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Lab Warfare

Scientists combat resistant microbes

PLATES OF HONOR
A memorial to last meals

TURNCOAT PROTEINS
What future blood tests may reveal

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Volume 7 Number 3 // oregonstate.edu/terra // Spring 2012

FEATURES

Julie Green memorializes final meal requests by death-row inmates who have been executed. See "Plates of Honor," Page 20. (Photo: Hannah O'Leary)

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Oregon State University is a leading public research university with more than $262 million in research funding in FY2011. Classified by the Carnegie Foundation for the Advancement of Teaching in its top category (very high research activity), OSU is one of only two American universities to hold the Land-, Sea-, Sun- and Space-Grant designations. OSU comprises 11 academic colleges with strengths in Earth systems, health, entrepreneurship and the arts and sciences.

Terra is published by University Relations and Marketing and printed with vegetable-based inks on paper with 55 percent recycled content (30 percent post consumer).

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On the cover
OSU researchers are culturing colonies of a soil bacterium isolated from the Indonesian blackwater ecosystem in an attempt to classify it and identify its bioactive compounds. See "Battling the Superbugs," Page 6 (Photo: Jan Sonnenmair)

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THE CULTURE OF INFECTIOUS IDEAS

It could be called the "Tale of Two Steves." Steve Wozniak was the technical genius. Steve Jobs was the visionary. Inspired by a local computer-users group and surrounded by technology giants such as Hewlett-Packard and Xerox, they created the first computer for people who were not engineers or computer-science majors. Like the discovery of gold at Sutter's Mill, the birth of Apple Computer marked an economic turning point.

It didn't hurt that the two Steves lived near Stanford University and its culture of infectious ideas. Proximity matters.

Oregon doesn't have quite the critical mass of Silicon Valley, but the same point applies. When creative people share ideas, new ventures emerge. A recent example in Corvallis begins with the "Tale of Todd and Scott." That is, Todd Miller, prototyping manager of the Microproducts Breakthrough Institute, and Scott Gilbert, chemical safety officer at the MBI. Both have expertise in the science of microfluidics, the behavior of flowing liquids confined in tight spaces.

Gilbert spent years in Switzerland working on a microfluidics approach to an analytical technique known as "liquid chromatography on a chip." He formed a company, Crystal Vision Microsystems (yes, inspired by the Fleetwood Mac song) and received support from the Swiss government. The market turned out not to be as receptive as he thought, and then came the dot-com bust in 2001. Over the next few years, Gilbert found new allies in the United States, but competitors had also advanced, and when the recession hit in 2008, he pulled the plug.

It was at a Portland meeting sponsored by the Oregon Nanoscience and Microtechnologies Institute (ONAMI) that Gilbert and Miller met. Gilbert was looking for a petrochemical "micromixer," a device that processes liquids through a honeycomb of tubes slightly wider than a human hair. Miller had developed prototypes that might do the trick. A partnership was born.

Today, Miller is president and Gilbert is chief technology officer of Microflow CVO™ (CVO is the flight code for Corvallis Municipal Airport). The company has licensed technology from Oregon State University and launched its website on May 1. John Turner, Microflow CEO and OSU College of Business instructor, estimates that the global market for such devices in the life sciences alone is about $2 billion and expected to grow to $3 billion by 2014.

It's a bit premature to put Microflow's founding up against the origins of Apple Inc. But an estimated 47 Oregon startup companies received private or public investment in 2011. The culture of infectious ideas is nurtured by statewide research initiatives such as ONAMI and Oregon BEST. Oregon State's land grant mission calls us to set the stage for their success.

Nick Houtman

Editor

[Editor's note: OSU MBA student Ken True interviewed Scott Gilbert about Gilbert's journey from Swiss inventor to Oregon entrepreneur.]

Hail Oceanus!

Marine research vessel switches coasts

It was a beautiful day for a shakedown cruise off the Oregon coast. For a crew based at Oregon State University's Hatfield Marine Science Center, March 7, 2012, was also a good day to get to know their new ship, the research vessel (R/V) *Oceanus*.

Scientists and crew took *Oceanus*, the sister ship to OSU's R/V *Wecoma*, under the Yaquina River Bridge and past the jetty into the Pacific where they practiced deploying water and sediment samplers and launched *Jane*, an autonomous underwater glider.

Since 1975, *Wecoma* has been OSU's marine science workhorse on research expeditions from the Arctic to the Antarctic. A recent evaluation of the two vessels revealed a need for expensive repairs to *Wecoma*, which was decommissioned after *Oceanus*' arrival from the Woods Hole Oceanographic Institution.

The College of Earth, Ocean, and Atmospheric Sciences will operate *Oceanus* for its owner, the National Science Foundation. OSU also operates the 54-foot *Elakha* and 85-foot *Pacific Storm* for near-shore research.

The Exercise Gender Gap

Men are more active than women

Men exercise more than women do — 18 minutes of moderate-to-vigorous activity for women versus 30 minutes for men, on average — a study has found.

This is bad news for women, who are more prone to "metabolic syndrome" — a cluster of risk factors including so-called "stubborn belly fat" often targeted in diet ads. Exercise is one of the best ways to prevent or shed extra tummy pounds along with twin health worries high cholesterol and high blood pressure. But that's not all. Exercise also can boost mood and buoy optimism, say the study's authors Bradley Cardinal of OSU and former OSU student Paul Loprinzi, now at Bellarmine University in Kentucky.

"Those who get at least 30 minutes of exercise a day are less likely to be depressed, less likely to have high cholesterol and less likely to have metabolic syndrome," the researchers conclude.

Exercise habits start in childhood. But even for adults, it's never too late to change. Pressed for time? Solutions can be as simple as spurning the elevator and climbing the stairs. Even pacing while talking on the phone can enhance your health, the researchers say.

Of Predators and Herds

Big meat-eaters mean healthy ecosystems

The health of any ecosystem starts with razor-like teeth and an appetite for meat. The "apex" predators — big carnivores like bears and wolves at the top of the food web — keep things in balance, OSU researchers have found in study after study in the western United States.

Now, the findings have been confirmed on a larger scale: the entire Northern Hemisphere. When big predators are wiped out, as wolves were in the American West during the last century, herds of plant browsers balloon, according to a survey of 42 studies from Canada, Alaska, the Yukon, Northern Europe and Asia. The elk, moose and deer — fearless in the absence of the furry lurkers — linger longer in riparian zones, trampling riverbanks and gobbling up young trees and other plants that sequester carbon, shade streams and shelter countless other animals, say William Ripple and Robert Beschta of the College of Forestry. Biodiversity plummets.

"The preservation and recovery of large predators may represent an important conservation need for helping to maintain the resiliency of northern forest ecosystems, especially in the face of a rapidly changing climate," they add.

Life-Saving Science

BY RICHARD SPINRAD, VICE PRESIDENT FOR RESEARCH

AT A RECENT MEETING OF the American Meteorological Society in New Orleans, I participated in a discussion of early warning systems that give the public time to take cover from tornadoes and to prepare for hurricanes. Today, we have hours or days to get out of harm's way. Contrast that with the hurricane in Galveston, Texas, in 1900: Inability to track and warn of the storm led to the deaths of more than 8,000 people. That event still ranks as the United States' most deadly natural disaster.

For me, the meeting stimulated important thoughts about scientific inquiry. If researchers save lives, are they "heroes"? One common concept of heroism refers to putting one's life at risk for the safety of others. We think of a firefighter rescuing a child from a burning building or a soldier risking death to save a comrade. While scientists do not always take chances with life and limb in field and lab work, their efforts often save lives.

Remember polio? By the early 1950s, the epidemic had killed thousands and left many more paralyzed. Most victims were children. As a boy, I watched a neighbor move slowly, awkwardly, with great effort, using metal braces and crutches. I remember standing in line with my classmates to receive a revolutionary dose of precaution. Vaccines developed by Jonas Salk and Albert Sabin eliminated new cases of polio from not only my community but from most countries and dramatically reduced its worldwide incidence. I name Salk and Sabin among my champions.

Design for Maximum Benefit

At Oregon State, I think of work by our Construction Engineering faculty, who focus on the safety of homes, buildings, roads, freeways and bridges. Rescuing someone from underneath rubble takes heroism, yet preventing disasters by thoughtful design and construction can also be heroic, with far-reaching benefits.

Take our students in Engineers Without Borders. They have brought clean drinking water to communities in Central America and are working today in Africa to reduce the death rate from waterborne diseases and to improve quality of life.

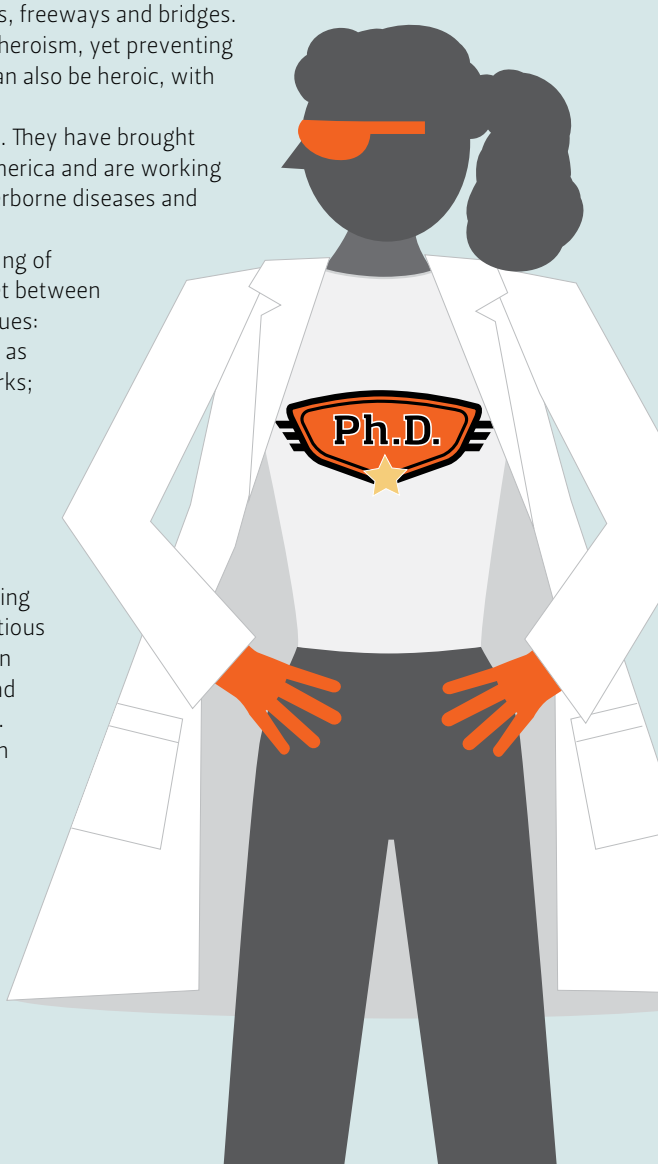
Oregon State's contributions to the understanding of tsunamis and earthquakes are widely heralded, yet between "events," many of us don't think about related issues: preservation of critical lifelines, such as key roads, airports and utility networks; seismic upgrades to buildings; and strategies to protect public safety during an event and to help a shattered region rebuild.

A hero is someone who has given his or her life to something bigger than oneself.

— Joseph Campbell

Maintaining public health is no less of a challenge. Researchers in our College of Pharmacy are developing new ways to prevent and treat infectious diseases. In the College of Public Health and Human Sciences, researchers address obesity, diabetes and cancer with sound science and with personal care.

Of the more than a quarter-billion dollars' worth of research conducted at OSU, a large percentage aims to protect human life. In my book, that makes our researchers a band of heroes. So I add my humble definition to Joseph Campbell's quote above: A hero is someone who dedicates his or her life to creating knowledge for a safer world.



Data Driven

Chris Patton uses computer modeling to help build world-champion racecars

BY CELENE CARILLO

The computer models Chris Patton wrote for Oregon State's Formula SAE team helped create a faster, more efficient car. (Photo: Robert Story)

WHEN CHRIS PATTON WAS HELPING his Formula SAE team design a racecar for international competition, he made an unusual suggestion: angle the rear wheels outward in relation to the car. Common knowledge would warn against that move. Turning the rear tires outward makes the car less stable.

But Patton, a Ph.D. student in mechanical engineering at Oregon State University, had a powerful tool at his disposal: the ability to simulate the impact of that move.

The results were surprising — and positive.

"We would tell design judges at the competition that we were doing this, and they wouldn't believe us. We would have to measure it in front of them," he says. "They'd tell us our car would be slow and undriveable. And then we'd go out and be the fastest car in competition."

Being the fastest is one of the reasons why Oregon State's Formula SAE team, in partnership with a student team at DHBW-Ravensburg in Germany, has been so successful. In 2011 the team won Formula Student Germany, which is widely considered to be the premier competition in the world. They also won back-to-back national championships in the United States in 2010 and 2011.

The trick for Oregon State's team, at least in part, has been computer simulation. During his seven years with Formula SAE (sponsored by SAE International, formerly the Society of Automotive Engineers), Patton has set the team apart by expanding the range of parameters used in designing its car. The flexibility of Patton's modeling structure is one of the key parts of his dissertation.

"We can basically program the car in a computer and make comparisons between different cars without having to build them," Patton says. "I can say, 'You want to add this parameter? And this parameter? Sure, just add it in.'"

By "program," Patton means he writes scripts in the programming language MATLAB that represent all the characteristics the team needs to consider when designing a car — whether to turn the rear wheels outward or to make the body of the car narrower or wider.

