BETWEEN A ROCK AND A NEW PLACE

With a wide-angle view of the world and a commitment to follow her fascination, this scientist is making imaginative connections between rocks, bacteria, and medicine.

by **Sarah C.P. Williams**
photography by Leah Fasten

DIANNE K. NEWMAN GREW UP EMBRACING TWO cultures. Born to American parents in Argentina (her father was a diplomat) she took to the transitions with ease: speaking English at home and fluent Spanish when she stepped outside in her adoptive cities throughout Argentina, Venezuela, and Panama. ¶ She learned early to let her passions guide her, and she has a gift for convincing others that her ideas are worth pursuing. With these talents, Newman, an HHMI investigator at the Massachusetts Institute of Technology (MIT), has become a scientific diplomat: an ambassador between the once-disparate fields of geology and microbiology.

She has mastered the languages, techniques, and cultures of both fields to get to the crux of her work: using modern bacteria to understand how the first bacteria on earth could have survived.

The only way to extrapolate how—and when—early bacteria thrived is to study the relics they left behind: rocks. So Newman is probing how bacteria interact with minerals. She's discovered how some bacteria produce energy from arsenic and iron and how they change their environments in the process. She thinks some of the oldest bacteria—those that existed before the atmosphere resembled its current, oxygen-dominated state—relied heavily on iron to drive their metabolisms. Today, the remnants of a long-ago iron-rich environment are visible as striking red bands on ancient canyon walls, and Newman's work is relevant for explaining those patterns.

"Choosing bacteria that can be worked with genetically really set her apart from her peers in the geosciences," says her former teacher Thomas Silhavy, a Princeton University microbiologist. "She realized that genetic analysis opens all the doors for molecular sciences. You could argue that she created the field of geomicrobiology."

Newman's work has crossed over into modern medicine and ecology as well, helping explain how modern bacteria thrive in unusual settings—from the mucus-filled lungs of cystic fibrosis patients to arsenic-contaminated streams. Learning what keeps the bacteria alive could lead to novel ways to thwart their growth.

FOLLOW THE FUN

As an undergraduate at Stanford University, Newman never guessed she'd end up as a microbiologist. She majored in German studies and took a lot of environmental and materials science classes. "I loved everything, that was my problem," she says. "I was an advising nightmare." She believed in doing what she loved, she says. If one day that was German and the next engineering, why not? That's still how she conducts research, following the ever-winding path of her interests.

But as graduation loomed, Newman had to nail down something to do next. She chose environmental engineering—a combination of some of the things that had fascinated her most at Stanford—and began a graduate program at MIT.

With no real engineering experience, she had to push to find a professor who would take her on. "Even though I said 'No thanks' six or seven times, she really wanted to work with me," says François Morel, who studies how microorganisms interact with metals—a topic that intrigued Newman. Her persistence paid off and Morel finally became her advisor.

In Morel's lab though, Newman says she didn't have the patience for the first project he gave her: studying how phytoplankton respond to silver. Beakers for these experiments needed to be washed repeatedly in acid baths to rid them of metal contamination. "I realized that multiple acid-washing would probably drive me crazy after a while," says Newman, "so I asked if I could switch."

Around that time, a senior student in the lab, who had gone all over Boston collecting bacteria that could metabolize high concentrations of arsenic, cleared off her desk. "She gave me one of her bottles of bacteria that was destined to be thrown away," says Newman. "And it was this really bright yellow color, and the only thing I knew how to do—from my materials science background—was to figure out what compound was making it yellow."

That's how Newman stumbled upon the molecules that allow bacteria to metabolize metals. These colorful compounds guided her budding career. But the real pivot point came when Morel moved his lab from MIT to Princeton. Though Newman had planned on only getting a master's degree and then pursuing patent law, she decided to accompany him and finish her Ph.D., for the fun of it. "I was doing things because I enjoyed them and I was lucky because the rest just took care of itself," Newman says.

She started seeking out courses in genetics and quickly saw its potential for studying bacterial processes. Newman's teacher of one short course, "Advanced Bacterial Genetics" at Cold Spring Harbor, was Bonnie Bassler, now an HHMI investigator at Princeton. Bassler says Newman caught her attention with her incredible energy.

