid to hear Rey's summary of the state of current human microbiome research.

Photos by Katrin Talbot MS'85



Across the life sciences, the microbiome is the buzziest of buzzwords, invoking a symphony of hope, hyperbole, and high expectations. Rey shares in the overall enthusiasm, but he is careful about the speculative details. Yes, the microbiome might even match our frothiest expectations. And no, he can't cure your diabetes or make you leaner, faster, or smarter. He can't even tell you if your microbiome is healthy. Not today.

Because nobody can.

In front of a large wall hanging of textile orange circles representing the bubbles of fermentation, he begins where he has to begin, very near the beginning. "Microbes are the most abundant form of life on this planet," he says, his thick Argentinian accent backlit by a docent's enthusiasm. "They can live in places where we cannot imagine life."

"Microbes outnumber us by many orders of magnitude. They power almost everything on the earth," he says. They convert as much carbon dioxide into organic compounds as plants do and emit more methane than the oil and gas industry. "Literally, there is no place on earth where there are no microbes,"he continues."It is impossible to get rid of them."

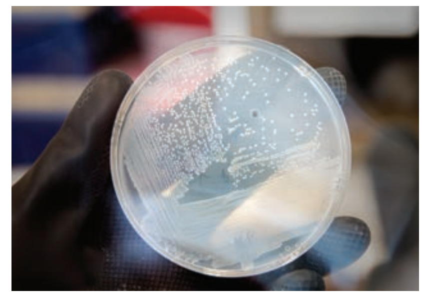
And despite our germophobia, they're mostly good company: "A very small fraction of microbes are pathogens. Most of them are commensal — they don't do good or bad — or they are beneficial for humans." These last ones, the microbes that fuel our fantasies of easy cures and everlasting health, truly capture Rey's interest.

Every surface on our bodies is colonized by some kind of microbe, and microbiologists have identified thousands of species of bacteria that can inhabit the human gut. Each of us, in turn, has a collection of between 100 and 200 different bacteria strains, comingled with other life forms from fungi and protists to viruses and archaea. These enteric ecosystems — different for every single human, even more unique than a fingerprint — each contain 100 times the genetic information of our own cells. They both supplement and interact with our bodily blueprints.

Deciphering who's who is not even half the problem. How exactly do our bodies gather these microbes? What shapes the resulting ecosystem? How do humans and microbes interact? In 2017 alone, Rey published new research about microbiome effects in diabetes, Alzheimer's, and the cycling of the nutrient choline (which may positively affect fetal brain development but also can lead to heart disease later). "Every single disease

(Above) Postdoc Lindsay Traeger, assistant professor of bacteriology Federico Rey, and research assistant Julia Kreznar stand in the data center at UW–Madison's Discovery Building, which houses the computers they use to sift through massive amounts of genetic information. Large cooling fans in each equipment rack create a windy environment.

(Left) Fermentation Fest, sponsored by the Wormfarm Institute, is an annual celebration of "live culture" held in Sauk County. These scenes are from the 2017 fest, where Federico Rey gave a presentation on the human gut microbiome.



Photos by Michael P. King

Julia Kreznar (left) inspects a germ-free mouse while performing cage maintenance. Sterile germ-free mouse facilities on the UW–Madison campus provide a controlled model in which to study the interactions of microbial communities within mammals and how they impact anatomy, physiology, behavior, and susceptibility to disease.

In the Rey lab, senior scientist Bob Kerby holds two sealed test tubes (top right) containing a pure strain of bacterium from a human fecal sample. The cloudy sample has been incubated for 24 hours; the clear sample has just been prepared. The Petri dish holds the bacterial colony.

or health condition scientists look at, they find a microbiome connection," he says.

And yet there is no single definition of a healthy microbiota. And what is healthy for you may not be healthy for me.

RESEARCH REVOLUTION

Federico Rey arrived in the United States in 1999 with advanced biological questions on his mind and little idea that microbes could hold the answer. As a research fellow at the Henry Ford Health Sciences Center in Detroit, he focused on hypertension and vascular disease. But when he moved to the University of Iowa for his Ph.D. in 2001, he met *Rhodopseudomonas palustris* during a lab rotation. These extravagantly versatile bacteria are known for their ability to use four different modes of metabolism to scavenge energy, nitrogen, and carbon from a variety of sources — with or without oxygen. Intrigued by the diversity and adaptability of microbes, Rey says he fell in love with the bacterium.

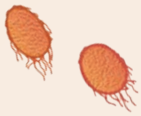
R. palustris was an obvious stepping-stone towards biofuels. But in 2005, Rey saw a talk by **Jeff Gordon**, a pioneer in the study of human-microbiome interactions. Gordon began examining the development of the mammalian gut in the 1980s. Eventually he realized that microbes were essential to the process, and he set out to untangle this complex relationship using early sequencing techniques and transgenic and germ-free mice.

Rey joined Gordon's lab at Washington University in St. Louis as a postdoc in 2006 just as microbiome science was gaining momentum. Tools for reading the genetic code were getting faster, cheaper, and more versatile. Computers used to crunch burgeoning data sets were growing in power as new statistical methods were increasing in sophistication.

One of the earliest hints of the power of microbes was that transplanting the microbiome from one mouse to another could also transfer basic metabolic conditions, such as obesity. It was in Gordon's lab that Rey first met CALS professor of biochemistry **Alan Attie** — through the microbes of his mice. In Attie's efforts to unravel the many mysteries of diabetes, his lab sent Gordon microbiome samples from genetically distinct mice that had been placed on a high-fat or a chow (i.e., grain-based) diet. It was known that both diet and genetics had a significant effect on the metabolic health of these mice. Gordon helped to show that the microbes played a role as well.

Rey took the project with him when he was hired by CALS in 2013, and he's been collaborating with Attie since. It's a task of daunting complexity: integrate two genetically complex systems that play a role in metabolic disease. Neither is close to being perfectly understood, yet they interact with each other, coalescing in each individual.

Hundreds of mammalian genes are already understood as part of the metabolic pathways



that go awry on the way to diabetes. The human microbiome, meanwhile, produces thousands of chemicals that act within the genetic framework of humans. We've long understood how these microbes help us break down the complex compounds in the plant-based foods we eat, providing about 10 percent more energy. More recently, we've learned how these microbial bioreactors produce molecules called short-chain fatty acids — acetic acid, propionic acid, butyrate, and other products of fermentation that signal our bodies in health-promoting ways.

Our bodies sense these molecules, helping regulate things like gastrointestinal motility. Less well understood are the thousands of chemicals that train our immune system and help regulate everything from kidney function to brain chemistry.

"This is one of the most important aspects of the microbiome that is revolutionizing biology," Rey says. But unraveling the interplay between host genetics and metabolism is anything but easy.

In work published in *Cell Reports* in 2017, Rey's student **Julia Kreznar** used eight different mouse strains and microbial transplants to help unravel this tangled web. The study found measurable differences in the microbiome established in the different strains. These microbes, in turn, influenced the likelihood that the mice would succumb to metabolic disease. The work also demonstrated a novel link between the gut microbiome and insulin secretion.

"We can show that microbiota affected pancreatic islet physiology and function," Kreznar says. It's a promising step, but it's also an indirect interaction. Identifying the mediators of these microbe-host interactions is really challenging.

"It's the dawn of a new field," Attie says. "We have 3 or 4 pounds of organisms that are producing so many molecules, and we don't know the least of them."

"I'm feeling daunted," he admits. "We had this idea that we would potentially connect the dots genetically. It is enormously complex, and it's hard. It's harder than we even thought it was going to be."