He starts with processing tire data collected by the transportation research company Calspan and the Formula SAE Tire Testing Consortium. To the uninitiated, it might seem like the raw power of the engine is what drives the car's motion. But tires, Patton says, are the foundation for the cars the team builds.

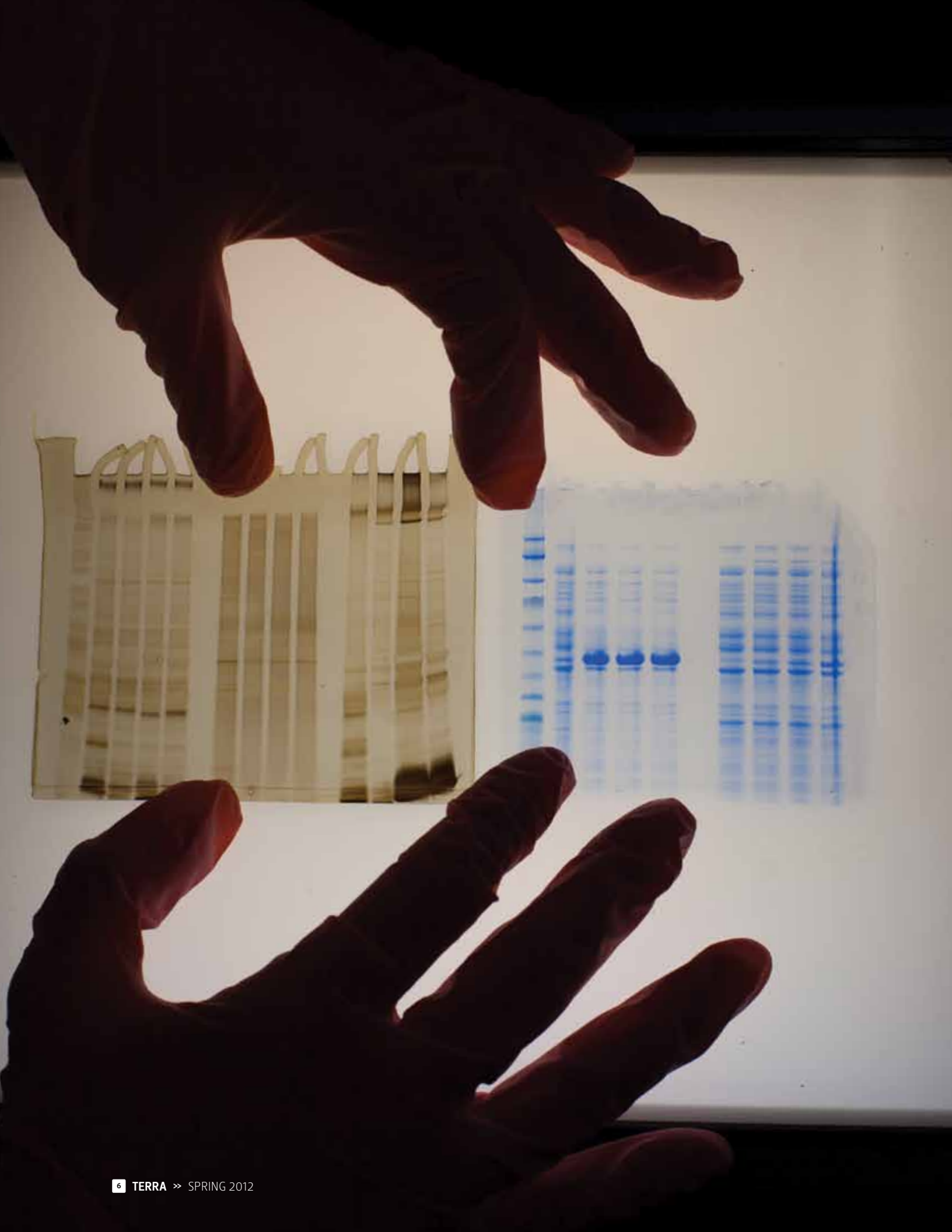
"Tires are where all of the motion of the car comes from," he says. "All of the forces that dominate the movement of the car come from the tires."

Tire data give him information about how the tires behave when they're in motion. For example, he gets measurements for friction against pavement, tire pressure and temperature, and how tires behave when the driver applies the brakes.

Having a detailed sense of what the tires will do ultimately gives the team a much better idea of how to design other elements of the car, and it helps them understand how those elements will behave in competition.

"I'm pretty confident that no other teams are doing the modeling at the level we're doing it. There might be some that are close, but I don't think it's very common. I would say that's something unique to us," Patton says.

ON THE WEB: See *Relentless*, a video about the team's success, oregonstate.edu/relentless



Battling the Superbugs

Science wages war on bacteria that are resisting modern drugs

BY LEE SHERMAN | PHOTOS BY JAN SONNENMAIR

This story has echoes of an epic journey, the kind told by Homer, J.R.R. Tolkien, L. Frank Baum and George Lukas — a story of heroes tramping the Earth (or the galaxy) on a quest to defeat the forces of darkness. Along the way, the travelers encounter strange creatures with remarkable powers. They endure harrowing tests of mental strength and technological prowess. In the end, they prevail, bringing down the enemy and discovering a truth that saves civilization.

It's not a huge stretch to say a story like this is unfolding at Oregon State University. Against legions of bacteria and other microbes that cause TB, cholera, malaria and other infectious diseases, a cadre of OSU scientists has taken up arms. Their light sabers are machines called chromatographs and mass spectrometers. Their droids are "high-throughput" plate readers and underwater robots. Their curative elixirs derive from weird and remote organisms like gelatinous "sea squirts" from Africa's Cape of Good Hope and giant tubeworms from the Axial Volcano a mile beneath the Pacific Ocean.

"Once life-saving medicines are increasingly having as little effect as a sugar pill. Microbial resistance to treatment could bring the world back to a pre-antibiotic age."
~World Health Organization, 2000

The story's ending has yet to be written. But so far, the odds are with the germs. As Earth's first inhabitants, bacteria have a 3-billion-year evolutionary jump on *Homo sapiens*. Superbly adept at adaptation, they've found genetic avenues into every ecological and biological niche, from polar icecaps to the human gut. They divide like crazy (some can double their population in nine minutes) and use an astounding array of strategies to make themselves at home. Many bacterial species do good things, like recycle waste. But other species, the ones scientists call pathogens, can invade and quickly overwhelm their host organisms, whether animal or plant. Miracle drugs like penicillin, once seen as impregnable shields against deadly infection, are losing their power as the bacteria regroup and recalibrate.

For all its brainpower and glittering technology, modern science is struggling to stay ahead of these microscopic shape shifters. The microbes have outmaneuvered just about every drug medical science has thrown at them.

This is the story of OSU's heroic battle to outwit these cunning adversaries. From running high-speed experiments in Corvallis, to surveying patients at Portland's Oregon Health & Science University (OHSU), to combing health-care databases for trends, the researchers are attacking infection and prevention from every conceivable angle. They search vast international databases for promising compounds. They decipher mechanisms for disease-promoting phenomena like bacterial sliming and swarming behaviors. They ponder unlikely-seeming disease pathways, such as those between pigs, fish and humans.

The eight professors in the colleges of Pharmacy, Science and Veterinary Medicine you will meet in these pages gather biweekly to trade insights and design collaborative investigations, ranging from microbes' molecular structures to hospitals' dosing protocols to urbanites' risks for drug-resistant infections. Here we look in on their journey, from lab bench to sickbed to public square.

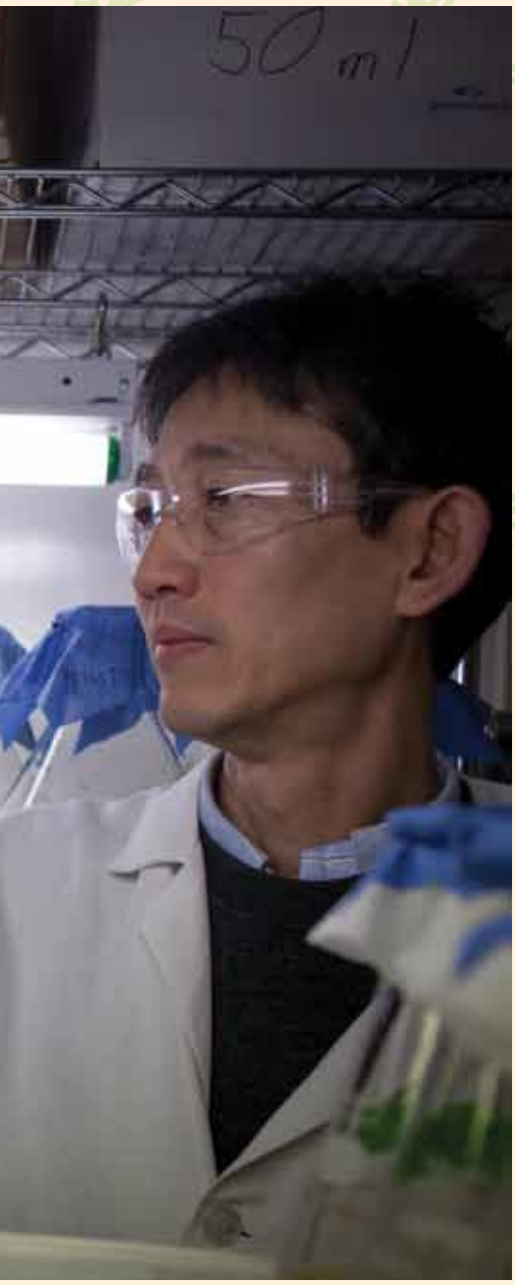
On a light box, an OSU researcher observes protein gels used in biochemical experiments.

In Brief

Pathogenic bacteria are becoming resistant to the arsenal of drugs developed to cure scourges such as malaria, TB, sexually transmitted diseases and even common staph infections. Thousands die annually when effective medications are unavailable or, increasingly, nonexistent. OSU scientists are taking a coordinated, multi-pronged approach to this global problem. They are testing novel bacteria for antimicrobial properties, finding new ways to disrupt bacterial defenses and calling for caution in the routine use of antibiotics in food production and other areas.

Kerry McPhail reaches into a Styrofoam cooler and lifts out a jagged black rock the size of a cantaloupe. "We collected this from an active volcano on the bottom of the Pacific, a mile deep," she says, her voice accented with the musical tones of southern Africa. Under her office's fluorescent lights, the rock's sharp facets shine like obsidian.

Her pride in this solidified chunk of deep-sea lava might suggest that McPhail is an Earth scientist. Why else would she join a 2009 NOAA expedition exploring the Axial Seamount 250 miles beyond Oregon's shore? So it's curious to learn that McPhail is neither a geologist nor an oceanographer, but a medicinal chemist in the OSU College of Pharmacy. Curious, too, is the fact that her research endeavors aboard the voyage were funded in part by the National Institutes of Health (NIH), along with Oregon Sea Grant.



In their natural-products lab, Kerry McPhail (left) and Taifo Mahmud examine a flask containing an antibiotic-producing red marine cyanobacterium growing in modified seawater. The cyanobacterium produces different toxins depending on the composition of the seawater.

What McPhail was seeking in those lightless depths, with the help of a diving robot named Jason II, was new sources of life-saving drugs. The black rock, grabbed by Jason II's mechanical arm from inside the caldera, was coated with billions of protozoa that thrive on super-heated sulfurous waters at vent sites, where magma bubbles up from the subterranean. As unlikely as it seems, this bluish "microbial mat" may harbor healing chemical compounds never seen before. McPhail and her team have brought home other promising vent-dwelling extremophiles, as well, collected from giant tube-worms, "snow blowers" (white clouds of microorganisms spewing out in 200-degree plumes), orange-colored biofilms (slimy layers of swarming microbes). Some of her specimens were collected during the famous 2008 NOAA expedition when a never-before-witnessed eruption of the underwater volcano was caught on tape by OSU scientists.

"There's an enormous diversity of microbes down there that people just had no idea about," she says.

But the cold Pacific isn't McPhail's only odd-organism goldmine. Closer to Zimbabwe, where she spent her childhood on an agricultural research station and later in the capital city of Harare, she has been collecting and studying gelatinous creatures called tunicates. Known colloquially as "sea squirts," these sac-like filter feeders are plentiful in the waters off South Africa. Having previously isolated potential anti-cancer compounds from tunicates, McPhail now has begun testing them for possible antibiotic properties. She also collaborates with OSU medicinal chemist Taifo Mahmud, who studies the curative powers of rare microbes living in the soils of "blackwater ecosystems" in the tangled jungles of Indonesia (see "Nature's Medicine Chest," *Terra*, Fall 2010).

Why are these strange and remote creatures so intriguing to McPhail? Why are deep-sea vent organisms significant enough for the NIH to award her one of its coveted "R21" grants for high-risk, exploratory projects? What makes tunicates worth the regular trips she makes to South Africa to collaborate with a fellow scientist at Rhodes University, where she got her Ph.D.?

It's their very rarity that makes them promising in drug discovery.

Resistance Times Ten

Pathogens resistant to one or more drugs are on the rise. Below are 10 diseases associated with antimicrobial resistance identified by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC).