"She came with little background in genetics but she knew she wanted to learn it. She was incredibly hard working, and unflappable. After long days of working and studying, everyone else would be too exhausted to move, and she'd bound out the door to go on a jog."

Leah Fasten

That vitality and enthusiasm hasn't faded; Newman's lab members nicknamed her "The Catalyst" (like an enzyme that increases the rate of a chemical reaction). "She injects energy into any project," keeping the lab both fun and successful, says graduate student Alexa Price-Whelan. "Even when she was exhausted on maternity leave, she'd come into the lab and have more energy than the rest of us combined."

Every lab member likes to mention the lab bench with Newman's name on it, a rarity among investigators who have teams of students to collect data for them. Though the countertop has become a storage area for unneeded equipment, Newman insists that the area is hers, and she plans to hunker down at the bench any day. "She wants to be right there in the thick of things, getting her hands dirty," says Paula Welander, another postdoctoral fellow in the lab. "We tease her about her lab bench a lot, but really it's very inspiring."

The 36-year old Newman exudes not only energy, but confidence. She could easily be mistaken for a graduate student: small with dark, untamed hair and glasses perched on her nose, she's dressed casually in brown and orange earth tones, except for a purple plastic watch. But she owns her lab like no graduate student could. At a recent lab meeting, midsentence talking about geology, she leans her chair back and rests her clog-adorned feet on the conference table. She's perfectly at home here, leading a lab.

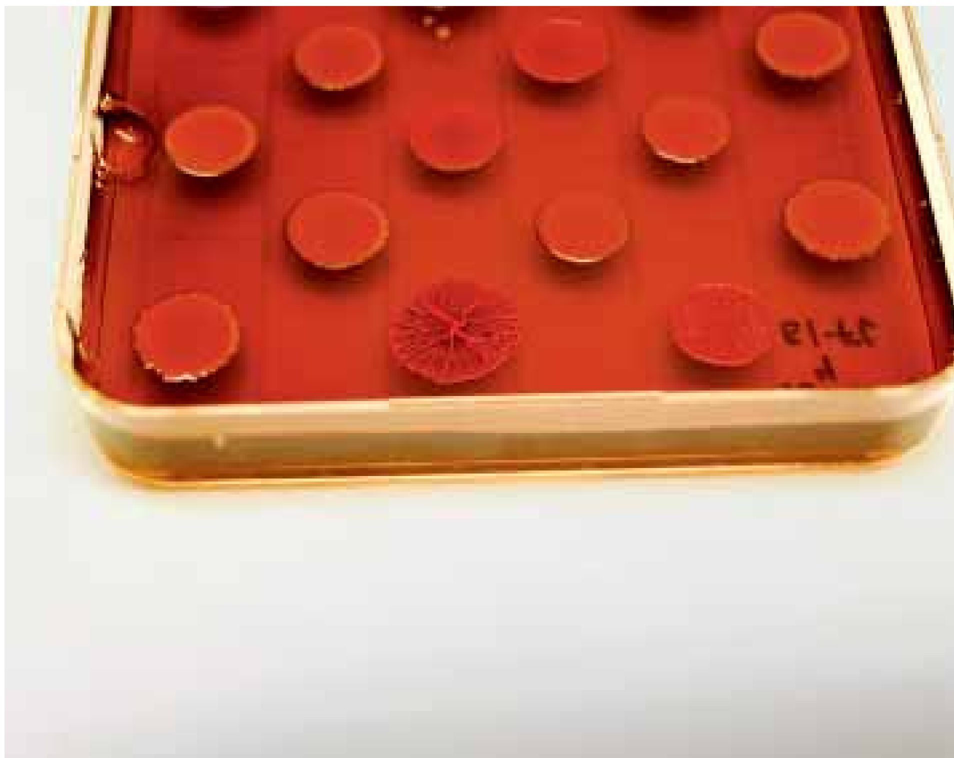
Her one-year old son Ronen occasionally makes the lab his home too. A pile of stuffed animals and a rubber duck sit on Newman's office floor next to a thick textbook entitled "Principles and Applications of Aquatic Chemistry." Although married to inorganic chemist Jonas Peters, she says science talk is rare at home—especially now, with the baby dominating their time. "Once in a blue moon we'll talk about science," she says. "Whenever I have a grant application that requires complex chemical structures, he double checks to make sure I've drawn the bonds right. Sometimes he just draws them for me."