A BIG GENETIC BLACK BOX

Back in Reedsburg, Rey knows the probiotic question is coming, so he makes a preemptive strike: "When I talk about microbiota, I'm not talking about probiotics. The probiotics that you can get at Walgreens are basically microbes from dairy, microbes that can live in milk. Microbes that are not adapted to live in our intestines."

If the microbiome has taught him anything, it's that generalizations are tricky. "If they work for you, you should continue," he emphasizes, trying to claim middle ground. Because of course probiotics are microbes, and there actually is a lot of evidence that some may provide immune benefits.

But you won't get a better microbiota by eating probiotics, and if you don't eat your yogurt on Saturday, by Sunday those yogurt microbes are pretty much gone. They just pass through. "The effect is good as long as you keep eating them. And that is the perfect model for a company, right?" he says, with a tone of innocent mischief.

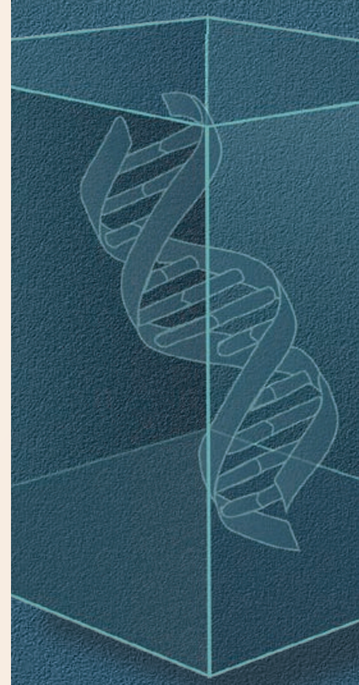
But if you look at probiotics through the lens of the microbiota, you have to acknowledge this essential truth: It's been a landmark decade, but we still don't have tools that are sophisticated enough to measure the microbiota in sufficient detail. We still don't have an adequate biological understanding of what makes a healthy microbiota. And we barely understand the complex dance these microbes do with our body. Add in the fact that probiotics are dietary supplements, and thus not well regulated.

"You have to be careful. You have to do your research," Rey says. "There are many different strains of probiotics, and there are big differences between different strains." This is further complicated by the difficulty of even properly identifying bacteria, which can evolve rapidly. "There is a big difference between George Clooney the actor and somebody named George Clooney who lives in Atlanta. They have the same name, but they are completely different people," he explains. "There are thousands of strains of *Lactobacillus rhamnosus*. Some may have an effect. Many of them probably don't."

In fact, it is our ability to identify these subtle differences in microbes that sparked the current revolution in microbiome science. First came 16S ribosomal RNA. Essential to the construction of proteins, 16S changes very slowly, which allowed scientists to, finally, reliably identify the members in a microbial community.

We talk about DNA as the book of life. At first, just reading a few pages was a chore. Then we developed machines to read more pages, faster. Then we learned how to read the sequels: DNA makes RNA, which makes proteins and enzymes responsible for carrying out cellular processes, including the making and breaking of sugar for energy. The technology responsible for reading these interrelated genetic codes is called next-generation

"Every single disease or health condition scientists look at, they find a microbiome connection."



sequencing, and it has powered this first golden age of microbiome research. The challenge now is sifting through that data to find biological meaning. Postdoc **Lindsay Traeger** Ph.D. '15 is one of Rey's primary number crunchers. "I'm attracted to very broad questions that we can throw a data hammer at and see what falls out," she says.

Right now Traeger is focused on the next stage of collaboration with Attie and several other UW–Madison faculty including **Joshua Coon** (biomolecular chemistry), **Karl Broman** (biostatistics and medical informatics), and **Brian Yandell** (statistics). "We know that the gut microbiome is influenced by diet," Traeger says. "But there is also this genetic component, which is a black box."

Using genetically distinct mouse strains is advantageous when you're trying to model a particular disease. But if you're trying to tease out broader biological principles, using a single strain of mice could lead to bias. That's why the labs are using a special breed called Diversity Outbred, a strategic genetic mash-up of common lab strains and some wild strains.

In one hand, Traeger has the genetic code of each individual mouse. And in the other, she has the genetic code of the microbiome of each mouse. Using advanced statistics, she's searching for patterns that suggest some molecular matchmaking.

"I'm trying to identify how the host is selecting for or deselecting for the presence and abundance of certain microbial functions. Because the microbes are interacting somehow with the host." One gene of interest is responsible for creating the important immune protein TNF-alpha, which plays roles in cancer and autoimmune disease. Early returns suggest that the TNF gene is also involved in sensing and responding to bacteria that have flagella.

Of course, the TNF gene is only one of about 23,000 genes, while the genes associated with bacterial flagella are just a few out of potentially hundreds of thousands. With numbers that big, there's a lot of noise to filter out. And lots of distractions. "It's a little hard to focus," she laughs. "I think I could just spiral off. [Rey] keeps me thinking about the biology." Rey's endless creative energy helps. "He'll just bust into the office and say, 'I have this idea!'"

The immensity of the black box also keeps the work exciting. "We do think we're going to find some interesting examples of interaction of host and microbiome," she says.

"Biology is never simple. If it's simple, you're missing something."

TWO T-BONES A DAY

The microbiome is a dynamic force. Change the diets of lab mice, and overnight the communities that live in their gut change dramatically. So why care what microbes are in your gut if you can switch it up that quickly?

Rey points to his classic Argentinian upbringing as an example. "I grew up eating a T-bone for lunch and a T-bone for dinner," he says. "Twenty-five years. And I miss it very much," he quips, evoking another laugh from his audience. "But if I became vegetarian long term, I would definitely select for different microbial communities. And I would likely have new microbes colonize me."

But even while your gut community is adaptable, the microbes in your gut can also have long-term consequences. That T-bone? "There are components in meat that microbes love and that cause problems," Rey warns. "But you might not have them." Which could mean several things: You've never been exposed to them, or you've been exposed but they didn't take. Or maybe they're there, but other microbes keep them in check. All of those are open biological questions, which now makes nutrition even more complicated.

In 2011, **Stanley Hazen** of the Cleveland Clinic published a paper linking microbes to the breakdown of lipid phosphatidylcholine (lecithin) into several choline-related compounds, particularly TMAO (trimethylamine N-oxide), a chemical already found to be a strong predictor of heart disease risk. Specifically, microbes metabolized choline into trimethylamine (TMA), which is then converted in the liver to TMAO.

While diet is a big part of this risk — eggs, milk, liver, red meat, poultry, shellfish, and fish are major dietary sources — the combination of microbial and host biology leading to TMAO accumulation intrigued **Kymberleigh Romano** Ph.D.'17, who decided to dig deeper for her doctoral work with Rey and was co-mentored by **Daniel Amador-Noguez**, an assistant professor in bacteriology with expertise in metabolomics. Despite years of lab experience, she'd never worked with lab animals before, but she knew the time had come. "A lot of the phenotypes we study exist only in the context of a host-microbe interaction," she says. "A test tube is never going to develop heart disease."

First she needed microbes. Harvard researcher **Emily Balskus** had identified the genes involved in microbial conversion of choline to TMA, and Romano began looking for them in human-associated microbes and constructing experimental mixes of microbes. As she tinkered she found that, in mice at least, you need a TMA producer present in the intestinal microbiota to see TMA accumulation. And as you add more TMA-producing species, less choline is left for the host.

Even though she'd narrowed down the difference to a single organism in her custom microbiota, it still wasn't enough. One bacterium contains anywhere from 3,000 to 5,000 genes — that's a lot of variables. Fortunately, her collaborator from Harvard had identified a genetically tractable choline consumer and knocked out the TMA production gene. "Now the only difference in my communities was a single gene."