1. ANTHRAX. Occurs rarely in humans. Caused by exposure to infected animals or animal products. Also has been used in bioterrorism weapons.
2. BACILLARY DYSENTERY. Caused by a bacterium called shigella. Kills more than 1 million people per year, mostly children.
3. BACTERIAL PNEUMONIA. A leading cause of serious illness among young children worldwide. Overuse of antibiotics contributes to emerging resistance.
4. CHOLERA. Sickens up to 5 million and kills more than 100,000 people per year. Many bacteria show resistance to some antibiotics.
5. GONORRHEA. A sexually transmitted disease infecting 62 million people per year. Strains may be resistant to penicillin, tetracycline and fluoroquinolones.
6. MALARIA. A mosquito-borne disease that infects 216 million people per year. Resistance, found in two of four human malaria parasite species, is fueling disease rates.
7. MENINGOCOCCAL DISEASE. An infection that can affect the spinal cord, brain and bloodstream. The first cases of fluoroquinolone resistance in the United States were reported in 2007.
8. MRSA. MRSA is a skin-based staph infection resistant to methicillin and other antibiotics. Serious or life-threatening infections occur most often in hospitals and health-care facilities.
9. TUBERCULOSIS. Second to HIV/AIDS as top infectious killer, taking nearly 1.5 million lives yearly. Multidrug-resistant TB is present in nearly every country surveyed by WHO.
10. TYPHOID FEVER. A food- and water-borne disease infecting 22 million people yearly. Increasing resistance to drugs, including fluoroquinolones, presents a treatment challenge.

Aleksandra Sikora, along with her husband and research partner Ryszard Zielke, is investigating ways to combat the germs that cause cholera and gonorrhea.

"Unique organisms from unusual, diverse ecosystems have unusual chemistry," says McPhail. "My lab is testing these organisms for unknown bioactive compounds — ones that target pathogens in unexpected ways. These compounds then can be used to design a new generation of drugs to fight infection."

Tracing the chemical "fingerprints" of these novel compounds against known compounds catalogued in databases and examining microbial growth patterns in Petri dishes are the first steps in drug discovery. Next, McPhail will move on to studying disease progression in animals. Once again, she's eyeing a singular creature. This time, it's the waxworm. Surprisingly, this caterpillar larva of the wax moth (a member of the "snout moth" family) has an immune system similar to that of mammals. That trait, along with being cheap and plentiful, makes the waxworm an excellent subject for drug discovery.

Nature of the Beast

In the global fight against infectious disease, new drugs are urgently needed. That's because bacteria and other pathogens are evolving day-by-day, minute-by-minute, to withstand the onslaught of existing drugs. They survive by creating mutant versions of themselves or by swapping whole chunks of DNA with other microbes. Not only have pathogens learned to foil single drugs, they're now fending off multiple drugs simultaneously. These multidrug-resistant germs have been dubbed "superbugs" in recognition of their ninja-like powers of intracellular infiltration and assassination.

Worldwide, nearly a half-million cases of multidrug-resistant tuberculosis take hold in human lungs each year, causing 150,000 deaths, according to the World Health Organization. (Learn about the TB research of OSU microbiologist Luiz Bermudez in "Targeting an Old Foe," *Terra*, Winter 2009.) Drugs also are failing to cure malaria in countries ravaged by the mosquito-borne protozoan, which annually kills 650,000 people, mostly African children. Other killers include cholera, typhoid and pneumonia. Dangerous staph infections resistant to an older antibiotic called methicillin, as well as many current antibiotics, are rampant in hospitals and making forays into the community at large. (see sidebar).

"For every antibiotic that's ever been used, resistance has developed," says OSU researcher David Bearden. "It's a hard game to play, because the truth is, the more you use it, the less well it's going to work. That's just the nature of the beast."

It's that beast's nature — elusive, mutable — that captures Bearden's imagination as a clinician. Infectious agents, he says, are a lot like those moving targets in the carnival booth. By the time you get one in your sights, a new one has taken its place.

"It's a foreign-invader scenario," explains Bearden, who chairs the Department of Pharmacy Practice. "You're giving drugs to the person to kill the living organisms that are attacking them from inside. And all the while, the thing you're fighting is changing."

Just outside the window of his 12th-floor Portland office, the aerial tramcars connecting OHSU's South Waterfront to Pill Hill creep up and down the forested slope like silver beetles. On the adjacent lot below, workers in hardhats are running cranes and positioning girders for the Collaborative Life Sciences Complex, a joint project of OHSU and the Oregon University System. Bearden and another dozen pharmacy researchers who work at the OSU Center for Health and Healing will join scientists and clinicians of OHSU and Portland State University in the new complex when it opens in 2014.

While McPhail and Mahmud are rummaging in some of nature's most peculiar ecosystems for new drugs, Bearden is looking for better ways to use the drugs already available. Resistance gets a boost when too many people take too many antibiotics, he points out. Patients suffering from colds and flu may request — even demand — antibi-

otics from their doctors. But because those common ailments are caused not by bacteria but by viruses, taking antibacterial drugs is an exercise in futility. Adding to the problem, many patients take their prescriptions inappropriately or stockpile antibiotics for future use. Remnant germs may lurk in the organs or tissues of their human host, building strength for another assault.

To combat the misuse and overuse of antibiotics, Bearden is looking into optimizing dosages and calibrating them for special groups, such as the obese. "Substandard dosing — concentrations that fail to inhibit or kill all of the bacteria — can induce or enrich resistance," says Bearden. "Say you have a population of 1 million bacteria, and maybe 1,000 of them are very resistant. If you kill off 999,000 of them, the rest of them have this nice, free niche to become the dominant population."

From her office a few strides from Bearden's, OSU epidemiologist Jessina McGregor elaborates: "Optimizing the choice of drug, the dosage, the duration of therapy and the route of therapy — whether oral, topical or intravenous — are the next steps in prudent antibiotic use after first cutting down on overuse. That's the focus of a lot of pharmaceutical research on infectious disease."

Bio-Bargain Hunter

When Aleksandra Sikora gets excited about a buy-one-get-one-free deal, it has nothing to do with the half-yearly sale at the mall. Rather, she does her bargain hunting in scientific supply catalogs, such as the dog-eared booklet from Greiner Bio-One that sits on her desk. By stretching dollars, the OSU microbiologist can run more experiments with the startup grants that currently fund her research on cholera (which sickens more than 300,000 yearly) and gonorrhea (the most prevalent infectious disease in the United States).

Opening a cupboard in her level-2 bio-safety lab in OSU's Pharmacy Building, Sikora takes out a crisp new package of clear-plastic trays, each about the size of a slice of bread.

"We use 20 to 30 of these sterile plates each time we run a screening for bioactivity," says Sikora, who grew up in Poland and has a Ph.D. from the University of Gdansk. "They're expensive, $3 to $4 each. If you buy them from Greiner Bio-One, you get one free for every two you order."

What she's after in those screenings are "hits" — that is, signs of bioactivity. A bioactive agent or compound is one that affects a living organism such as the gonorrhea-causing bacterium *Neisseria gonorrhoaeae* or the cholera-causing bacterium *Vibrio cholerae*, Sikora's current subjects of study. A hit can show up as a faint glow ("bioluminescence"), which some microbes emit as they send chemical signals back and forth. It can also show up in patterns or rates of bacterial growth. Lack of growth, too, can tell a story.

If she gets a hit, she can see it almost instantly on a computer screen. Thanks to her pricey plastic trays and an even-pricier BioTek plate reader she ordered for her lab soon after arriving at OSU last fall after her post-doctoral training at the University of Michigan Medical School, the whole process is automated. She can run nearly 3,000 tests in just minutes using the high-speed robotic machine, which purrs with perfect precision. That's because each plate contains 96 "wells" — little troughs that hold samples of bacteria inoculated with whatever compounds are being tested — and the plate reader holds up to 30 plates. Scientists call this type of ultra-fast screening "high-throughput" — in other words, putting samples through chemical and biological analyses at accelerated rates (compared to the old days, when researchers had to run them manually, one at a time).

The gleaming stainless-steel gear gracing Sikora's lab will let OSU's team of infectious-disease researchers create their own "compound library." To that end, Sikora is testing extracts and bioactive compounds from McPhail's vent organisms and sea squirts and Mahmud's blackwater bacteria, along with her own experiments.

Sikora's target in the infectious-disease battle is the microbe's cell wall — the point of contact between the pathogen and the host. It's where virulence gets a toehold. Instead of targeting the whole cell with a drug designed to kill it outright, Sikora and Ryszard Zielke, her husband and research partner, hope to block "virulence factors," the actions of bacteria that cause disease. Toxins and other proteins secreted from the cell wall, as well as the wall's composition, are of particular interest.

Chatty Bacteria

In the pantheon of weird sea creatures, the Hawaiian bobtail squid ranks near the top. This 2-inch "stealth bomber of the ocean," as *Natural History* magazine calls it, is worthy of Dr. Seuss's imaginary bestiary. This tiny nocturnal squid even has a biological buddy, a bacterium called *Vibrio fischeri* that dwells inside a sort of built-in lampshade on the belly of the eight-legged cephalopod. The squid nourishes the dense bacterial populace, which repay the favor by glowing just enough to cancel out the squid's silhouette as it swims, rendering it invisible to predators. "Interestingly," OSU microbiologist Martin Schuster notes, "the bacteria don't glow when they're out in the open ocean by themselves."

How do these one-celled wonders accomplish this astonishing feat of

variable bioluminescence? As biologists discovered in the 1970s, they do it by sending chemical signals back and forth. These bacteria essentially talk to each other in a process called "quorum sensing," a stunning discovery that led to a paradigm shift in microbiology: the realization that microbes aren't loners but rather social creatures that communicate and cooperate with each other.

"Microbes talk," says Schuster. "And we're listening in."

The discovery of quorum sensing in *Vibrio fischeri*, a microbe beneficial to its host, set off a flurry of new findings. Cell-to-cell communication, it turns out, is common in disease-causing bacteria, too. This includes *Pseudomonas aeruginosa*, the primary organism under study in Schuster's laboratory. This notoriously antibiotic-resistant bacterium causes serious hospital-acquired infections and is the main cause of death among people suffering from cystic fibrosis.

Schuster is studying how germ-to-germ dialog fosters disease-causing actions among bacteria, such as secreting harmful toxins or enzymes that break down host tissue. Biofilm formation, a gabfest among millions of microbes, is another. These "cities of microbes" can be up to 1,000-fold more resistant to antibiotic treatment than free-floating bacteria and are the source of many chronic infections. They build a slimy coating that shields the germs deepest within the biofilm. They draw strength from their surrounding compatriots.

"Biofilms and nasty toxins that harm the host are produced by bacteria as a group," Schuster says. "It's a concerted effort."

What Schuster hears as he eavesdrops on these secret chemical conversations constitutes a novel approach in antibiotic design: disarming rather than killing the pathogen with so-called anti-virulence drugs. "With traditional antibiotics, you basically wipe everybody out," says Schuster. "Only the resistant clone remains and then just explodes."

From Bedside to Public Square

Drug-resistant staph infections go viral

"The 'nice' thing about serious S. aureus *infections is that they can occur in anyone at any time for no good reason."*

~Mark Crislip, M.D.
Infectious Disease Compendium

Most of Portland is still punching the snooze button when morning rounds begin on Pill Hill. By 6 o'clock, teams of doctors, residents and medical students have draped their stethoscopes around their necks, collected their clipboards and greeted their first patients at OHSU's teaching hospital. Joining one of the white-coated clusters, the family-medicine team, is OSU pharmacy researcher and clinician Ravina Kullar. "I'm the main drug person onboard," she explains. "I have a great role, educating residents on infectious disease, antibiotics, dosing of medication. It all comes together at the patient's bedside."

After growing up in London and then Pittsburgh, Kullar earned her infectious-disease credentials at ground zero, Detroit Medical Center. "Detroit is the mecca of infectious disease," she says. "It's where resistance developed."

A big worry facing the health-care system is a bug called MRSA (methicillin-resistant *Staphylococcus aureus*). A common bacterium that lives on the skin, *S. aureus* is usually harmless. When it does cause infection, the cure used to be simple: prescribe a penicillin-type antibiotic. But staph infections are getting tougher to treat as the bacteria dodge drug after drug.

So far, Oregon has seen less MRSA than many other states, according to OSU pharmacy researchers at OHSU. But even in Oregon, MRSA is mounting. At OHSU, Kullar estimates, at least 75 percent of the patients she sees have some kind of resistant staph infection. "Almost everyone turns up with a positive culture for MRSA in their skin or bloodstream," she says. " It's the top organism for skin and soft-tissue infection in hospitals."

But it's not just health-care settings where MRSA thrives these days, according to the Oregon Health Authority. Resistant infections such as boils, abscesses and cellulitis are gaining ground in the general community, too — so-called "community-associated" MRSA, as opposed to "health-care-associated" MRSA.

This new strain, warns Portland physician Mark Crislip in his online *Infectious Disease Compendium*, "is sweeping the world," causing "plagues of boils, necrotizing soft-tissue infections and hemorrhagic pneumonia."

Kullar has seen MRSA patients from all walks of life, from IV drug users to teenage athletes. "There was even an outbreak in a football team," she reports.

One drug user in his 30s was suffering from endocarditis, an infection of the heart valve. He had been given vancomycin, but failed to get well. Based on her work in Detroit, Kullar switched him to daptomycin. "There was a lot of IV drug use in Detroit," she says. "I knew vanco wasn't going to work, so we went to a second-line agent." So far, the patient is doing well.