GEOLOGY GOES GENETIC

That summer at Cold Spring Harbor changed the direction of Newman's research.

"I realized this huge power in genetics that could solve all these problems I was considering," she recalls. Once at Princeton, she started characterizing the arsenic-metabolizing bacterium, which she named *Desulfotomaculum auripigmentum* for its gold-colored pigments. At that point, she couldn't genetically modify the microorganism, but she held on to that goal for later.

Though she worked in a geosciences lab, Newman frequented molecular biology labs to absorb techniques and advice, says Princeton's Silhavy, who had Newman as a



student in his graduate genetics course. "When there were things to learn, she took it upon herself to learn them," he says.

Newman thought that together microbiology and genetics could tackle questions that geologists had been grappling with. "A lot of geology-related microbiology until then had been very descriptive, and here was finally a way to get at underlying mechanisms."

In 1998, Newman landed a postdoc position in the microbiology lab of Roberto Kolter at Harvard Medical School. "Her background really caught my eye," says Kolter, who prides himself in having a diverse team. "I'd never had anyone with a degree in German studies apply to my lab." She proposed to study bacteria that metabolize not arsenic, as she'd studied with Morel, but iron.

"I must say that I had never thought of studying this," says Kolter. "When she first brought it up I thought 'What's the big deal? Why is this important?' but after a few minutes with her I was convinced this was the project she should do."

Iron is noteworthy because it was much more biologically available in the ancient, oxygen-depleted earth than it is today. Most bacteria need oxygen to survive because chemical reactions that give bacteria energy produce excess electrons. Oxygen, an electron acceptor, can collect these spare electrons. Other compounds—like iron—can accept electrons too but the mechanism was unknown before Newman started studying iron-metabolizing bacteria.

Newman had an inkling that the bacteria produced molecules that acted outside the cell as electron shuttles—carrying electrons from the cell and dumping them on iron. Her suspicions were right—she discovered evidence for such an electron shuttle by screening mutants that couldn't metabolize iron. With that finding, Newman suddenly had a plethora of options for her future.

"She arrived in my lab in January, and after she had been there less than a month, she came into my office and told me that she had three job interviews," says Kolter. "This is how impressive she was. Nobody else at the time was thinking of combining environmental microbiology and genetics. She paved the way for a new field."

Newman stayed in Kolter's lab for two years, though, learning everything she could about genetics before accepting a job at the California Institute of Technology—a joint appointment in geological and planetary sciences and biology.

ANCIENT RECORD, MODERN LUNGS

Today, oxygen makes up a fifth of the atmosphere of the earth and most life forms rely on it. But 3.8 billion years ago—when the earliest evidence of life is recorded in ancient rocks—oxygen was scarce. Nailing down exactly when, and how, the atmosphere transitioned to oxygen requires probing the fossil record for the appearance of microorganisms that produced oxygen. "Dinosaur footprints only go back a short ways," says Newman. "If you want to understand the evolution of life on earth billions of years before that, you need to understand microbiology."

Typically, geologists have used molecules called 2-methylhopanoids as markers of oxygen-generating life. They've been found in rocks that some claim are 2.7 billion years old. But other geochemical measurements do not find evidence for appreciable oxygen on the earth at that time. At Caltech, and now at MIT, where she moved her lab in 2007, Newman has probed this discrepancy by investigating the role of 2-methylhopanoids in modern bacteria. Her lab has found that the ability of modern bacteria to make these compounds is not related to their ability to generate oxygen. Although more work needs to be done before ruling out 2-methylhopanoids as oxygen markers, Newman says the "case doesn't look very good."

The biggest focus in the Newman lab now is one that started as a side project: how the bacteria *Pseudomonas aeruginosa*

Image: Lars Dietrich / Newman lab Photo: Leah Fasten

Bye-bye Biofilm. LEFT: *P. aeruginosa* use phenazines to breathe in low-oxygen environments, like the mucus-filled lungs of cystic fibrosis patients. With no phenazines available, the bacteria form shriveled colonies (front, center) so that every bacterium has access to oxygen. RIGHT: One strain of *P. aeruginosa* makes green-pigmented phenazines. The bottles on the left contain bacteria engineered to lack the molecules.

metabolizes iron. *P. aeruginosa* produces colorful phenazines—compounds Newman identified in her search for molecules that shuttle electrons to iron. But *P. aeruginosa* isn't relevant only to the ancient earth—it's the bacteria that most often infect the lungs of people with cystic fibrosis.