Cardiovascular risk aside, choline is an underappreciated nutrient contributing to the process of epigenetic regulation of gene expression, and those without enough of it are more likely to suffer metabolic disease. In mice and rats, there is even a two-day window during pregnancy where lack of choline can impact fetal brain development. "Biology is never simple," says Romano. "If it's simple, you're missing something."

EAT YOUR VEGETABLES

Talking about poop makes people laugh, and as Rey wraps up in Reedsburg, the crowd has stayed engaged, surviving even his brief foray into 16S sequencing.

His advice for microbial health is folksy and charming. "Spouses share more microbes than people that don't live together," Rey tells the crowd. "We have found that spouses who get along together share more microbes than spouses that don't. There is a lot of exchange going on there." (In fact, if you've had to take antibiotics, he suggests family time will do more to restore your microbes than probiotics.)

And, noting that the most diverse microbiomes are found in places like the Amazon, he says being exposed to dirt is probably a good thing. "Get your hands dirty working in your garden," he says. "I think that's a health habit that we have lost over the years."

Still, stubborn ideas persist among those gathered in the room. About a dozen times people bring up their pet microbiome theories for validation: probiotics, kombucha, fermented food, raw food, red wine vinegar, minimal vegetable washing, fecal transplants.

"The microbiome has come to mean anything you want it to mean," Rey says disarmingly, for another laugh.

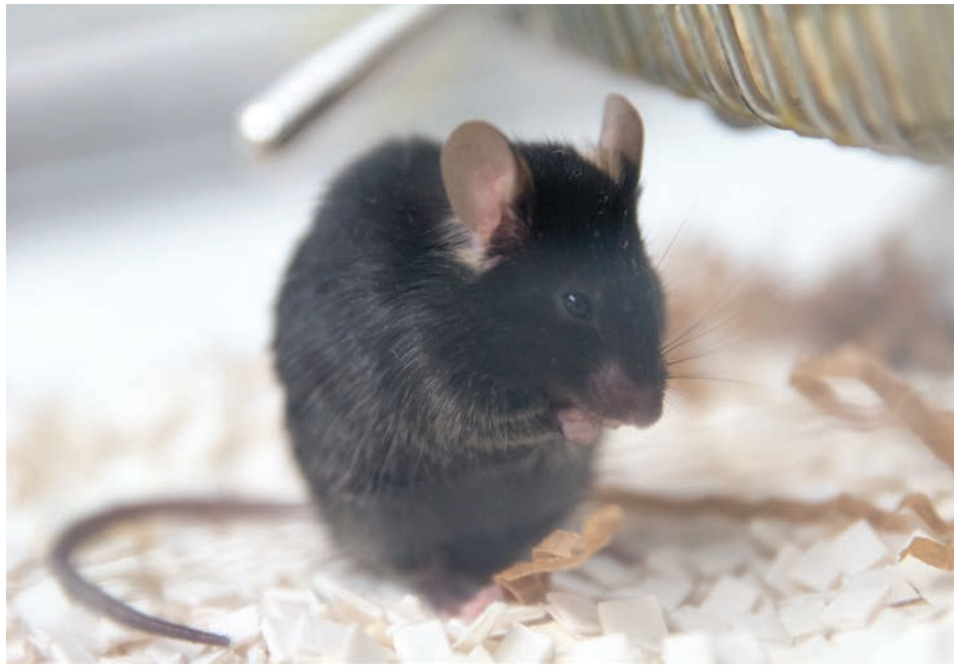


Photo by Michael P. King

A germ-free mouse in its sterile quarters on the UW–Madison campus.

But "I don't know" is his most honest answer. It's a conundrum: The microbiome is hot in part because of some stunning findings. Most remarkable is the use of fecal transplants to cure drug-resistant *Clostridium difficile* infections, with cure rates running above 90 percent in some studies.

That extraordinary outcome certainly got the attention of both the medical community and the fad diet community. And even as it validates the power of the microbiome, that outcome actually runs against the grain of all the variation Rey is trying to figure out. "My lab is very interested in understanding the consequences of our interpersonal differences," he explains.

"I can sequence your microbes, and I would not be able to tell you what vegetables to eat," he says. "Maybe in 5 or 10 years personalized nutrition will be a reality, but it is not today. The one recommendation we can give right now is try to think about feeding your microbes. Because we cannot tell you what will be the best for your microbiota."

In other words, eat your vegetables. Let's say you eat pizza, with regular flour dough and cheese. Your body can digest every single ingredient of that pizza. By the time it reaches your large intestine, where most of your microbes live, your body has absorbed everything of nutritional value.

"You're not sharing any of your food with your microbes," he explains. "That's one of the things we are doing with our Westernized diets: we are starving our microbes."

"Maybe broccoli is the best for your microbiota whereas cabbage is the best for my microbiota," he concludes. "But in general, if you eat a diverse diet that contains plant polysaccharides, eventually you are going to help the good guys." g

Gerry Weiss stands in a soybean field that was planted using only two tilling passes (instead of a typical four to seven), narrower rows, and a preemergent herbicide to yield a fuller crop that blocks out weeds. It's just one example of the innovation found at his Grant County farm.

THE METHOD MAKER

Gerry Weiss, a Grant County farmer, scientist, and permaculturist, recounts a lifetime of innovation and collaboration with CALS and UW Cooperative Extension

BY DAVID TENENBAUM

PHOTOS BY MARK HIRSCH

Gerry Weiss BS'67 admits he knew nothing about the steep-valleyed fields of southwestern Wisconsin when, back in 1975, he bought 350 acres in Grant County and started raising forage, row crops, swine, and beef cattle. A native of flatter lands in Dane and Columbia counties, he knew the unfamiliar geography would present a true challenge, perhaps decades of trial and error. But Weiss began farmwork at age five, and he was taught to appreciate an experimental attitude right from the start.

"My father and my two uncles were innovators," says Weiss, now 72, as we sit at his kitchen table, stacked high with papers, research studies, and farm magazines. "I learned that you advance by being more efficient, more focused. They told me, 'The answers are in front of you. Keep your eyes open.'"

Following their advice helped him earn agricultural accolades at an early age. He reveals to me that he is still the only FFA member to be named State Star Farmer, State FFA Speaking Contest winner, and State FFA Officer all in one year. That prodigious resume, combined with his incisive nature, propelled him to earn a B.S. (with honors) in animal sciences at CALS and a doctorate from Iowa State University, though he occasionally mocks his Ph.D. as standing for "piled higher and deeper."

Weiss is intelligent, erudite, and challenging, with an unpredictable, probing sense of humor and a proclivity to pun in English and German — a vestige of his time as a postdoctoral researcher in the Netherlands and Germany in the 1970s. He followed his work abroad with a stint as senior meat scientist at Union Carbide and then a job as assistant to the president, focused on technology and science integration, at Dubuque Packing Company.

His education and private sector career did not, however, teach Weiss much about permaculture, rotational grazing, humane ways to wean cattle, or a hundred other systems, tactics, and processes that he invented, honed, or proved on his land and in his barns. Thinking of these innovations, I suggest to Weiss that he seems to have carved his own furrow, but he balks at my words. "I have not plowed a single furrow in Grant County," he says.

What he means is that, in 40 years of farming, he has not used a moldboard plow — the device that John Deere invented in 1837 and is still used today. By turning over the soil and exposing it to rain and wind, the moldboard plow raises conservation questions, at least to a visionary like Weiss.