True to their nature, the resistant bacteria continue to evolve. It wasn't long ago that vancomycin was a reliable second line of defense against resistant staph infections. But vancomycin-resistant germs already have turned up in Detroit. It's just a matter of time before the new superbug, VRSA, shows up at Oregon's door. Kullar is ready. The wilier the bacterial adversary, the more she relishes the hunt. "Infectious disease is like a puzzle or a mystery," she says. "It makes me feel like a detective."

Oregon State University pharmacy researcher Ravina Kullar rides the Portland tram between her office on the waterfront and OHSU's teaching hospital on the hill, where she collaborates with doctors and medical students in the treatment of infections such as MRSA.

Scientists generally assume that if bacteria aren't threatened with annihilation, they won't work so hard to create new versions of themselves. Minus this "selective pressure" — evolution's relentless push for genetic adaptation to environmental threats — resistance won't develop. This assumption had never been tested experimentally, until now.

What would happen, Schuster wondered, if he shut off the bacterial chatter? Could he halt the behaviors that bolster the disease process? Could he slow the evolution of resistance, the looming problem with traditional antibiotics? The answer to both turned out to be yes.

Graduate student Brett Mellbye ran a number of "evolution-in-a-test-tube" experiments, mingling drug-resistant bacteria with non-resistant bacteria. The non-resistant bacteria, Mellbye discovered, got ahead by "cheating" — that is, by exploiting the nutrients and other resources supplied by the resistant bacteria. The cheating put the brakes on resistance.

"The suppression of resistance is contingent on the targeting of cooperative behaviors," Schuster cautions. The next step in verifying these findings is to move the experiments from test tubes to animal models.

Fishy Germ Swap

How could an Atlantic whitefish caught off Boston pass a germ to a pig on an Iowa hog farm that winds up infecting a teenager in Seattle? It hasn't happened yet, as far as we know. The pathway from fish to hog to human is not a straight line; it zigs and it zags. But OSU veterinary microbiologist Dan Rockey says it's just a matter of time before all the dots connect.

The reason: Antibiotic overuse isn't limited to hospitals and doctors' offices. Factory farms and feedlots,

which routinely give antibiotics to healthy livestock to promote growth and prevent disease, can become breeding grounds for resistant germs. As a rule, pigs and cows don't pass those dangerous germs to people. That's because bacterial species rarely jump from animals to humans, or vice versa. For instance, chlamydia, the disease Rockey studies, is common across the animal kingdom, yet each animal has its own version of the germ. "A single chlamydia species generally dials in to a single animal species," he explains. "The organisms that infect a koala bear or a horse or a lizard or a frog — those don't cross over."

Infectious Science

The National Institutes of Health is supporting Oregon State University researchers with $4.5 million spread across 16 active projects. Among them:

- Jon Furuno, College of Pharmacy, studies the incidence and severity of MRSA in hospitals and long-term care facilities.
- Margaret Dolcini, Department of Public Health, studies the behaviors and attitudes of urban African-American youth at risk of HIV/AIDS. Her goal is better prevention strategies.
- David Williams, Linus Pauling Institute and Department of Environmental and Molecular Toxicology, focuses on the interaction between genes and drug effectiveness in anti-malarial treatments. He aims to maximize drug effectiveness and minimize toxicity.

But as we know, bacteria everywhere are hardwired to adapt — even on an Iowa pig farm. That's where Rockey and some colleagues from Iowa State and the University of Washington recently discovered a strain of bacteria resistant to tetracycline, the most common antibiotic used to treat humans suffering from chlamydia (a range of diseases affecting eyes and sexual organs). The researchers traced the microbe to the pigs' diet: fishmeal. It appears that a complex DNA switcheroo among fish pathogens created a genetic perfect storm for tetracycline resistance.

"One fish pathogen had all the right genes coded in the right sequence," he says. "Lo and behold, crazy but true, this other fish pathogen, unrelated to the first pathogen, has a complimentary set of genes. Somehow, the two fish pathogens got together and then got into the chlamydia that infects pigs, which often are fed fish waste, especially in the Midwest. This story tells you how complicated it is for antibiotic resistance to spread between humans and animals."

So far, chlamydia in humans remains treatable with tetracycline and other antibiotics. But Rockey's research suggests that a day will come when the human chlamydia germs *C. trachomatis* and *C. pneumoniae* join the ranks of resistant germs. In his lab, Rockey was able to engineer a tetracycline-resistant human chlamydia strain using DNA from the resistant pig strain. If science can do it in the lab, nature can do it in the wild — and sooner or later, it will.

"If tet-resistance were to get into the human strain, it could spread around pretty quickly," Rockey says. "Tetracycline is a primary drug of choice against chlamydia infections. This could really be a problem, especially in developing countries."

Evidence is mounting that animal-human crossover can and does occur. Rockey cites a significant paper by the Phoenix-based nonprofit TGen (Translational Genomics Research Institute) describing how the creation of methicillin-resistant *Staphylococcus aureus* (MRSA) likely was generated by contacts among humans, pigs, bacteria and antibiotics. Here's what the study found: Pigs acquired a strain of *S. aureus* from humans, a strain that initially was treatable by antibiotics. But because pig farms are awash in antibiotics, the strain quickly developed resistance inside the pigs. Today's MRSA problem may well have originated with the next step in that chain of infection: the bacterium's jump back to humans, this time in its resistant form.

Lance Price, the TGen study's lead author, sounded a warning. "Our findings underscore the potential public health risks of widespread antibiotic use in food animal production," he said in announcing the study results in February. "Staph thrives in crowded and unsanitary conditions. Add antibiotics to that, and you're going to create a public health problem."

Skin-to-Skin Contact

Factory farms and feedlots aren't the only "crowded and unsanitary conditions" that promote staph infections. Gyms, dorms, barracks, playgrounds, day-care centers — close quarters where people have skin-to-skin contact — are a growing worry in health-care circles. In most cases, *S. aureus* is usually a harmless hitchhiker on healthy human skin. But sometimes it invades its host, often through a cut or abrasion. The boils, carbuncles, pimples, yellow crusts and milky pus associated with staph infections, while unsavory, are usually treatable. However, adding MRSA strains to this mix leads to "more and more stubborn infections at which doctors throw more

and more drugs," Rockey says. Sometimes, patients fail to respond. Sometimes, they die.

This trend gives a sense of urgency to researchers like McGregor, an OSU microbiology graduate who came back to join the faculty after getting her Ph.D. from the University of Maryland School of Medicine. Like Bearden, her colleague down the hall, McGregor is captivated by bacteria's warp-speed knack for adaptation.

"You can actually observe evolution happening!" She leans forward in her chair, the energy in her voice rising as she contemplates the awesome power of microbial communities. "You can directly observe the bacteria's response to evolutionary pressure. With larger organisms, you would have to watch for decades or millennia to witness evolutionary change."

As an epidemiologist, McGregor scans, not populations of microbes in Petri dishes, but populations of humans in all sorts of settings — cities and states, hospitals and doctors' offices, residential-care facilities and outpatient clinics. She studies long-term data and looks for trends. She plumbs the numbers to stem the threat of resistant disease.

One solution is outreach. Hand-in-hand with the Oregon Health Authority, she and OSU pharmacy students have spearheaded a local project under the national AWARE (Alliance Working for Antibiotic Resistance Education) umbrella, which fans out across the state with brochures, games, videos and face-to-face conversations for local communities. Other solutions may emerge from her current studies of urinary-tract infection patterns at Kaiser Permanente Northwest and OHSU, as well as infection rates among inpatient-versus-outpatient settings.

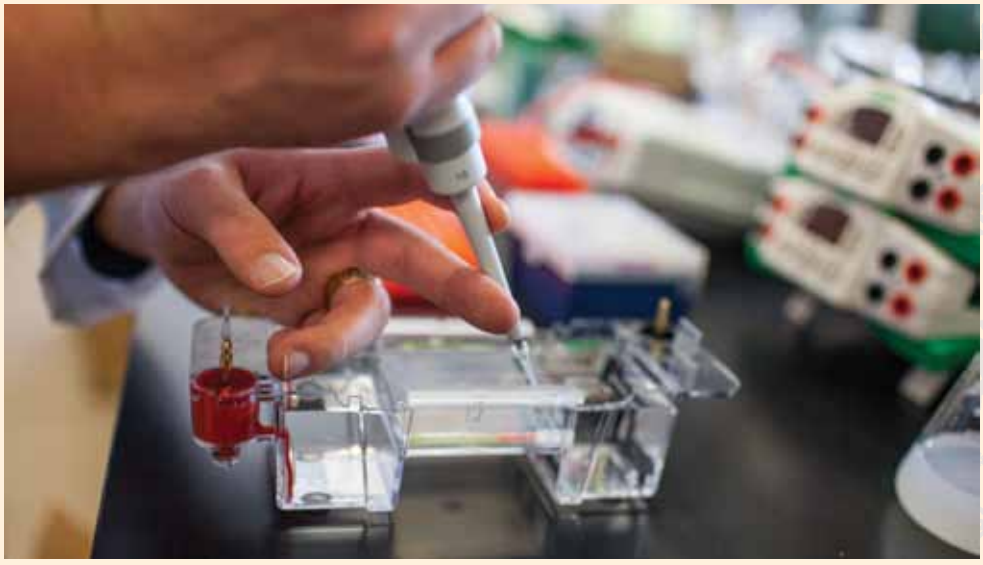
So far, McGregor says, Oregon and Portland have dodged the full force of resistance hammering other states and cities. "What's happening in Oregon is very different than in other places in the U.S.," she explains. "We have very different prescribing patterns here. Oregon is one of the lowest antibiotic utilizers per capita, behind only Alaska. That definitely helps us out.

Having locally specific information to guide our policies is important. We don't need to be reactionary ahead of the curve."

Now More Than Ever

Ironically, the escalating demand for new drugs coincides with declining dollars for antibiotic research. That's because pharmaceutical companies are concentrating on "blockbuster" medicines for patients with long-term conditions, like elevated cholesterol and high blood pressure. Antibiotics don't pencil out on the balance sheet, say six sponsors of a bipartisan bill currently before Congress. "The development of any new pharmaceutical costs hundreds of millions of dollars for basic and clinical research," write the sponsors, three Democrats and three Republicans from six states. "For antibiotics, revenue is limited because they tend to be prescribed for short-course therapies that are completed in days or weeks." If it passes, the GAIN Act (Generating Antibiotic Incentives Now) will create incentives to encourage R&D and speed up drug discovery.

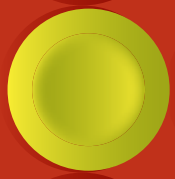
The bill's sponsors mince no scary words, spare no sobering statistics. "The antibiotic pipeline is dwindling, and a global crisis looms," they write. "Each year, antibiotic-resistant infections are responsible for tens of thousands of deaths, hundreds of thousands of hospitalizations and up to $26 billion in extra costs to the U.S. health-care system. Just when we need innovation the most, the pipeline of drugs to replace ineffective antibiotics has dwindled to a trickle."



A lab technician separates and analyzes DNA fragments isolated from a bacterium in an experiment to find natural-product biosynthetic genes.

To turn that trickle into a life-giving river, infectious-disease research at OSU and other universities is more urgent than ever. Taifo Mahmud sums it up simply: "We are running out of drugs. We have no other choice than to keep moving."

After all, a hero perseveres, no matter the cost, no matter the odds. terra



Turncoat Proteins

Scientists scope out the earliest signs of disease

BY NICK HOUTMAN

It's one of life's little ironies. The proteins in our bodies fight infection, carry messages, ferry oxygen and build tissue. But then, like double agents in a spy novel, they can betray us. They overreact to a virus and attack our own organs. They promote cancer, help clog arteries or set up roadblocks in the brain. We may never know until symptoms appear — a lump, chest pain, severe memory lapses — and irreversible damage is done.

Who wouldn't like to get ahead of these heart-stopping scenarios? By detecting proteins gone awry or elevated in the earliest stages of disease, scientists are opening up the possibility of effective therapy before health is compromised. The standard checklist on the annual physical — temperature, blood pressure, reflexes, lung function, skin condition — is already backed up by blood tests for molecular markers such as cholesterol and other proteins. What researchers envision is an inexpensive, accurate and rapid test that can be performed in a doctor's office and provide unprecedented views of our biochemistry on the fly.

Oregon State University chemist Vince Remcho likens the search for proteins to fishing. "Ultimately, you are searching for one particular protein or other molecule in a vast soup of molecules, so you have to choose the right bait. My group is in the bait business, bait and hook," he says.

In Remcho's lab in OSU's new Linus Pauling Science Center, some of that bait consists of short relatives of DNA known as aptamers. If the research team has prepared their devices properly, they will attract big fish, proteins and other molecules that fit into the nooks and crannies of a particular aptamer and no other. Remcho and his international team (hailing from Indonesia, China, Nigeria, Thailand and the United States) develop new tools — lab-on-a-chip technologies, microfluidics and nanosensors — for scientific, medical and precision manufacturing purposes. But their goals can't be achieved by chemistry alone, so at OSU, they rely on the expertise of physicists, engineers and molecular biologists to advance sensing science.

Marked Molecules

Knowing how to catch proteins is one thing. Knowing which proteins to catch is another. The U.S. Food and Drug Administration recognizes nine biomarkers for use in clinical diagnosis of cancer, and researchers have identified markers for kidney and liver disease, Alzheimer's, rheumatoid arthritis, tuberculosis and other illnesses. "There are new markers coming out every day from different labs," says Arup Indra in the OSU College of Pharmacy.