The minuscule cellular brushes that normally sweep the lungs clear of mucus are missing in people with the disease. Their lungs build up layers of mucus, a fertile place for bacteria to thrive. These thick layers of mucus have low concentrations of oxygen, resembling the oxygen-deprived atmosphere of the planet billions of years ago.

"Pseudomonads colonize the lungs just like they colonize other surfaces," says Newman. "They aggregate into multicellular communities that become increasingly resistant to antibiotics with time."

Since Newman suspects that phenazines are critical to *P. aeruginosa*'s survival in these deep layers without oxygen, she hopes that blocking phenazine cycling might be a way to combat lung infections.

A RAINBOW OF BACTERIA

Thanks to the bright colors of phenazines, it's easy to see whether bacteria are producing them. Newman's postdoctoral fellow Lars Dietrich shows the drastic effect of oxygen on phenazine production by pulling two beakers of murky bacterial soup off a shaking platform that keeps the liquids constantly churned and exposed to oxygen. One beaker, filled with unmodified *P. aeruginosa*, is the color of green Kool-Aid (other natural *P. aeruginosa* strains produce blue, orange, red, and yellow phenazines). The other beaker, full of almost transparent fluid, is chock full of bacteria that were modified so they can't produce phenazines. Dietrich sets the beakers on his lab bench and immediately the green in the first sample begins to fade.

"Since it's not being shaken around to get lots of oxygen, it's using up the phenazines," he explains. "Having phenazines is like having a snorkel to breathe underwater." The bacteria are dumping extra electrons onto the phenazines, which carry the electrons out of the cells.

Phenazines also affect whether *P. aeruginosa* can form biofilms—colonies of bacteria encased in a slimy goop of extracellular matrix. Bacteria banded together into biofilms exist on unbrushed teeth, on slimy rocks, and in the lungs of cystic fibrosis patients. Since bacteria in the deepest layers of the biofilms don't have access to oxygen, they need phenazines to breathe. In the bacterial strain that Dietrich has blocked from making phenazines, the colonies form not smooth films but curly, bumpy, surprisingly predictable shapes that expose every bacterium to oxygen. It's another finding that links back to cystic fibrosis: if the bacteria without phenazines can't form normal biofilms when oxygen is limited, they can't survive in mucus-filled lungs as easily.

Morel says Newman's diverse background is what allows her to make these imaginative connections. "Her background gives her a lot of different things to think about when she looks at a problem," he says. Ask Newman how she's come to make such creative connections in her work, and she brings it back to her parents: "I have to credit them as people who always appreciated new things and encouraged my wide-ranging interests." On weekends they drove her to high school debate tournaments, and helped her track down materials for science fair projects that emitted horrible noises from the basement, which she says they tolerated happily.

The way she charts her own path is a lesson that resonates strongly in her students. Tanja Bosak, one of Newman's first students at Caltech and now an assistant professor at MIT, says she tries to model parts of her own lab after Newman's.

"She let me really develop my own project the way I wanted but was always there to support me and answer questions," explains Bosak. "She taught me that you can have fun and do science. And that it's really important to run a lab the way you want—you don't have to try to be something you're not."

Whether it's the quick switch from English to Spanish to order a sandwich from a Latino cashier at an MIT café, her ability to bridge geology and microbiology, or juggling her work life and home life, Newman moves with ease across several worlds.

"She's gone from being a student, when I first met her, to the head of a huge lab and a leader in her field," says Bassler. "But to me she seems exactly the same as that day she walked into Cold Spring Harbor. Her science has certainly grown and changed, but in her spirit, she's one of the brightest lights in the bacterial community. Her modesty and enthusiasm and talent are always a breath of fresh air."

As for the future, Newman hesitates to predict where her next research projects will take her, beyond the obvious continuation of her foray into cystic fibrosis. "My hope is that in the longer term, my research will take me in directions I can't even imagine now," she says, "because that's what makes this so fun." ■