"WE ATTITUDE"

Weiss's sloping farm, located just a few miles from UW–Madison's Lancaster Agricultural Research Station, sits inside Wisconsin's Driftless Area. The region is known for its exceptionally rugged terrain due to the utter lack of glacial bulldozing (i.e., drift) and for the meandering paths that the Wisconsin and Mississippi rivers and their tributaries have slashed through the landscape.

Many Wisconsinites look upon this unique geography — and the adaptations necessary for living within it — with genuine pride. Likewise, many are proud of the connections between CALS and the economic engines of farming and food processing. These linked industries are vital to the state; they employ 413,500 people and generate $88.3 billion in economic activity.

Weiss resides at the heart of all of this — a born innovator who adjusts to the conditions thrust upon him and exemplifies the connection between academic experts and those who make a

The seven pastures on Weiss' terraced farmland converge at this point (above) to promote the easy movement of his herd of Gelbvieh cows (left). "After five days of grazing in one pasture, they come here to let me know they're ready to move," he says. "All you have to do is swing a gate. No trap pens, no catching cattle, no hauling them to the next pasture." The use of this system of rotational grazing in Wisconsin was cultivated by Richard Vatthauer, an emeritus professor of animal sciences, and Bill Paulson, former superintendent at UW's Lancaster research station, Weiss says. Rotational grazing keeps weeds in check while stimulating grass growth, which helps prevent soil erosion.

living raising crops and animals. And it's a pipeline that flows in both directions. Weiss credits **Bill Paulson**, former superintendent at the Lancaster station, with valuable suggestions for weed control and a seed mix for improved pastures and other conservation practices, such as waterways, that still thrive today. It was the first of many connections that have benefited Weiss — and CALS — over the course of four decades.

Some of this collaboration pertains to permaculture, that basket of approaches to farming that develops sustainable agricultural ecosystems through thoughtful observation and creativity. Despite the name, permaculture is not, Weiss says, a "set-and-forget" operation. It takes real work to manage acres of permanent pasture. Fortunately, Weiss is energetic — and relentless.

"I have never worked with terraces that have had so much constant maintenance," says Grant County soil conservationist **Kevin Lange**, who has worked with Weiss for almost 30 years. "He'll fix the rodent holes, scrape the soil back to the top."

Weiss does all of this in addition to testing the soil, fertilizing as needed, winning the war on weeds, and conducting his own research. The last one, according to Lange, is special — most farmers lack the time for it. "If they are interested in research, they are interested in reading somebody else's work," he says. "He's always checking in, always got something new he wants to try."

Any success he's had, Weiss attributes to what he calls a "we attitude," a propensity for collaboration. This mentality has led to fruitful partnerships with two land-grant institutions (UW–Madison and Iowa State University) and their associated extension units and agricultural research stations, as well as the Natural Resources Conservation Service (NRCS) at the U.S. Department of Agriculture. "I don't know all of the answers," he says. "And if I don't know it, I'm on the phone, and I'll admit that I don't know it."

To find the answers, Weiss asks some tough questions. Lange admits that he can be an acquired taste. "Sometimes when he calls, you have to take a certain amount of his guff and give back a little bit of lip of your own," he says. "But it's not too insulting. That's just our thing. Somehow, I got to be his guy."

"THE ANIMALS TAUGHT US"

Weiss's agricultural education, and his unusual approaches to the hurdles of farm life, began with his father's wisdom

"My father and my two uncles were innovators. I learned that you advance by being more efficient, more focused. They told me, 'The answers are in front of you. Keep your eyes open.'"

about "open eyes." One outcome of that observant nature appears as soon as we enter Weiss's cattle housing. At first, I wonder whether I'm in a barn or a carnival fun house lightly scented with manure. The floor is nowhere close to level, the gates are built to telescope to different lengths, and odd angles are as common as right ones.

These peculiar features are all designed to get cattle to move where he wants, Weiss says, and they're built to suit the innate tendencies of a herd. "The animals taught us," he says. "They like to stick together, to walk along the wall, and to walk downhill. We don't use sticks or prods to move them. Don't need to."

The highway guardrails outside the barn also represent lessons learned from the cattle. They're part of a humane, common-sense system that started with fence-line weaning, the practice of allowing cows and their young to associate — but not nurse — to ease a traumatic separation. The technique presented itself as the solution to an obvious need if your eyes — and ears — were open, Weiss says.

After weaning, "You could look at the anxiety of the calf and its mother and could tell it was pretty high," he says. "The calf would stand in the gate area, bellering until it lost its voice, and the cow would stand at the pasture gate somewhere and beller. Nobody was happy. You could bring a baton and direct the orchestra."

But the whole equation changes if the pair can see, smell, and even touch each other. "They have less stress," Weiss says. "Baby can talk to its mother, and she can look through the fence [or guardrail] and see that her baby's okay." Within days, both sides have quit singing the separation blues.

Decades later, fence-line weaning is gaining acceptance in beef operations. The benefits, Weiss says, are measurable. "We weigh when we wean and again before we sell the calves as feeders. They are gaining 1.8 or 2 pounds per head per day. With high-stress weaning, they are pacing, bellering. They're pretty wound-up little critters, and the gain is more like 0.75 or 1 pound per head per day."

Defying conventional weaning wisdom led to another example of the "Weiss method," one designed to address what he calls "another part of the horrible tradition" with calf weaning. "You would jab them with needles for antibiotics and vaccine," Weiss says. "Talk about making a calf feel great! It would take four to six weeks to get past all that."

That was the way it had always been done. But Weiss had better ideas, many of them related to vaccinations. In the late 1970s, he helped Norden Labs of Lincoln, Nebraska, demonstrate a protocol designed to prevent *E. coli* infection and rotavirus in calves, a method that involves no stressful catching or needle pricking. "We administered this to the beef cows two weeks prepartum to generate maternal antibodies for the mom to pass on to the newborn calf," Weiss says. "Our calf scour [diarrhea] incidence dropped to zero and has remained at zero since our working with this vaccine."

"That vaccine … which originally goes back to the Norden product, is one of the most, if not *the* most, commonly used methods to prevent *E. coli* and rotavirus diarrhea in calves," says **Simon Peek**, a clinical professor of large animal internal medicine at the UW–Madison School of Veterinary Medicine. "It's something pertinent, relevant to the state, and it's definitely made a big contribution."

"WE DEVELOPED BIOSECURITY BEFORE IT WAS A WORD"

To Weiss, continuous improvement is simply common sense. "You make advances step by step," he says. "We saw the same attitude at CALS and at Iowa State. Once you do something, you see an opportunity to do it even better."

He learned this method early through his father and uncles, who were early adopters of farrowing crates for swine. "Originally there was a 5-foot by 7-foot pen, but we transformed that to put mother in a more confined area so it would be harder to lay on her little ones," he says. "Then we hung a heat lamp to draw them away from mother. Then we raised the farrowing crate to keep the young pigs off the cold concrete floor, and manure would fall through the grate so the babies stayed clean."

Demonstrating the ingenuity that has helped drive Wisconsin to the forefront of animal agriculture, the Weiss farmers developed a system that involves washing the sows to remove worm eggs and manure and then washing the crates as well. "A clean mom with a clean udder is a whole lot better than a dirty mom," Weiss says. "We progressed to a much-improved, higher-growth performance with a much lower load of bacteria and worms. We helped develop biosecurity before it was a word."