The Indra lab is one of them. In 2009, he, Gitali Indra and collaborators at OSU and in France reported a new biomarker for head and neck cancers. With funding from the National Institutes of Health, they conclusively linked a protein known as CTIP2 to squamous cell carcinoma. Squamous cells are flat, plate-like cells in the skin and the lining of internal organs. When it occurs in the head and neck, squamous cell carcinoma is the sixth most common form of cancer worldwide — promoted by exposure to tobacco, alcohol and human papillomavirus.

Can this thing be automated, take the human interpretation out of it? That's a big challenge.

— Ethan Minot

It is aggressive and hard to treat. Despite advances in chemotherapy and surgery, five-year survival rates have not improved over the past 20 years. And until the CTIP2 discovery, researchers had had limited success in identifying biomarkers for use in clinical oncology.

In December 2011, the Indras and their colleagues Mark Leid of OSU and French biochemist Joseph Abecassis received a U.S. patent for the use of CTIP2 in cancer diagnostic tests. "Cells that are dividing rapidly express more CTIP2," says Arup Indra. "It is a marker of cell proliferation. We don't know for sure if it is a cause of cancer, but we suspect strongly that it is." The protein has also been called a "master regulator" because it influences cell development in skin, teeth, the brain and immune system.

In storage tanks cooled by liquid nitrogen, the Indras maintain human oral cancer cell lines that overproduce CTIP2. With partners at OSU and the Oregon Health & Science University in Portland, Gitali Indra leads studies on its role in the development of normal tissues as well as cancer. "CTIP2 is expressed in normal cells but at much lower levels," she says.

Personal Proteomics

"A higher-than-normal level (of CTIP2) indicates that an individual could be at risk," adds Arup. "If you are getting more than a normal detectable level, you could determine that she requires monitoring."

Before CTIP2 becomes useful in the doctor's office, its function needs to be studied in animals and then human subjects. "We need to understand how disease progresses in animal models, how levels of a given biomarker are changing," says Arup.

Moreover, no protein acts alone. Each operates in a network. So the ideal biosensor will be capable of monitoring many proteins at once. The hope is that such devices will enable every person to have a composite protein profile, a biochemical fingerprint, for evaluating health as we age.

Researchers will need better technology to reach that goal. While the Indras can analyze CTIP2 and other proteins through existing laboratory techniques, their efforts bump up against detection limits. They need a better way to pick out one molecule among thousands and to see small

Ethan Minot and his team use light to analyze the structure of carbon nanotubes grown in the lab. (Photo: Jan Sonnenmair)

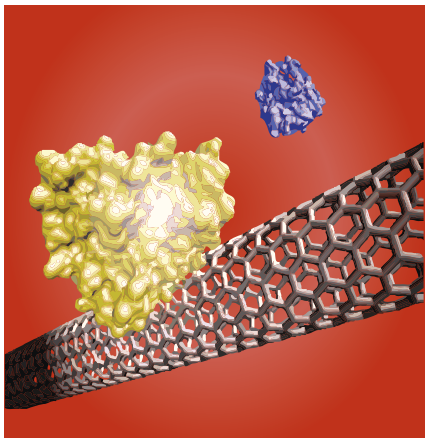
but possibly significant trends. Just as the Indras identify biomarkers and the Remcho lab develops ways to catch them, Ethan Minot is working on a new type of fishing line for CTIP2 — a more sensitive detection system made of carbon nanotubes.

Planting Nanotubes

These slender threads of pure carbon are hollow and so tiny that they are invisible to the naked eye, even under the most powerful light microscope. But they conduct electricity with such sensitivity that physicists can measure the tiny change in electric current that occurs when a single molecule lands on their surface. That makes them good candidates for the kind of detection system needed by the Indras and other molecular biologists. However, despite their size, making and developing a nanotube-based detection system is no small matter.

With support from the Oregon Nanoscience and Microtechnologies Institute (ONAMI) and OSU startup funds, Minot has established a lab in the OSU Department of Physics for studying nanotubes and graphene (one-atom thick carbon sheets). He and his team sow nanotube "seeds" — catalysts that sequester carbon atoms from gases such as methane and ethylene — onto a silicon chip. At about 900 degrees Centigrade, carbon nanotubes grow in only a few minutes.

But it can take hours of painstaking work to determine exactly what kind of tubes the researchers have made. "When you bind carbon atoms together into the nanotube structure, there are at least 100 different ways to do it. So the diameter can be different and every one has slightly different properties," says Minot. Carbon bonds also take a variety of angles as they grow. These so-called chiral angles affect the way a nanotube conducts electricity and binds to other molecules.



Proteins tumble in solution and bind to a nanotube. Events like these can modify the nanotube's resistance, allowing the device to be used as an electronic biosensor. (Image: Landon Prisbrey)

Fortunately, physicists have more than a few tricks up their sleeves. Working with the Remcho and Indra labs, Minot and his team are developing ways to bind small molecules — the bait — to nanotubes and then detect biomarkers such as CTIP2 — the fish — in a simple saline solution.

Something that has so far eluded the Minot lab's grasp is the successful detection of a protein in a blood sample. "If you have a mixture that you're sensing, like real blood, there are thousands of different types of proteins. Most of them you want to bounce right off the sensor. One out of a thousand (proteins) has the right chemical structure to stick to it. That's the ideal situation," he adds. "Sensors will pick up anything unless you treat the surface correctly."

Out of the Lab

In January 2012, Minot's and Remcho's labs and a colleague at UC-Santa Barbara reported nearly tripling the speed of a prototype detection system. Their advance stemmed from preventing proteins in the system from sticking to other surfaces.

While refining biosensor chemistry is hard enough, the electronics present another major hurdle. "If anything stops this from being commercialized from the electronics point of view," Minot adds, "it's the fact that if you wait a half hour, there are slow changes in baseline resistance. When we do an experiment, it might last five minutes, and we bind proteins onto the surface in that amount of time. We see a very clear signal over that period of time.

"But commercial devices don't have the same luxury as a research experiment. They don't have a grad student, who knows exactly what's going on, watching over it."

Meanwhile, Oregon businesses are expressing interest in OSU's developing technologies. Minot is working with Voxtel in Beaverton on methods for controlling nanotube properties in manufacturing. And a company known as mAbDx, Inc., a spinoff from the University of Oregon, has taken an option on an antibody to CTIP2 based on work by the Indras and Leid.

Nanotubes are just one of the technologies in development. Other approaches at OSU include magnetized "nanobeads," the focus in Pallavi Daghat's lab in the School of Electrical Engineering and Computer Science. Working with Remcho's group, Daghat has developed a way to turn ferromagnetic iron oxide nanoparticles, extraordinarily tiny pieces of rust, into sensors. Such particles not only can detect chemicals with sensitivity and selectivity, but they can be incorporated into a system of integrated circuits to instantly display the findings. The applications could extend to homeland security and environmental monitoring as well as to medical diagnostics.

"It doesn't have to be nanotubes," says Minot. "Maybe somebody else is going to get it. But there's a lot of excitement that we're moving this way. Someone is going to nail it." And when they do, the proteins that betray us will have nowhere to hide. terra

Plates of Honor

Julie Green memorializes final choices by death-row prisoners

BY ANGELA YEAGER

Cooking and sharing food connect OSU artist Julie Green to family and Midwestern roots. (Photo: Ha Lam, courtesy of Whole Foods Market)

In 1997, Julie Green had just moved to Norman, Oklahoma, when she sat down to read the local paper with her morning tea and toast. As she was looking at the column of news from around the state, she was riveted by an item describing an execution that had happened the previous night.

The column said a man, whose name Green does not recall now, died at 11:59 p.m. by lethal injection and that, at the time of death, his legs shook and his eyes became glassy and closed to a crescent. The story ended simply: "And his final meal was six tacos, six glazed doughnuts and a cherry Coke."


Texas
NONE
30 March 2010

"I was stunned," Green says. "Of course, I had heard of last words. But I hadn't heard last meals described in such detail."

A newly hired artist in the University of Oklahoma's art department, Green began clipping all the execution notices in *The Norman Transcript*. Oklahoma has the highest execution rate per capita in the United States, so she often was clipping several items per week. At the time, she wasn't sure what she would do with this information. She only knew she felt compelled to keep collecting them.

"I collected the menus for a while, and I can't really pinpoint why — it just bothered me," Green says. "The meals brought me into this issue. I grew up in a family of wonderful cooks, and there was a lot of tradition with meals passed down through generations. And the idea of a meal whose purpose is not to sustain life, or be shared, but seems to have this other symbolic meaning, just compelled me."

An Idea Is Born

When she accepted a position in the Oregon State University Department of Art in 2000, she began The Last Supper, a project that would translate her feelings into a public statement. Her first piece was a portrayal of those tacos and doughnuts that had caught her attention in Norman. Expressed through blue mineral paint fired on white porcelain plates, the series now has more than 500 pieces depicting last supper choices by death-row inmates.

The work has been exhibited widely in the United States and internationally, most recently at the University of Nebraska at Omaha. The Corvallis Arts Center plans a show in early 2013. National news media including *Ceramics Monthly*, *Gastronomica* and National Public Radio have featured The Last Supper, as has *Dark Rye*, an online magazine produced by Whole Foods Market. OSU-Cascades artist Henry Sayre has included text and images, as well as Green's narrative tempera paintings, in the 2012 edition of his textbook *A World of Art*, published by Prentice-Hall.

At Oregon State, Green teaches painting, drawing and contemporary issues in art. In 2011, she received grant support from the Joan Mitchell Foundation. Its prestigious award is given to only 25 contemporary artists a year to acknowledge painters and sculptors nationwide who create work of exceptional quality.

Green paints The Last Supper plates in her studio in a cozy historic bungalow in Corvallis, which she shares with her husband, artist Clay Lohmann. Every month or two, she loads newly painted plates into a dish rack and drives a slow half-mile to the home of artist and collaborator Antonia "Toni" Acock, who fires them in her ceramics kiln.

At home, Green is a warm hostess, welcoming guests with a pot of tea and a delicious dessert freshly baked, or a bowl of fruit picked from the trees and raspberry vines on their property. She attributes her hospitality to Midwestern family roots. Born in Japan to a naval officer father, she grew up in Des Moines and received both her undergraduate and graduate degrees from University of Kansas.

"My art was always encouraged, but I am from practical people," Green says. "My grandmother taught in one-room school house and my mother taught home ec before she had children. I could sew before I could walk." Home crafts — sewing, cooking, quilting — were an essential part of Green's household.

"I never saw the difference between museum art and quilts," she says. "Perhaps that is why the plate project, and combining conceptual ideas with very basic visuals, is something that doesn't intimidate me."

As a college student, Green worked with Roger Shimomura, an acclaimed artist with more than 80 pieces in permanent collections around the world. Shimomura's paintings and prints have decidedly political overtones that address Asian-American sociopolitical issues. He has followed Green's development of The Last Supper.

"It's important work, important because it deals with subject matter that no one else has dealt with

< *Death-row inmates make simple food choices: pizza, roast chicken, a pastry — or nothing at all.*

> *"My art was always encouraged, but I am from practical people," says Julie Green. (Photos: Hannah O'Leary)*

Green applies blue mineral paint on white porcelain to create each plate. (Left photo by Hannah O'Leary. Center and right photos by Ha Lam, courtesy of Whole Foods Market.)

in such creative terms," Shimomura says. "Not only is it original, but it is well-crafted, thoughtfully considered and politically forthright. Good work that takes chances politically always draws attention."

Green has said in media interviews that she plans to add 50 new plates to The Last Supper project each year until capital punishment is abolished. Does she ever worry that she has over-committed herself as an artist to such an overwhelming task?

"I did say I would continue until capital punishment is abolished, and I meant it. But if I felt like I wasn't doing the project justice or I wasn't connected to the work, I would take a break," she says. "Because this is work that has to be meaningful, it can't be me just going through the motions. I have to honor the painting and honor the memory of these people."

Devotion to Story

In order to keep the project fresh and herself creatively inspired, Green spends six months per year working on The Last Supper plates. She devotes the rest of the year to her narrative paintings which are less well-known but, for her, just as essential.

"Contemporary issues inspire me, and it comes out in my other work," Green says. "I need that break from the plates, and I need to express myself in other ways."

Green's narrative paintings often have a whimsical tone. For example, in the summer of 2011, she painted a series of iPhones collected from friends and colleagues. More recently, she has started a series depicting figurative imagery on decorated plates, mostly drawn from memory.

One of Green's signatures is her use of egg tempera, a painting technique that uses colored pigments mixed with egg yolk as an emulsifier. Known for their rich colors and durability, tempera paintings survive from the first century. Green is one of the few art professors on the West Coast to teach this style.

Tala Madani, a 2002 OSU alumna, took an egg tempera workshop with Green and also accompanied her on a trip to tour art facilities in China. Madani is an Iranian-American artist who has gone on to international acclaim and splits her time between New York and Amsterdam.

"Visually, her work is very subtle; you get wheeled in and suddenly you don't know what hit you," Madani says. "Personally, I respond strongly to Julie's other works. Her surrealist imagery and translucent paintings with egg tempera have always struck a very strong chord with me."

Green has just finished another batch of The Last Supper plates, which includes a group from Virginia, the state with the second highest annual execution rate after Texas. When she began the project, she received last meal documentation through the prisons through fax or mail. Now, last meal menus are often posted online, and she can be painting a plate within 24 hours of the execution.