Weiss found other ways to focus his creativity on animals. In 1994, he built a specialized pig barn designed for scientific investigation. As proprietor of the on-farm science business Progress Plus LLC, Weiss has used the barn to perform contract research for the late **Mark Cook**, professor of animal sciences, as

The entrance and exit to special swine housing on Gerry Weiss' farm sits at trailer height for ease of loading and unloading pigs. The ramp has shallow steps that are easier for animals to navigate and makes a 45-degree turn so pigs are urged on by their own curiosity rather than being driven. "They want to know what's around the corner," Weiss says. "I have never carried a weaned pig up that ramp." The system, which he says he borrowed from Madison's Oscar Mayer plant where he made swine deliveries in his youth, reduces stress for pigs and hassle for farmers and processors.

well as private firms in the hog industry. The building has five rooms, each with its own feed supply and manure pit, to enable side-by-side comparisons of input and output in swine.

"There are so many variables, so this barn was ideal for conducting complex trials quickly," Weiss says.

It's also the perfect place for a data-obsessed farmer-scientist, one who listens to an inner voice and never settles for "good" when "great" is begging to be invented.

"I DIDN'T KNOW ANYTHING ABOUT THIS STUFF"

As we cruise Weiss' farm on a tractor road, I notice the ride is exceptionally smooth — no ruts, wallows, or washouts. So he tells me about the 10-inch layer of breaker run and gravel beneath his pickup. The overkill design is not needed on this dry summer day, but when he has to tend the cattle or haul manure in the rain, it prevents wheels churning through the mud, which would translate into erosion.

Even after July's staggering rainfall, there's no mud, no hint of a gully, no erosion in sight throughout our drive.

The subject of erosion returns us to the 1970s and to the role of publicly supported science. "I grew up on the Arlington prairie," Weiss says. "I didn't know anything about this stuff out here." From the USDA NRCS, he received advice on filling gullies and constructing terraces, diversions, and waterways to halt soil erosion that had measured 13.1 tons per acre per year on his land. Some of those gullies, he says, were deep enough to hide the bulldozer that he hired to repair them.

A despiser of waste, Weiss was loath to take the waterways out of production, and he figured hay or conservation practices would yield a saleable crop while preventing erosion. And so, unembarrassed by his ignorance, he contacted Bill Paulson, then the superintendent of UW–Madison's nearby Lancaster experimental station.

"USDA had its own seeding specifications," Weiss says, "but the difference was that Bill had actually done it. He'd perfected the seed mixture; it was an unbelievably positive addition to what we were doing. Bill knew what would work here."

Thirty-eight years later, Weiss continues to do soil tests and fertilize as needed, but he has not had to reseed his pasture. "We just take the hay off," he says. When waterways and terraces are always covered, soil and stream bank erosion are practically zero.

"It may seem obvious, but I've never had anybody mention [hay harvest from waterways] to me," says **Dan Schaefer** BS'73 MS'75, longtime head of the Department of Animal Sciences, when asked about Weiss' permanent seeding of these erosion protections. Meanwhile, Weiss is happily hauling hay, which is profitable in today's market.

This initial interaction with Paulson led to many more collaborations with CALS. Weiss has opened his own land and crops for pesticide trials conducted by the departments of agronomy and entomology. Last summer, the only row crop on the farm was a soybean trial that assessed weed resistance to herbicide. All in all, Weiss has taken part in more than 220 research trials related to animals and crops.

"PEOPLE THOUGHT I WAS NUTS"

Decades ago, the process of accounting for homegrown organic fertilizer became another element of the Weiss method. Working with UW researchers, he developed systems to track the nitrogen and phosphorus added to the soil by manure and legume crops.

"I was one of the first to utilize manure in a nutrient management plan, working with [Grant County] UW Cooperative Extension agent **Ted Bay**

MS'80," Weiss says. In two growing seasons, using soil analyses from the Marshfield Agricultural Research Station, he cut his fertilizer bill by 70 percent. As with his work with cattle, one improvement begat another. To maximize savings, Weiss bought a manure spreader able to change application rates to supplement nutrients based on variations in soil tests.

But the simple logic in favor of buying only as much fertilizer as you need would have been plowed under had Weiss listened to his neighbors — or his fertilizer dealer. "People thought I was nuts, yes, for 25, 30 years," Weiss says, "but we were supported by the agronomy and soil science faculty in Madison."

If you spend enough time with Weiss, you begin to assume that any allusion to conventional wisdom will be chucked to the wayside if not squarely onto the dung heap of history. It's how he stays ahead of the curve. Today, the "nutrient credits" that can reduce fertilizer use and environmental damage are required on many Wisconsin farms. They're also integral to SnapPlus, a software program created by experts at the Department of Soil Science.

"He's a land-grant creation. To me, he epitomizes the application of science to agriculture."

"SnapPlus solves several problems at once, related to distributing manure and fertilizer efficiently, while meeting guidelines for protecting groundwater and surface water," says associate scientist **Laura Good** MS'88 PhD'02, who has led its development and testing. "The program helps to maintain crop fertility without wasting money or endangering natural resources."

Just like manure, legumes are a critical part of permaculture. Aided by soil microbes, plants like alfalfa and clover absorb nitrogen from the atmosphere and put it back in the soil to make it more fertile. Decades ago, when most farmers dedicated fields to pasture or row crops, Weiss planted legumes in his permanent pastures and pioneered the use of "rotational grazing." Moving cattle from field to field not only protects the pasture from trampling and overgrazing but also reduces tilling and hauling of feed and manure. At the same time, it increases fertility and productivity, so any given field can support more animals. The practice of moving cattle is now a mainstay of organic and other low-impact agriculture.

"YOU DON'T NEED TO DO THIS!"

Weiss's collaborations with CALS have also involved planting innovations. At a time when planting and cultivating corn entailed at least a half dozen passes across the field, he teamed up with frequent collaborator Paulson, soil science professor **Larry Bundy**, and agronomy professor **Ron Doersch** BS'58 MS'61 PhD'63 to develop a two-pass corn-planting system.

"You disk in manure and cornstalk residue with a heavy disk, doing primary tilling in one pass," he says. Then, aggressive trash whippers on the planter clear a seven-inch row for the corn as the planter sprays a preemergent herbicide.

"We found that most years, with normal rain, we got such tremendous activity from the preemergent herbicide that we did not need a second pass of spraying, but a very limited number of people have picked that up," Weiss says. "They are locked into four to seven passes for tilling, planting, spraying, and then spraying again. People, you don't need to do this! We are reducing labor, soil compaction, and fuel burn, and also recreational tillage."

But having a motive to disbelieve can overpower the evidence of open eyes, he adds. "I've had salesperson after salesperson come here to look at a field after the soybeans have been drilled and shake their heads," Weiss says. "The field is still relatively rough, which I want for rain erosion prevention. I've had many of these guys come back at harvest, and say, 'This is really a tremendous plant environment.' When I respond, 'But four months ago, you told me this was a disaster,' they get real quiet. But it always seems easier to criticize than to try to understand why I keep doing it."

A different attitude, both positive and more open-minded, prevails at UW–Madison and the other land-grant institutions, Weiss says, and the attitude is mutual. "He has always been respectful of faculty, though he will speak out if someone has a loony idea," Schaefer says. "He's principled, all about accurate data, accurate communication. There's no varnishing, no window dressing.

Gerry Weiss surveys his farm from the seat of his pick-up truck while parked at a high point in one of the pastures.

'Tell it to me the way it is.'"

In this way, Weiss has managed to survive in the ever-changing farm economy for 40 years. Today growing forage is profitable, so hay is what he sells, usually delivered to horse owners in small bales.

The swine barn is now empty — another victim of harsh market conditions — so the Gelbvieh cows that Weiss collaborated to import from Germany in the 1970s are his only livestock. Having grown to understand (so I think) the many labor-saving and cow-saving innovations on the farm, I ask why he has only 60 head. As the question hovers above the kitchen table, I immediately realize that I have plunged into the manure pit called conventional wisdom. Bigger is not necessarily better, and the answer is in front of my face, though Weiss is kind enough not to mention that.

"I match the cow herd to the rotational grazed pasture program," he says. "Sixty head is my carrying capacity with my current 68 acres of permanent pasture, but we have plenty of room for more pasture here."

Such an expansion, Weiss says, would best be carried out by the next generation of stewards of his land. He is now on the hunt for a "very special person or people" to continue where he leaves off. When students of the agricultural sciences visit his farm to learn from its innovations, he tells them his successor just might be among their ranks.

"I also tell them," Weiss says, "that I haven't made all of the mistakes yet, but I'm getting close."

"THE BARBS ARE QUITE DULL; THEY ARE JUST GERRY WEISS"

Thinking back, Weiss' meticulous attention to the land and his characteristic dry wit are both on display the moment we first meet. I drive onto the farmstead with my road bike racked behind my economy Honda and approach a weathered, white-haired guy pitchforking Canada thistles from the back of a white Ford pickup.

By way of introduction, I ask, "Aren't you too old for that?" He responds, "Oh, I think we're going to get along just fine. You can give it back."

Later that day, as we tour the fields, I tease Weiss about a lone Canada thistle proudly blossoming above a pasture. Even a city fellow knows that those splendid purple flowers are one of Wisconsin's premier pasture pests, and Weiss immediately promises to annihilate it to block it from reseeding.

I mention the thistle to Lange, the Grant County conservationist, and he remarks, "I'm surprised that he did not write down the location. If he was younger, he would have put it on GPS, but I'm sure it's gone by now." Indeed, when Weiss later meets me for lunch in Spring Green, he hands me a thorny, withered thistle. "Some salad from the farm!" he says.

"He's very conservation conscious," says weed expert **Jerry Doll**, professor emeritus of agronomy. "He once called after an 8-inch rain, happy that his grass waterways and terraces had no visible erosion, while his neighbors were looking at gullies."

"His mind is always churning," Doll adds. "I don't know how he sleeps at night. I know his power of observation. When he sees something he can't explain, he's on the phone."

Like Doll, others who have worked with Weiss typically cite his inquiring mind and diligence, as well as his devotion to conservation. They also like to mention his low-grade combative nature.

"Gerry is very bright and quite self-deprecating," Schaefer says. "He can be prickly and takes pride in barbed comments, but he does that mostly for effect. He wants to know if he's getting through to you. The barbs are quite dull; they are just Gerry Weiss."

But underneath Weiss' thorny exterior, Schaefer sees the embodiment of a precept of the great Midwestern public universities. "He's a land-grant creation. To me, he epitomizes the application of science to agriculture." g

in the field

BY GILLIANE DAVISON

DARYL BUSS MS'74, PhD'75

Daryl Buss grew up on a small Minnesota farm where he enjoyed daily work with a variety of animals. On the farm, Buss quickly realized the importance of the local veterinarian and regarded him as an early role model. This early fascination with veterinary medicine propelled Buss down a path of academic accomplishments, beginning with a veterinary medicine degree from the University of Minnesota and followed by a lifetime of accomplishments at UW–Madison. Buss received his master's degree from the Department of Veterinary Science in 1974 and rolled straight into his Ph.D., focusing his research on the cardiopulmonary system. From there, Buss held a variety of academic and research positions at numerous institutions such as the Max Planck Institute for Physiological and Clinical Research in Germany and the University of Florida, Gainesville. In 1994, Buss returned to Madison and was hired as the dean of the UW School of Veterinary Medicine. He served for 18 years and helped solidify the school's position as one of the top professional schools of veterinary medicine in the country. Today, Buss utilizes his years of expertise as the editor-in-chief of the *Journal of Veterinary Medical Education*. "After many years in academic administration, this role has offered a new and complementary venue for continued national and international engagement with veterinary medical education," Buss says.

KRIS ELLINGSEN BS'79

Spending your workday surrounded by fluffy felines may sound like a fantasy for cat lovers, but for **Kris Ellingsen** it's just another day at the office. As a veterinarian with a special interest in cat care, Ellingsen enjoys interacting with both the feline patients and their owners while helping make cats better understood and cared for properly. Her journey to feline medicine began at age 16 with her first job, working for a local veterinarian — a job she kept while pursuing her CALS undergraduate degree in bacteriology. After the UW School of Veterinary Medicine (SVM) opened in 1983, Ellingsen realized she could combine her passion for medicine with her love for animals. She applied and was accepted into the Class of 1988. After graduation from the SVM, she headed to the Pacific Northwest, where she spent 11 years in Seattle and the past 18 in Portland, Oregon. In Seattle, Ellingsen found her ideal position at Cats Exclusive Veterinary Center, one of the first feline-only clinics in the U.S. She currently lives in Portland, where she works as a veterinarian for Cat Care Professionals. Aside from her daily veterinary medical practice, Ellingsen has also been involved with the non-profit Feral Cat Coalition of Oregon since 2001. In 2008, she was elected president of the organization, which helps to feed, treat, and spay or neuter more than 6,000 feral and stray cats annually.

KATHY HUNTINGTON MS'91

If you ask **Kathy Huntington** how she chose a career in animal pathology, she may argue that it chose her. "Pathology is like a big puzzle to figure out, and I love that challenge," she says. "That, along with my love of wilderness and wildlife, makes it a pretty amazing combination for me." In hindsight, it seems like an obvious fit, but her path to pathology wasn't so simple. Huntington began her career with a degree in zoology before coming to the UW–Madison campus, where she received a D.V.M. followed by a master's degree in veterinary science and wildlife diseases. She relocated to Alaska upon graduation and began practicing as a small animal veterinarian. After a few short years, Huntington was sure of two things: she loved Alaska, but she was not content as a small animal veterinarian. Luckily, her degree in wildlife diseases was there to rekindle a forgotten passion and jump-start her career in wildlife pathology. Huntington now works as a diagnostic pathologist and owner of Alaska Veterinary Pathology Services. There she acts as a consultant and research pathologist on projects with marine and wildlife agencies such as the Alaska Department of Fish and Game, the U.S. Geologic Survey, and the U.S. Fish and Wildlife Service. In the field, Huntington is able to learn all about the diverse species that inhabit what she calls one of the United States' most transformative and scenic states.

About *In the Field* | *CALS graduates highlighted here represent the depth and breadth of alumni accomplishments. Selections are made by* Grow *staff and are intended to reflect a sample of alumni stories. It is not a ranking or a comprehensive list. For more about CALS alumni, visit* ***cals.wisc.edu/alumni****.*

Alumni making their mark in VETERINARY MEDICINE

TRAVIS KUHLKA BS'03

Travis Kuhlka became interested in animal agriculture when he was a freshman in high school. He accepted a job at a local hog farm, where he found his niche caring for sows and piglet litters. When it came time to choose a career, Kuhlka stuck to his experience and pursued a bachelor's degree in animal sciences from CALS. Here he worked as a large animal reproduction technician for a campus lab and acted as the head student veterinarian at the UW–Madison Veterinary Medical Teaching Hospital. This clinical experience solidified his career path into veterinary medicine. Upon graduation, Kuhlka applied to the UW School of Veterinary Medicine, where he earned his D.V.M. Today, Kuhlka lives in North Dakota and practices as a large animal veterinarian through his private company TK Veterinary Services. Though his technical training is in veterinary medicine, Kuhlka credits CALS for his foundational skills, such as how to safely handle cattle, relate to farmers' lifestyles, and understand clients' needs. "I attribute my background in livestock handling to my relationships and experiences with those in the Department of Animal Sciences," Kuhlka says.