National Survey

In 2005, she received a fellowship at the OSU Center for the Humanities, which allowed her to delve more deeply into the history and sociopolitical consequences of last meals. Along with a research assistant, Green contacted every

state that had capital punishment and asked questions such as: Do you have a final meal? What is its purpose? What are the rules (do you allow restaurant meals, what is the spending limit)? She found many states have a $20 maximum spending limit; others, like Oregon, with fewer executions, don't limit the amount.

"Many prisons I called said that meals were given for 'good behavior,'" Green says. "If you don't make a scene, you get a meal. And others had some interesting traditions. For instance, in Louisiana, your family can join you for the last meal."

Texas, which accounts for more than a third of all executions in the U.S. since 1976, eliminated last meals for death-row inmates in September 2011 after a state legislator called the meals a waste of money. The irony, Green says, is that most inmates have very simple requests, such as a hamburger and fries or a slice of pepperoni pizza.

"In part it is because many of the inmates are from lower income backgrounds and that maybe is the meal they want," Green says. "Many pick comfort food items, things they associate with home. They don't have time to digest it anyway, and it's not as if the meal is meant to sustain them. So what they do with it is their choice, I think."

The OSU Center for the Humanities has awarded Green a fellowship to write a book titled *The Last Supper* in 2013.

Green is starting a new group of plates on which she repeatedly paints the words "Declined last meal." That is what the documents she was sent from Virginia claimed the prisoners wanted.

She says it is perhaps best she didn't know what she was getting into when she clipped that newspaper column while having her morning tea and toast in 1997. Maybe if she had known, she would have never jumped into the fray. But now as meal notices keep coming in from all over the country, the sense of urgency is as great as ever.

"Once I started, and I saw that this was a way to humanize those who have been portrayed as monsters by making visual something we all share — the love and comfort of food — I couldn't stop," Green says. "It opened my mind and made me an activist, so my hope is that this work somehow does that for others." terra

Death Penalty Statistics

Last execution in Oregon: **1997**

Number of executions in the U.S. in 2011: **43**

Peak year of executions: **1999 (98)**

Number of states with the death penalty: **34**

States without the death penalty: **16, including Washington, D.C.**

States with highest number of executions since 1976: **Texas (481), followed by Virginia (109)**

Death-row inmates by race: **white (43 percent), black (42 percent), Hispanic (12 percent), other (2 percent).**

Source: http://www.deathpenaltyinfo.org

From Wood to Watts

Forest-based fuels could fire up rural development, but at what cost?

BY DAVID STAUTH | ILLUSTRATION BY CELIA JOHNSON

About a million years ago in South Africa, a *Homo erectus* cave dweller used fire on purpose, and some charred bones at the site suggest it may have been for cooking.

Thus was born the biofuels industry — and also the first known barbecue.

The name of that cave, Wonderwerk, means "miracle" in the Afrikaans language, and indeed biofuels were a miracle. From cooking to heating and light, fire aided the evolution of the human race. The biofuels industry even preceded *Homo sapiens* and anatomically modern humans by about 800,000 years.

Over time, barbecue techniques made steady progress, achieving ultimate perfection in South Carolina pulled pork. However, despite their importance and a few innovations like fireplaces and metallurgy, biofuel technologies tended to stagnate for about 999,000 years. In the developed world, biofuels were eventually dwarfed by fossil fuels like coal, oil and natural gas, and challenged more recently by solar, nuclear, wind and even wave energy.

Now, we've come full circle.

Biofuels are back, hotter than ever, the source of billions of dollars in new investments. From corn ethanol to biodiesel and now forest products, biofuels are often touted as a sustainable fuel source that will lessen our dependence on imported oil and provide domestic jobs. It's ideally seen as win-win, and researchers all over the world are trying to perfect new technologies, increase efficiency and make biofuels more cost-effective.

It had also been proposed that biofuels could help mitigate climate change — that substituting them for their fossil-fuel counterparts would reduce "greenhouse gas" emissions into the atmosphere — but that assumption is facing challenges both locally and globally.

Jet Fuel

This is not your caveman's biofuel. A U.S. Department of Agriculture program that was announced last year will bring $80 million to Pacific Northwest industry and universities, $9.8 million of it to Oregon State University, for a diverse program of research and education to create aviation fuel out of tree plantations and low-value wood products. Through the miracle of cellulosic ethanol, some jets of the future will fly on fuel made from Pacific Northwest trees.

"We could take material that isn't now being used and create a new billion-dollar industry in the Pacific Northwest," says John Sessions, a distinguished professor of forest engineering at Oregon State and principal investigator working on the Northwest Aviation Renewables Alliance.

"At the same time, we could help thin forests that are unhealthy and overcrowded, benefit wildlife habitat, reduce the risk of catastrophic fire and provide some badly needed jobs in communities that have lost their historic base in timber production," Sessions says. "This won't solve all of the nation's energy concerns, and we shouldn't say that it will. But it could make an important contribution."

Sessions is quick to point out that "not all biofuels are created equal" and that thinning forests will cost substantially more than just using residues from existing logging operations — although the cost issue would look much better if commercial timber from small trees were harvested along with residue. One of OSU's primary roles in the new initiative is to identify ways to get wood out of the forests more efficiently, and Sessions says that cutting logistical costs by 30 percent or more is a reasonable target.

However, questions about the modern biofuels industry have been raised almost since its inception, and as the debate enters the forest-products industry, it's getting more intense. Cost is a big issue. So is what many ecologists consider the single most serious environmental threat in the world today — global warming, or the greenhouse effect.

In Brief

Biofuels provide a domestic energy source that creates jobs and spurs economic development. However, current technologies are heavily subsidized and increase greenhouse gas emissions. Oregon State University researchers are analyzing the efficiencies and economics of biofuel production and its role in a broad forest management strategy that includes fire risk and rural communities.

Carbon Emissions

Some early proponents of biofuels suggested that they could be "carbon neutral" or even better, meaning they will not compound concerns about greenhouse warming and might even reduce it. Since they are produced from crops or trees that "sequester" carbon from the atmosphere as they grow, the theory was that sequestration would offset most or all of the carbon they release when they are turned into one type of fuel or another.

"Different sides in this debate tend to pick the numbers that best support their arguments," says Mark Harmon, a professor of forest science at OSU and one of 18 researchers in the nation advising the U.S. Environmental Protection Agency on biogenic carbon. "The truth is more nuanced."

The bottom line, Harmon says, is that almost any harvest of existing forest trees will cause a net increase of carbon to the atmosphere and that it may take decades or even centuries to "pay it back" with future tree growth. For global-warming concerns that are real and immediate, that's a problem.

"This is a dilemma, and there won't be any magic fix," he says. "Forests are renewable, but only over very long time spans. Biofuels from tree harvesting would create a carbon debt that would be very difficult to pay back, like borrowing on one credit card to pay off another. The enthusiasm for them may have gotten ahead of the science."

Harmon has estimated that, in an Oregon Coast Range stand, if you removed solid woody biofuels for the reduction of catastrophic fire risk and used them to produce cellulosic ethanol, it would take 339 years to reach a break-even point in carbon sequestration.

Another study last year at OSU, the largest and most comprehensive yet done on the effect of biofuel production from West Coast forests, echoed these concerns. It found that an emphasis on bioenergy would increase carbon-dioxide emissions from these forests at least 14 percent, if the efficiency of such operations were optimal. Harvest increases, for any reason, would result in increases in greenhouse emissions.

An analysis just published in the journal *Global Change Biology/Bioenergy* raised even more doubts, if forest biomass were to reach its ultimate potential. The authors, who included Beverly Law, a professor of global change forest science at OSU, wrote that a major global commitment to forest-biomass energy "would result in a reduction of biomass pools that may take decades to centuries to be paid back by fossil fuel substitution, if paid back at all."

Reported emission savings from forest bioenergy are based on erroneous assumptions, they added, and a large biofuels industry would push forest management to ever-shorter rotation lengths, with depleted soil nutrients and fertility, increased erosion and flooding, and degraded fish habitat in streams. Even the economics may become more difficult, according to this analysis. In Europe, where bioenergy is subsidized, the cost of woody biomass from conifers surged in price from 300 percent to 600 percent between 2005 and 2010.

"Based on review of the literature, the paper concluded that large-scale bioenergy production from forests is neither sustainable nor greenhouse-gas neutral," says Law, who is also a co-author of the National Research Council report on methods for quantifying and verifying greenhouse-gas emissions. "These issues have not been thought out very fully."

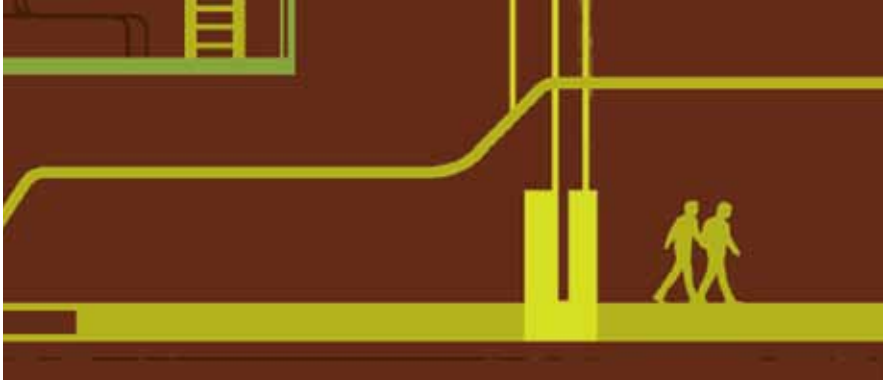
By the Numbers

That's about the same perspective held by William Jaeger, an OSU professor of agricultural and resource economics who has studied the economics of biofuels for the past five years.

"Biofuels were being seriously promoted before two main areas were thoroughly analyzed," Jaeger says. "Those areas are net carbon analysis and economic constraints. People looked at this somewhat superficially. They said, 'We can grow our own energy; why buy it from Saudi Arabia?'"

Biofuels, he says, were seen at first as such a win-win by most groups that they engendered almost no opposition. Political leaders loved them, environmental groups went along, jobs were being created and crop prices went up for farmers.

Under Jaeger's analysis, however, the facts are less rosy. He analyzed ethanol produced from crops and switchgrass cellulose, including some approaches that are simpler and even less costly than the current move toward forest-based cellulosic ethanol. Jaeger concluded that existing policies have been very costly, produce negligible reductions in fossil fuel use and increased greenhouse-gas emissions.



His bottom line?

For complex reasons, the growth of a biofuel industry is doing almost nothing to reduce use of fossil fuels. And if you wanted to reduce gas consumption by 1 percent, U.S.-produced biofuels would cost 20 to 31 times more than energy-efficiency improvements. Meanwhile, the cost of taxpayer subsidies for some of these programs is extraordinary: Current ethanol subsidies to operate a 100-million-gallon ethanol plant translate to about $1 million per job, per year. Depending on the type of biofuel, there are risks of local pollution, heavier demands on land use and higher food prices for the poor.

Will some of the research being done around the world, and in the Pacific Northwest, change that? Some researchers believe it will. At least incremental improvements in efficiency and cost are probable. Whether they will be enough to offset the huge obstacles is more problematic. But while subsidizing a whole industry right now is questionable, even Jaeger points out that investment in research often has a very high payoff.

Forest Investment

"Until we work on them, we really won't know what improved technologies will be able to do," says Claire Montgomery, an OSU professor of forest resources. "And some of these costs have to be kept in perspective. We're spending billions of dollars to protect our access to fossil fuels, and the cost of fire suppression in the U.S. has tripled since the mid-1990s to $1 billion a year."

Other issues aside, Montgomery says, Pacific Northwest forests and rural communities are struggling. Decades of fire suppression have led to overcrowded forests, insect and disease epidemics are increasing, rural communities have high unemployment levels, and there's little money to do anything about it. A biofuels industry could help all of these.

In her research, Montgomery is trying to identify where a supply of wood that could fuel an industry most closely matches up with the communities that need help. "Displacing fossil fuels is good," she says. "Creating jobs is good. Helping rural communities is good."

But a biofuels industry is not simple, certainly not as simple as once envisioned. And the issues of greenhouse warming, high societal costs and other environmental concerns are not easily dismissed.

Biofuels still make for a great barbecue. But it's safe to say the caveman who invented this industry a million years ago had no idea, before it was all over, just how complicated the business might get.

terra

Wood or Oil?

"The world is a complicated place and there are consequences for every choice we make," says Hal Salwasser, dean of the Oregon State University College of Forestry. "The research cited here shows what some of those consequences, good and bad, might be when we transform wood, a carbohydrate renewable over a scale of years to centuries, into heat or fuel.

"Compare that to getting that heat or fuel from a hydrocarbon, renewable only on a scale of many millennia. Both create jobs and cause environmental effects, and both are heavily subsidized. Where are those jobs most desired, where do environmental effects have the least impact and what subsidies are most reasonable? We can expect more to come on these questions as the research rolls in."

Hal Salwasser spoke to participants at the 2007 Fernhopper celebration at Oregon State. (Photo: Caryn Davis)

Business Partners

Entrepreneurs leverage OSU research in startup companies

BY NICK HOUTMAN | ILLUSTRATION BY MARY SUSAN WELDON

One sunny spring afternoon, friends sat together in the backyard of a Corvallis home sipping wine, bemoaning the recent hike in gas prices to $3.50 per gallon. Among them were a former product-development specialist for Hewlett-Packard and an Oregon State University chemist. Perhaps inspired by the bioethanol in their glasses, what might happen, they wondered, if they could turn local agricultural by-products — grass and wheat straw, fruit and vegetable processing wastes — into fuel? Thus was born the idea for a new company, Trillium FiberFuels.