GAYLE LEITH MS'85

Gayle Leith says she has achieved her childhood dream. "I grew up in southern California riding horses and was fortunate to realize my career goals as an equine veterinarian at a very young age," she says. Leith earned her master's degree in veterinary science and D.V.M. at UW–Madison. Today she is an owner and partner of an equine referral practice through Arizona Equine Medical and Surgical Centre. There she acts as a self-named "family practitioner for horses," making routine and emergency visits to stables. But these stables aren't always nearby. Once a year, Leith organizes a group of veterinarians and hikes into the Grand Canyon to provide veterinary medical care to the horses of the Havasupai Tribe. "My favorite part of my work is helping horse owners maintain the health of their four-legged friends," Leith says. Now a seasoned veterinarian, Leith enjoys passing on her expertise to students and interns. In 2010, Leith took her passion for teaching a step further by completing a master of arts degree in learning with technology, and she has been teaching an undergraduate science class at Ashford University ever since. Keeping horses healthy and happy may be her dream, but Leith also enjoys a rewarding life outside of the office. She loves to travel and enjoy the outdoors with her husband, Preston, and daughter, Jordyn, but horses never stray too far from her mind. Some of her favorite equine activities include trail rides with her family and training her young thoroughbred gelding for the show ring.

DAVID LUNN MS'87

David Lunn was born in Wales and received his bachelor's degree in veterinary science at the University of Liverpool in 1982. After spending two years practicing as a veterinarian, he ventured to America and earned his master's degree in veterinary science from UW–Madison. In 1988, he returned to the U.K. and received his Ph.D. from the University of Cambridge in 1991. Just a year later, Lunn became a certified diplomate of the American College of Veterinary Internal Medicine and returned to UW–Madison. Here he served as a professor in the School of Veterinary Medicine for nine years before accepting a job as an associate dean and director of the UW–Madison Veterinary Medical Teaching Hospital. Today, Lunn serves as the dean of the North Carolina State College of Veterinary Medicine. He is a renowned expert in equine immunology and infectious disease, backed by more than 90 academic publications, 16 book chapters, and service on countless boards, committees, and review panels. At NC State, he enjoys a busy but exciting career. As the veterinary medical college's dean, Lunn is responsible for many, many things, but student education continues to be his top priority. "Our most important role is making better vets," he says. "We are constantly trying to find ways to improve education at every level and find the best opportunities for these young people." Even the busiest careers require occasional rest and relaxation. In his downtime, Lunn hikes with his wife, Kathy, raises terrier pups, and skis inexpertly but enthusiastically.

Catch up with…
Anna Snider BS'98 Horticulture

Anna Snider's recent volunteer work has taken her to Nigeria, Bangladesh, and beyond, but her love of horticulture and farming started in Wisconsin. She grew up in a rural area outside of Fond du Lac, where she served as president of the local FFA chapter and spent most of her time outside — either in the garden or at her uncle's and grandparents' farms.

At UW–Madison, Snider immersed herself in her horticulture major. She became president of the university's Horticulture Society and organized its first tour of Costa Rica with the help of faculty mentor **Jim Nienhuis** PhD'82. That trip marked the first of many related to the world of international agriculture. As a volunteer with the USAID-funded Winrock International Farmer-to-Farmer program, she travels to developing countries all over the world to provide technical assistance for farmers, farmers' organizations, and agribusinesses.

Photo courtesy Anna Snider

Anna Snider meets with a family in Abuja, Nigeria, following a workshop in which she taught methods for growing vegetables in sacks to conserve space and improve household nutrition.

HOW DID YOU BECOME INTERESTED IN WORKING IN AGRICULTURE AND FARMER-TO-FARMER LEARNING?

After my undergraduate degree, I worked for horticulture professor Jiwan Palta, and that was my first job with international experience. I managed projects in Wisconsin, California, Ecuador, and Florida, and it prepared me for international work. During my master's degree work, I became fascinated with the social issues that affect agriculture and food security in developing countries. I wanted to understand the reality in these countries, including how agribusinesses and consumers in developed countries can have a positive influence on environmental and social conditions. When I started working for Cornell Cooperative Extension, I felt that there was really a lack of experience in sustainable agriculture in many places, and I wanted to help.

WHAT HAVE YOU DONE ON YOUR TRIPS WITH THE ORGANIZATION?

My earlier projects focused mainly on sustainable production practices and composting. Those projects were in Kyrgyzstan, Lebanon, and Bangladesh. In Nigeria and Senegal, I worked with the leaders of farmers' organizations on strategic planning, leadership, and engaging women and youth in entrepreneurship. Farmers' organizations in these countries rely heavily on funding from the government or support from nonprofit organizations, and we work together to figure out how they can become more self-reliant and resilient.

WHAT DO YOU LIKE BEST ABOUT THE WORK?

I love working with farmers to solve problems. I also love that it gives you opportunities to see places, interact with locals, and understand the country in a way that you never could if you were just traveling. For example, in Senegal, I was invited to the hut of the village chief to discuss challenges and concerns with the administrative council of the local banana cooperative. The group was quite frank about the problems of trust or conflict among the members and how they deal with that according to their cultural traditions of arbitration with tribal elders. It was fascinating.

Farmer-to-Farmer is always looking for volunteers. Visit ***winrock.org*** *to find opportunities.*

—Caroline Schneider MS'11

Photo courtesy UW–Madison Department of Dairy Science

Dan Truttmann (foreground), owner of Truttman Dairy, answers questions from "Team Guernsey" — students Abigail Martin, Courtney McCourt, and Anthony Schmitz — during the 2015 Badger Dairy Challenge.

'Dairy Challenge' Offers More than Competition

There's no better place than America's Dairyland for a dairy farm management competition that helps undergraduates learn firsthand about the industry.

The Badger Dairy Challenge, hosted by the Department of Dairy Science, brings teams of four or five students together to analyze real farm records, cow management data, and nutritional information. After a site visit, the teams then develop suggestions for improvement and present them to a panel of industry professionals. The challenge was last held in fall 2015 in partnership with the University of Minnesota and will make its return to campus later this year.

After seeing the benefits of the North American Intercollegiate Dairy Challenge for many years, faculty associate **Ted Halbach** established the Badger Dairy Challenge in 2012 to give a broader range of students an early opportunity to immerse themselves in the field.

"The idea is for beginning-level dairy science students to get involved," Halbach says. "Students starting their education in dairy management have an opportunity to be mentored in the Badger Dairy Challenge, and it's less about competition and more about experience and learning."

Senior dairy science major **Anthony Schmitz** BSx'18 competed in his sophomore year and is hoping to gain a spot on the national team this year. "You have to work your way up and try out," Schmitz says. "It's competitive, actually, because a lot of students are interested in it, and it's a good way to use the skills and the knowledge that we have learned in the classroom in a practical, real-life situation."

While there are similar programs at schools across the country, as well as regional and national dairy challenges, Halbach believes that Wisconsin is best positioned to provide a positive impact on the careers of these students.

"Within a half-hour [drive from campus], we have multiple farms that we can call on that are different than [those that participated] a year ago," Halbach says. "There aren't many schools that have that resource, so we're very fortunate for the willingness of those farms to participate."

Halbach puts a lot of work into it, but it takes more than human resources to sustain the program. The challenge receives funding from a mix of dairy organizations and CALS alumni. For example, an annual golf outing raises between $25,000 and $30,000 each year for scholarships and high-impact learning opportunities.

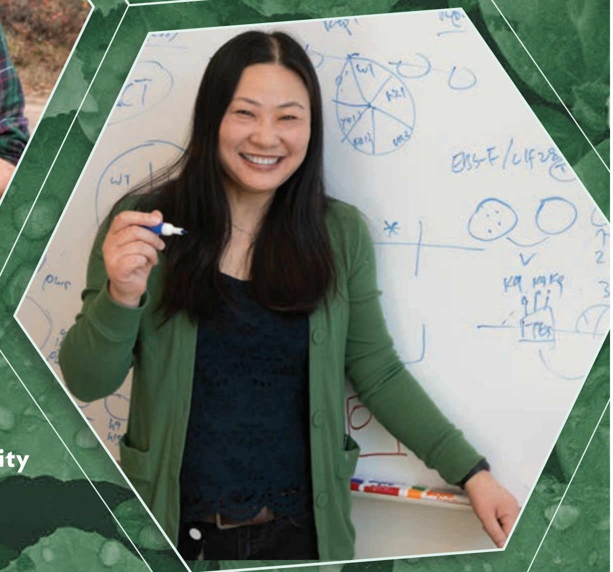
"Our alums have either financially supported the program or they're very willing to contribute their time to serve as officials or mentors for the students during the events, which is every bit as valuable," Halbach says.

There are also incentives for people in the dairy industry to be involved in the competition. According to Schmitz, the program provides a convenient opportunity for employers to make connections with potential hires, and vice versa.

"It's a great way to get your name out there because the contests are officiated by industry professionals, so it's a really good way for you to make an impression on that kind of person," Schmitz says. "Most of the students competing have already been locked in by somebody because they are sought-after talent."

—Andrew Pearce

YOU CAN SUPPORT THE BADGER DAIRY CHALLENGE with a gift to the Dairy Science Department Fund. Visit **supportuw.org/giveto/dairyscience** and add "support for Dairy Challenge" in the text field. Or contact Development Director **Jodi Wickham** at **jodi.wickham@supportuw.org** or **(608) 308-5315.**



From food systems to healthy ecosystems, from bioenergy to community development. These are just some of the fields where CALS faculty, staff, and students are leading the way with new discoveries and innovations. We are grateful to sponsors like Covance for helping to make these advancements possible.

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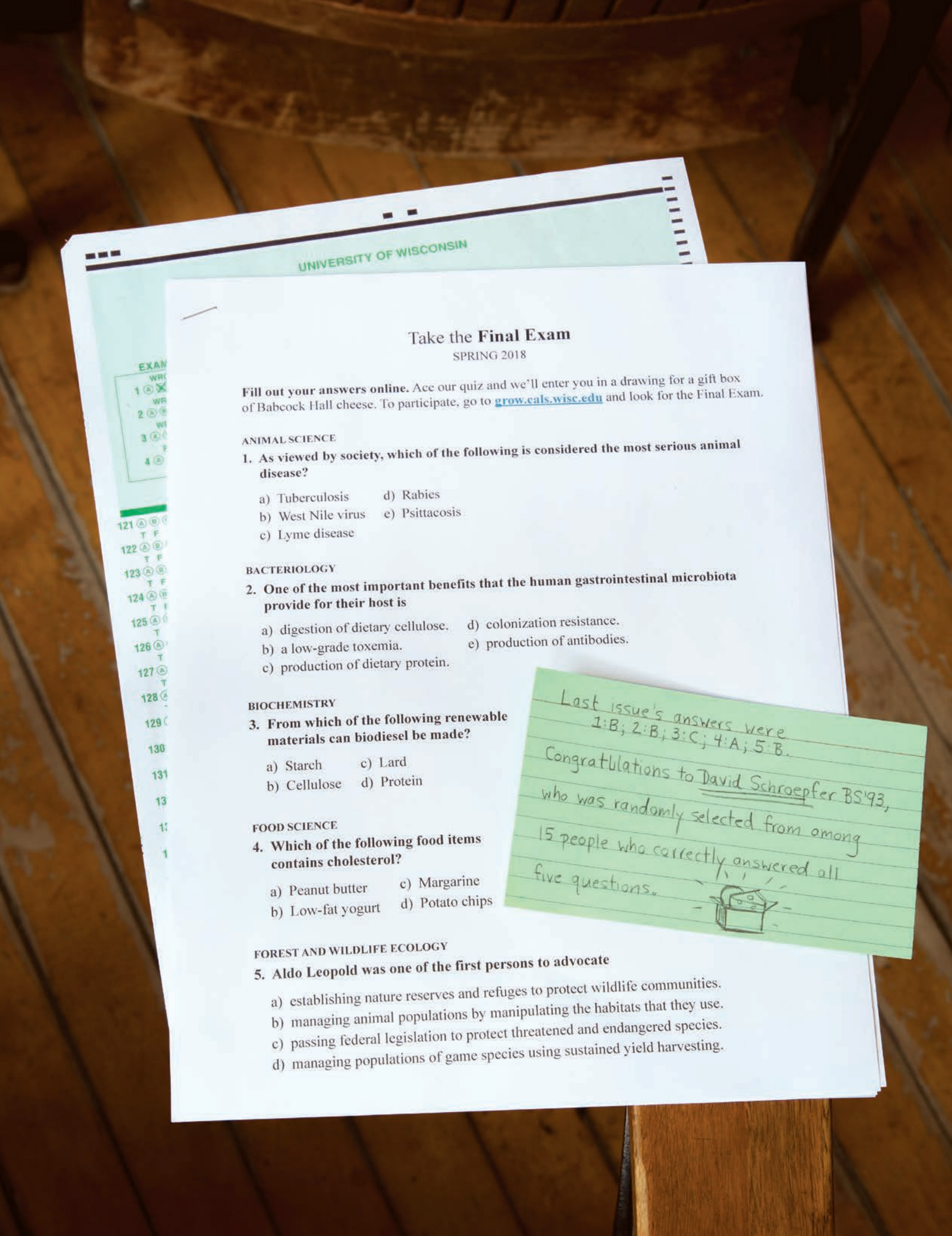

Take the **Final Exam**

SPRING 2018

Fill out your answers online. Ace our quiz and we'll enter you in a drawing for a gift box of Babcock Hall cheese. To participate, go to **grow.cals.wisc.edu** and look for the Final Exam.

ANIMAL SCIENCE

1. As viewed by society, which of the following is considered the most serious animal disease?

a) Tuberculosis
b) West Nile virus
c) Lyme disease
d) Rabies
e) Psittacosis

BACTERIOLOGY

2. One of the most important benefits that the human gastrointestinal microbiota provide for their host is

a) digestion of dietary cellulose.
b) a low-grade toxemia.
c) production of dietary protein.
d) colonization resistance.
e) production of antibodies.

BIOCHEMISTRY

3. From which of the following renewable materials can biodiesel be made?

a) Starch
b) Cellulose
c) Lard
d) Protein

FOOD SCIENCE

4. Which of the following food items contains cholesterol?

a) Peanut butter
b) Low-fat yogurt
c) Margarine
d) Potato chips

FOREST AND WILDLIFE ECOLOGY

5. Aldo Leopold was one of the first persons to advocate

a) establishing nature reserves and refuges to protect wildlife communities.
b) managing animal populations by manipulating the habitats that they use.
c) passing federal legislation to protect threatened and endangered species.
d) managing populations of game species using sustained yield harvesting.

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A wide range of plants, from fruits and vegetables to grains and spices, are studied at the Walnut Street Greenhouse on the UW–Madison campus. The research primarily benefits Wisconsin agricultural crops.

PHOTO BY SEVIE KENYON BS'80 MS'06