They didn't intend to compete against the rapidly expanding corn-ethanol industry. As of 2010, more than 200 facilities, mostly in the Midwest, were churning out about 13.5 billion gallons of corn ethanol a year. The Trillium co-founders' hope was that they would develop a more environmentally sustainable product (lower greenhouse-gas emissions, less water pollution), provide another revenue source for rural Oregon landowners and contribute to the national energy goal of producing 36 billion gallons of biofuel annually by 2022. Trillium had entered the cellulosic-ethanol business.

Research Leads to Products

More than two dozen startup and established companies have leveraged OSU research over the last decade. Here are six examples:

- **Inpria Inc.** is developing high-resolution, etch-resistant lithography to enable advances in semiconductor manufacturing. It grew out of the Center for Sustainable Materials Chemistry, an OSU-University of Oregon collaboration.
- **Home Dialysis Plus** is developing a portable kidney dialysis machine, based on OSU research in micro-fluidics, that will free people from frequent and lengthy visits to treatment centers.
- **NuScale Power** is developing a next-generation modular nuclear power plant that addresses concerns over safety, cost and security.
- **Columbia Forest Products**, the nation's largest manufacturer of hardwood plywood, is producing formaldehyde-free panels using adhesives developed in the OSU College of Forestry.
- **BASF** licensed "Clearfield" wheat, which was developed at OSU through traditional breeding and resists herbicide treatment. It has become a prominent wheat variety in the Pacific Northwest.
- **HP** has licensed OSU transparent metal-oxide semiconductors, which enable higher resolution 3-D displays and more efficient solar energy systems.

Priority No. 1 for any new company is to stay alive. So Trillium succeeded in competing for federal and state grants and spun off another small business along the way. In a small wood-frame building just off Highway 99 north of Corvallis, the company has developed a method (known as xylose isomerization) to ferment the 20 percent to 40 percent of plant biomass that resists being turned into ethanol by yeast. Trillium president Chris Beatty credits research by OSU Distinguished Professor Stephen Giovannoni, who isolated and sequenced the genome of a microorganism used in the company's experiments.

The goal is to produce cellulosic ethanol at a competitive price and ramp up production quickly. "If you're going to make a dent in this business, it's either grow big or stay home," says Vince Remcho, Trillium co-founder, OSU professor of chemistry and affiliate scientist with the Pacific Northwest National Laboratory. Other co-founders include Beatty, Steve Potochnik and Grant Pease, all with former or current ties to HP.

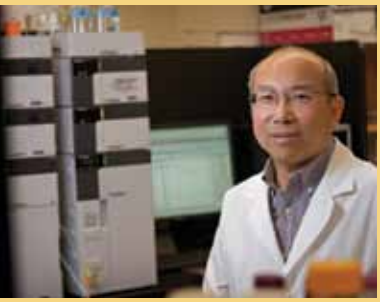
Priming the Pump

Trillium isn't the only business collaborating with OSU to have grand ambitions. Spun directly out of research or boosted by patented OSU technology, others are aiming to grab significant shares of business and consumer markets. Some of their products are already coming off farm fields and manufacturing lines.

Through their relationships with OSU, these and other companies create jobs, diversify the Oregon economy and respond to market demands for more sustainable, consumer-driven technologies. And in turn, OSU benefits. Students gain experience through internships. Faculty stay up-to-date on industry practice. And licensing revenues provide new research funds. "The purpose of our efforts is impact," says Ron Adams, executive vice president for research. "It relates to our land grant mission, so we're furthering economic development and social progress. We're partnering in R&D that will result in new products and business opportunities."

Sowing seeds for business

Startup companies and entrepreneurs work hand-in-hand with researchers



Xihou Yin, president, AGAE Technologies

Scott Gilbert, chief technology officer (left); Todd Miller, president, Microflow CVO

(Photos: Karl Maasdam)

AGAE Technologies

Surfactants enhance cleaning, dispersion and emulsification in paints, household cleaners and other products. However, many are known to be toxic. Based on research in the OSU College of Pharmacy, AGAE Technologies has developed a biological method for producing surfactants that are environmentally benign and biodegradable. Based on licensed OSU technology, the new product is known as a "rhamnolipid" and is produced by a strain of the common bacterium, *Pseudomonas aeruginosa*.

Microflow CVO

The problem seems simple: mix two liquids with consistently uniform results. Manufacturers usually perform this step in vats where batches of liquids are stirred and then processed. Through research in OSU's Microproducts Breakthrough Institute, Microflow CVO has developed stainless-steel micromixers that achieve high-quality mixtures by pushing liquids through channels slightly larger than a human hair. The dime-sized devices can be scaled and adapted to manufacturing needs in the pharmaceutical, petrochemical and personal-care product industries.

Applied Exergy

Renewable energy sources tend to be intermittent: They produce power when the sun shines or the wind blows. Based on research in the OSU College of Engineering and the Microproducts Breakthrough Institute, Applied Exergy is developing methods for storing energy as "low-grade heat," temperatures from 40 to 80 degrees Centigrade. The technology has multiple applications: energy recovery from steam plumes, integration with carbon capture systems and energy storage for use during peak demand.

Still, working with businesses isn't like serving students or competing for research grants. Adams and others are mindful that entrepreneurs and business managers face rapidly changing risks and protect their interests accordingly. "The people who are investing their lives and money in those enterprises are not depending totally on us to get it done," Adams says. "If you're an entrepreneur running one of these companies, you want 100 percent control."

While companies do look to universities for innovation and skilled, well-educated employees, "we're not an economic development organization," adds Brian Wall, director of the Office of Commercialization and Corporate Development. "We are an economic driver through our graduates, research partnerships and licensing. We're always on the lookout for discoveries that offer opportunities for commercialization and new business investment. This is an important area of growth and impact."

The rules that define that process — agreements on copyright, licensing, royalties and other steps — are based on policies created by the Oregon State Board of Higher Education.

Show Me the Money

Private-sector partnerships show up as support for problem-oriented research. Nationally, according to the National Science Foundation, industry funded nearly 6 percent of the roughly $55 billion in research performed in institutions of higher education in 2009. At Oregon State in 2011, studies funded directly by industry totaled about $5.4 million, or 2 percent of the university's $261.7 million in grants and contracts. However, that doesn't include contributions from research gifts, agricultural commodity groups, the forest-products industry and testing services, which bring the total close to $13 million, or about 5 percent.

What about return on investment? Perhaps the most dramatic comes from the agricultural sciences, which helped Oregon farmers and ranchers to earn a record $5.2 billion in farm-gate sales in 2011. Oregon beef topped the list as the state's most valuable agricultural commodity. Ranchers have a long history of working with OSU researchers through Agricultural Experiment Stations in animal and rangeland science on feed, herd health and cattle management.

Impact also comes from fledgling startup companies like Trillium. Over the past eight years, new OSU-assisted companies have raised $160 million in private investment and created 350 jobs, says Rick Spinrad, vice president for research. New businesses proceed through stages, he adds, from research-inspired startup to venture-funded, revenue-producing and growth-focused.

At every step is a major hurdle: money to pay for product development, market analysis and management expertise. Among the sources of funding that help young companies transition from one stage to another are the Oregon Nanoscience and Microtechnologies Institute (ONAMI), the Oregon Built Environment and Sustainable Technologies Center (BEST) and the OSU University Venture Development Fund. The latter leverages tax-deductible contributions from private citizens. The OSU Foundation conducts fundraising, and the OSU Research Office manages investments. Recent examples include:

- Ultra-high-temperature water pasteurization for another startup, Home Dialysis Plus ($182,700)
- Market analysis of a landmark new LCD display by Inpria Corporation ($100,000)
- Development of a thermal energy storage system by a new company, Applied Exergy ($148,514)
- Proof-of-concept display for a new type of diode that could replace silicon and reduce energy, leading to a new company, Amorphyx ($150,000)

Trillium FiberFuels, meanwhile, announced in April 2012 that it received a $150,000 Small Business Technology Transfer grant from the U.S. Department of Energy (DOE) to develop a commercial-scale enzyme production process for the cellulosic biofuels industry. Based on manganese peroxidase, which is found naturally in white-rot fungi, the new process emerged from the lab of OSU researchers Christine Kelly and Curtis Lajoie. The company has also received funding from sources such as the U.S. Environmental Protection Agency, the National Science Foundation, U.S. Department of Agriculture, ONAMI and Oregon BEST.

"There is a reason to invest in research in biofuels," says Remcho. "It will play a role in U.S. and worldwide energy needs in the future. So it's coming. We just need to do it intelligently." terra

Engineered for Employment

Oregon State University is a top-tier recruiting source for HP. Over the past 10 years, the company has hired about 100 OSU students and provided internships for another 200.

Bits & Pieces

News briefs from OSU

Red Rover. A geologist who once helped discover rock-eating microbes a mile beneath the ocean floor soon will be looking for rocks in the other direction: up. More than 36 million miles up, in fact. NASA has invited Martin Fisk to join a 28-person team to guide *Curiosity*, the rover currently en route to Mars. When it lands in August, it will scan the red planet for samples of soil and rock — and signs of water and life.

One-Cell Meal. The food web, it turns out, is more complex than anyone knew. In a stunning discovery, researchers found that the tiny life forms called *Archaea* (unknown until 1977) nourish organisms higher up on the meal chain. Vent worms eat the one-celled microbes, which in turn feed off methane seeping from the ocean floor, reports Andrew Thurber, a post-doc in ocean ecology.

Dilemma Zone. Stop or go? When the traffic light turns yellow, drivers have only seconds to decide. That uncertainty can be dangerous, even deadly, researchers say. So transportation engineers have developed ways to minimize driver mistakes by bringing more precision, consistency and uniformity to the danger zone. "We want conscientious drivers to know what is the right thing to do," says Professor David Hurwitz.

Viral Coral. Seeking clues to the die-off of coral reefs around the world, scientists have turned up a possible culprit: viral disease. While investigating pathogens that might explain the alarming rate of coral decline, microbiologist Rebecca Vega-Thurber discovered viruses in the herpes family living among the coral. Whether these viruses are actually causing disease is not yet known.

For more on these stories, see "In the News" at **oregonstate.edu/terra**

Parents Should Chill Out

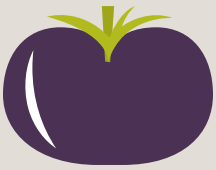
Toddlers whose parents anger easily tend to throw more tantrums and become upset, a new study shows. Looking into the nature-versus-nurture question long debated in childrearing, researchers found a clear link between over-reactive parenting and negative emotions in young children.

"You set the example as a parent in your own emotions and reactions," says researcher Shannon Lipscomb at OSU-Cascades. "Parents' ability to regulate themselves and to remain firm, confident and not over-react is a key way they can help their children to modify their behavior." Genetics, however, does play a role, Lipscomb and her colleagues found. Children may remain at risk for negative emotionality as an inheritance from their birth parents, despite being raised in low-stress adoptive homes.

The Power's in the Purple

A new type of tomato that's "as black as an eggplant" is being touted for its health-enhancing properties. Poetically named "Indigo Rose," the new variety was bred at OSU as a powerful source of antioxidants — micronutrients known to fight the harmful "free radicals" implicated in cancers and other diseases. It's the purple pigment, in fact, where the beneficial compounds called "flavonoids" reside.

But does it taste good? Yes, according to horticulturist Jim Meyers. "It has a good balance of sugars and acids and tastes just like a tomato," he says.

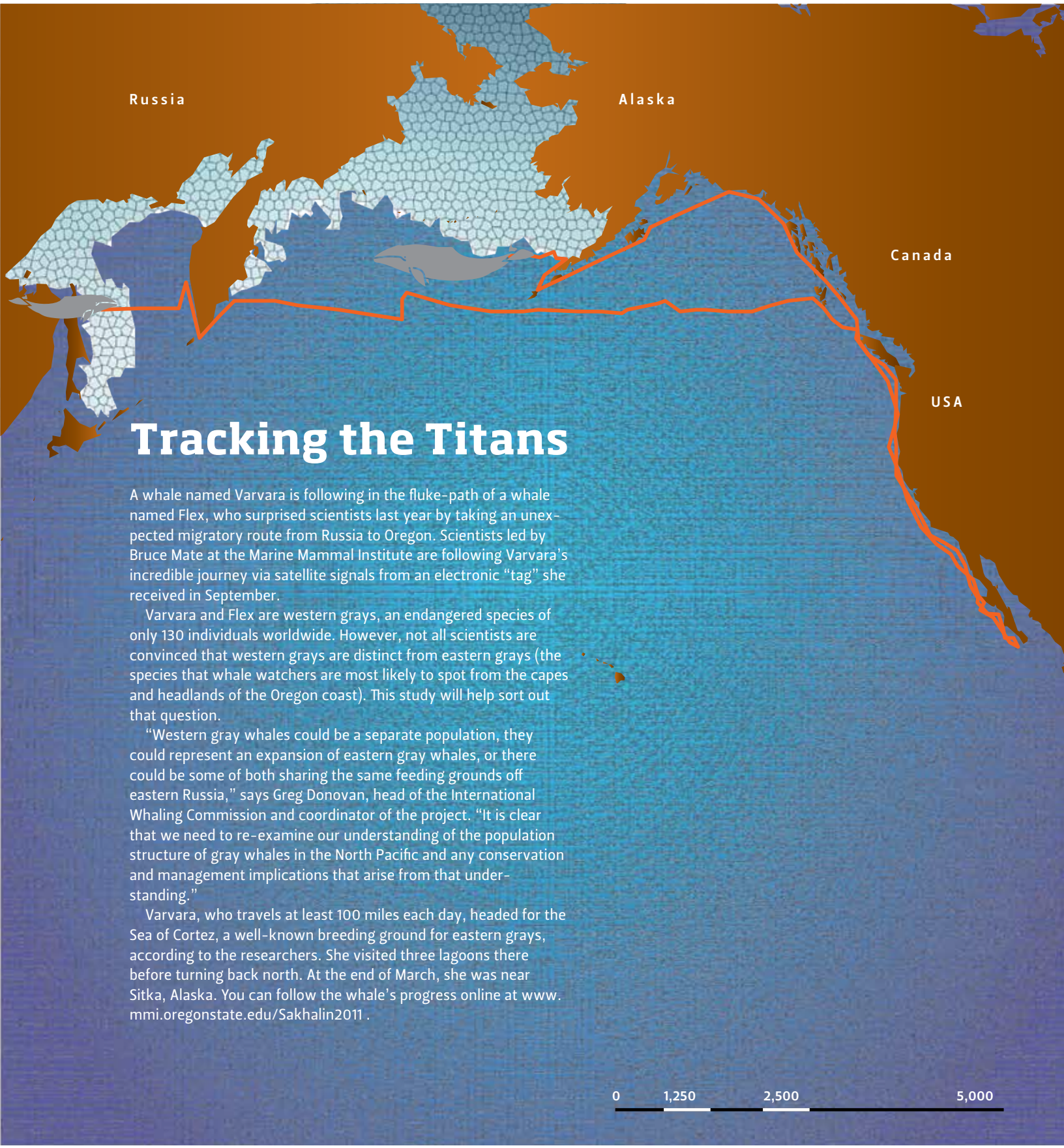


Indigo Rose has been a long time in the making — some 40 years, in fact. Its recent arrival in Oregon gardens and supermarkets can be traced to its exotic genesis in two wild species, one from Chile and the other from the Galapagos Islands.

The Oh! Zone

Far-out findings from science

Ancient Blood Brothers. Like the "sloth moth," which lives only in the fur of the ambling two-toed and three-toed mammals, the "bat fly" exists only in the fur of the winged, cave-dwelling mammals. Now scientists know that the flea-like, blood-sucking fly has been hanging around with bats for at least 20 million years. That's because an unfortunate bat fly became entombed in a sticky glob of tree sap eons ago and has been there ever since, preserved in the solidified amber. Bat flies coevolved with bats, explains one of the world's leading amber experts, OSU zoologist George Poinar Jr., who discovered the fossilized fly in the semi-precious stone from the Dominican Republic.



Tracking the Titans

A whale named Varvara is following in the fluke-path of a whale named Flex, who surprised scientists last year by taking an unexpected migratory route from Russia to Oregon. Scientists led by Bruce Mate at the Marine Mammal Institute are following Varvara's incredible journey via satellite signals from an electronic "tag" she received in September.

Varvara and Flex are western grays, an endangered species of only 130 individuals worldwide. However, not all scientists are convinced that western grays are distinct from eastern grays (the species that whale watchers are most likely to spot from the capes and headlands of the Oregon coast). This study will help sort out that question.

"Western gray whales could be a separate population, they could represent an expansion of eastern gray whales, or there could be some of both sharing the same feeding grounds off eastern Russia," says Greg Donovan, head of the International Whaling Commission and coordinator of the project. "It is clear that we need to re-examine our understanding of the population structure of gray whales in the North Pacific and any conservation and management implications that arise from that understanding."

Varvara, who travels at least 100 miles each day, headed for the Sea of Cortez, a well-known breeding ground for eastern grays, according to the researchers. She visited three lagoons there before turning back north. At the end of March, she was near Sitka, Alaska. You can follow the whale's progress online at www.mmi.oregonstate.edu/Sakhalin2011 .

Evidence for Change

Rigorous climate science trumps our senses

BY PHIL MOTE, DIRECTOR, OREGON CLIMATE CHANGE RESEARCH INSTITUTE

Some people take a dim view of the idea that Oregon, as well as the rest of the world, could be expected to continue warming in coming decades. They may cite March snowfall in the Willamette Valley or unpublished comparisons of mean temperatures over a given time period in specific places. Appealing as it is, such evidence hardly constitutes proof that the region is cooling and does not trump rigorous, peer-reviewed science.

It's important to ask the right questions about data used to reach a conclusion. Are there gaps, either geographically or through time? Were robust statistical methods used to determine if a specific event was indeed unusual? Peer-reviewed research has shown that short periods of cooling can easily be embedded in longer-term warming trends; it's simply a statistical fact in a time series with a positive trend and a variable system.

Recent cool weather notwithstanding, Oregon has undergone a substantial warming trend over the last 50 to 60 years. What are now considered exceptionally cool seasons were normal 75 to 100 years ago, and seasons now considered normal were exceptionally warm in the same period. If one arbitrarily selects the climatically insignificant period of 5 to 10 years, one can incorrectly conclude that there is no evidence of warming. But further research also shows reasons for the slight decline in global (and Oregon's) temperatures: A combination of La Niña (when eastern equatorial Pacific sea surface temperatures are 3 degrees to 5 degrees Celsius cooler than normal) and solar minimum (a low point in solar activity) temporarily overcame the gradually increasing effects of greenhouse gases.

Globally, 2011 was the warmest La Niña year ever. Research clearly points to a resumption of the warming as the recent spate of La Niñas wanes and as the solar cycle moves toward maximum. In short, rigorous research tells us so much more than the comparison of averages over arbitrary lengths of time.

The larger point that concerns me is how easily many people dismiss rigorous research in preference for subjective observation. Both are valid ways of adding to the sum of human knowledge, but sometimes the results of research can be counterintuitive and can even contradict what we see with our own eyes.

Take, for example, the patient whose doctor tells him he has a treatable form of cancer. If he feels fine, should he rely only on his subjective feelings? Would he be wise to conclude that his doctor is in "the cancer camp" and wait for clear physical evidence before doing anything?

Or what about the roofer who tells a homeowner that her roof is badly worn and could start leaking in the next storm. Would she be wise to dismiss him as part of the "leaky-roof camp" and ignore him until she actually sees the water trickling through her dining room ceiling?

Why do some of us so flippantly dismiss scientists studying the health of our only planet? Why argue against taking prudent steps now?

Some people may wish that global warming is nonsense. So do I. But I have to accept the evidence provided by thousands of honest, hard-working scientists, meticulously documented during the past 120 years, that says otherwise.

Running Clear

Gary Klinkhammer turned water analysis into environmental protection

BY CELENE CARILLO

The Arctic Ocean, 1997. Gary Klinkhammer had strapped a water chemistry analyzer onto the hull of a retired U.S. Navy nuclear submarine to measure carbon. He had come to this bleak and desolate place looking for organic matter, fertile detritus dumped into the ocean by massive rivers in Siberia and North America.

"The Arctic in a lot of ways is more like a big lake than an ocean. It's more isolated," says Klinkhammer, a professor in the College of Earth, Ocean, and Atmospheric Sciences at Oregon State University. "Following carbon in the Arctic turns out to be a very powerful thing," he adds, because it can reveal details about the chemical and geological processes that drive ocean life.

Gary Klinkhammer (Photo: Susan Klinkhammer)

But Klinkhammer felt hampered by his equipment. His analytical tools could produce a lump-sum measurement of carbon, not a detailed picture of the dissolved and particulate forms that emanate from sources such as forests or farms, peat bogs or cities.

Following his Arctic expedition, he got to work on a better way to analyze water quality. What he learned about tracking carbon and other materials led him to create a Corvallis-based technology company that is advancing water-quality protection in the United States and abroad.

Today, in addition to his role as director of the W. M. Keck Collaboratory for Plasma Spectrometry at OSU, Klinkhammer is founder and chief scientific officer of ZAPS Technologies, which designs and sells an analytical system, LiquID™, based on his research. Through optical analysis of flowing water, the system can rapidly monitor over 100 constituents in water-supply and wastewater systems and the environment.

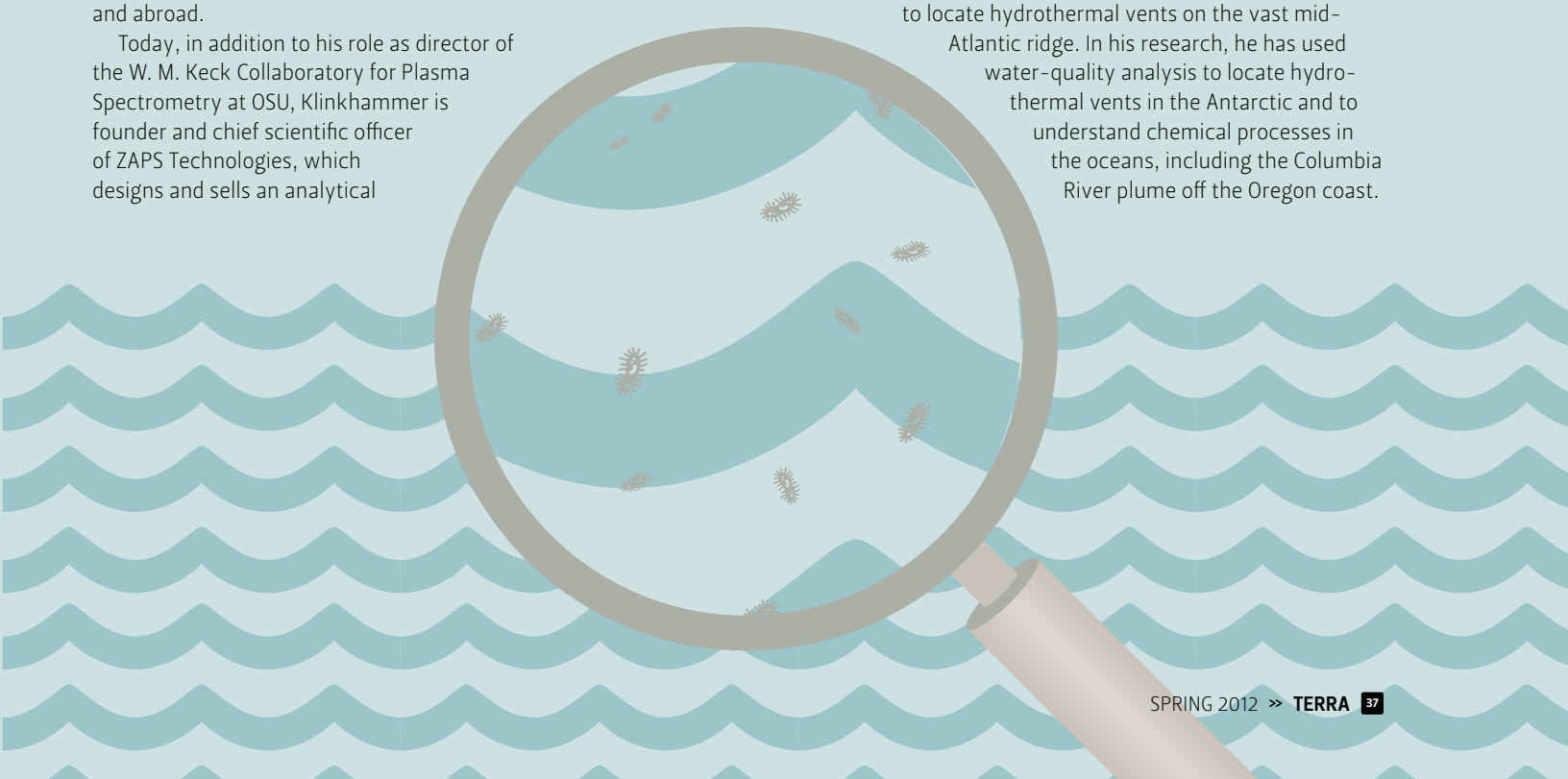
"If you're looking at the Santiam River or something like that, you don't really know where that carbon is coming from," he says. "Some of it's coming from groundwater. Some of it's coming from a reservoir. There are multiple sources that it can come from."

Pinpointing the identity and source of organic matter and other constituents is a critical step in protecting public health. For example, storms and floodwaters can pollute drinking-water supplies with sediment and disease-causing microbes. One of the most famous cases occurred in 1993 when the microbe *cryptosporidium* contaminated the drinking-water supply of Milwaukee, Wisconsin. The Centers for Disease Control estimates that more than 400,000 people got sick and 69 died.

Klinkhammer's analytical innovation provides both rapid optical analysis and online display of data. It monitors chlorophyll, algae, *E. coli* and other materials 24/7 in real-time. It can even track inorganic materials such as nitrate, chlorine and ammonia.

Currently, ZAPS employs more than 20 people and has installed monitoring systems in Corvallis, Albany, Seattle and Lafayette, Indiana. Others are scheduled for San Diego and Australia.

Klinkhammer started working with sensors as a graduate student at the University of Rhode Island. His goal then was to locate hydrothermal vents on the vast mid-Atlantic ridge. In his research, he has used water-quality analysis to locate hydrothermal vents in the Antarctic and to understand chemical processes in the oceans, including the Columbia River plume off the Oregon coast.



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Medicinal chemist Taifo Mahmud uses a nuclear magnetic resonance spectrometer in his investigations into the chemical structure of natural products, such as antibiotics. See "Battling the Superbugs," Page 6. (Photo: Jan Sonnenmair)