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April 13–17, 2016 | Seattle, Washington

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Root and Gut Microbiomes Are Strikingly Similar
Marcia Stone
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Safer? Healthier?

Social and professional perspectives on risky practices have changed dramatically over the past century with the emergence of Health and Safety as a paradigm of our times

Bernard Dixon

I might have been, but was not, alarmed last night when hearing on my car radio about a piece of research that had revealed the considerable danger of *Escherichia coli* acquired from car steering wheels. A university researcher had been to a car park with some cotton wool swabs which, taken back to the lab and plated out on nutrient medium, had revealed “astronomical” numbers of *E. coli* cells in 9 out of 10 vehicles. “Although *E. coli* can be harmless,” the reporter said, “it also causes not only severe gastrointestinal infections but also life-threatening conditions such as kidney failure.”

Back home, I went to the Internet and quickly found four other reports of the same general sort. Each one reflected eager microbiologists’ efforts to enumerate a variety of harmless organisms, from soil bacteria to normal components of the skin flora, in locations such as door knobs and shop counters.

On reflection, it occurs to me that this sort of thing has become much commoner with the emergence of our modern obsession with health and safety. While entirely appropriate when applied with judgement, the notion of health and safety seems in recent years to have extended into the domain not only of the exaggerated but of the frankly unreal. The key question, of course, is where to draw the line in these matters.

A little historical context may help. Think of a man without medical qualifications, who treats a child who may (or may not) be suffering from a potentially fatal disease, using material whose composition and toxicity are (to say the least) uncertain. In this and other cases, he makes no attempt to secure “informed consent” from patients—whose names, addresses, and personal circumstances he then publishes to help in publicizing some astounding claims. But he does not tell all. Like fraudulent quacks everywhere, he keeps the details of his “treatment” secret, so its validity cannot be checked independently.

Perhaps worst of all, this man performs horrendous experiments on human beings—injecting them with a particularly virulent microorganism—before he has revealed details of, or even carried out, the same tests in animals. Some patients die as a result. A distinguished collaborator up to this point (who is a medical doctor) rebels against what his colleague is doing, and dissociates himself from the work.

Louis Pasteur was the chemist who took these risks, and not only rode the inevitable criticism but ended the day with worldwide acclaim for his astonishing success in defeating rabies and other terrible maladies. I was interested to see what an independent observer, the historian Gerald Geison, made of the affair many years later. His analysis (*Hastings Center Report*, 8:26, 1978) concentrated on Louis Pasteur’s treatment of the rabies victim Joseph Meister in 1885 and showed that the great man did indeed violate several ethical and scientific precepts, including one he had himself publicly espoused.

Pasteur started to give the little Alsatian boy “aged” spinal marrow, thought to contain attenuated rabies virus, in July 1885—a month before he began investigations with the same material in animals previously infected with the disease. Success in those experiments was only “partial.” Pasteur suspected, but could not be sure, that his spinal cord tissue contained the rabies germ. What he did know was that at the end of his series of inoculations with increasingly virulent potions, the boy was receiving material even more dangerous than that obtained directly from rabid dogs. Pasteur had previously refused to treat a bitten child because he had not yet established his method in animals and had insisted that “proofs must be multiplied *ad infinitum* on diverse ani-
mal species before human therapeutics should dare to try this mode of prophylaxis on man himself.” That was the golden rule he abandoned, to the displeasure of his colleague Emile Roux, when confronted by Joseph Meister and his mother.

But there were, as Geison suggested, mitigating circumstances. Rabies has long been considered an especially mysterious and horrible disease. Its victims, usually children, are often reduced to total physical and mental degradation as they lose their sanity and become quivering, convulsive, animal-like shadows of their former selves. Long before Pasteur came along, the fear of rabies was sufficient to make people submit voluntarily to virtually any plausible therapy, even one as excruciating as cauterization by fire or acid. What does the modern concept of “informed consent” mean in these circumstances?

Then there is the extraordinarily long incubation period of rabies—from six weeks up to a year—during which treatment can be commenced. Coupled with a high degree of uncertainty as to whether the disease will develop in a person bitten by a known rabid animal, this generates a unique ethical problem. Probably most bitten individuals could forego medical attention without suffering anything untoward. So every case of post-exposure vaccination against rabies is a form of human experimentation which might well be unnecessary.

Historically, Pasteur appears to have been justified regarding “informed consent” and privacy. None of his opponents criticized him on these grounds. He was attacked for practicing medicine without a medical degree—but covered himself by ensuring that licensed physicians always performed the injections. And he made short shrift of attacks from two other quarters—the anti-vivisectionists (who wished him to do fewer, not more, tests on animals) and the anti-vaccinationists, who objected to his work on principle.

More telling, to modern eyes, was the criticism that Pasteur’s vaccines, unlike those of the English pioneer Edward Jenner, came from the laboratory rather than from nature. In 1796 Jenner too had done something which now appears intolerable. He inoculated cowpox matter into the arm of a healthy lad, James Phipps, and gave him smallpox pus six weeks later. But the cowpox material did come from nature, and Jenner’s confidence was founded on ample observations on the natural relationship between the two infections. What Pasteur did was very different; there was a real prospect that, by manipulating presumed rabies virus, he could have created a novel, artificial form of the disease.

Gerald Geison concluded with canny ambivalence: It was “an act of immense courage and humanitarianism” for Pasteur to treat Joseph Meister: had the exercise failed, his reputation would have been seriously damaged. But it is also “a form of courage and humanitarianism” to refuse to use a potentially beneficial procedure in the face of resolvable uncertainty. Was it the pleading of Meister’s family that made Pasteur back his hunch that his “vaccine” would work? Or was it that uncanny affinity with material and ideas (comparable to the gardener’s green fingers or the creative science of ham-fisted nuclear pioneer Lord Rutherford) which here and on countless other occasions led Pasteur to take considerable risks—and win?
RESEARCH ADVANCES
Polymyxin Resistance in China Renews Worries of Pan-Resistant Pathogens

Jeffrey L. Fox

The newly recognized mcr-1 gene, which confers resistance to polymyxin antibiotics, is already widespread among Enterobacteriaceae circulating among both pigs and humans in China, according to Jianzhong Shen of China Agricultural University in Beijing and collaborators in China, the United Kingdom, and the United States. This plasmid-borne drug resistance gene now joins forces with other resistance traits, notably those conferring resistance to carbapenem as well as other kinds of antibiotics. Their increasing presence in gram-negative bacteria is stirring renewed anxieties among clinicians and public health officials, who are concerned there will soon be little left to protect patients who become infected with these pathogens. Details describing this investigation appeared 18 November 2015 in *The Lancet Infectious Diseases* (doi:10.1016/S1473–3099(15)00424–7).

Nearly simultaneously, another research group in China reported finding hypervirulent strains of carbapenem-resistant *Klebsiella pneumoniae* infecting hospital patients in Zhejiang Province. Several similar strains circulating in that region are causing serious as well as fatal infections, particularly among surgical patients, according to Sheng Chen of Hong Kong Polytechnic University and collaborators at Zhejiang University in Hangzhou, China. These strains are “hyper-virulent, multidrug-resistant, and transmissible,” they note. Details appeared 16 November 2015 in *Antimicrobial Agents and Chemotherapy* (doi: 10.1128/AAC.02173–15).

Separately, officials at the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta, Ga., recently reported findings from ongoing efforts to monitor relatively rare U.S. cases caused by carbapenem-resistant Enterobacteriaceae (CRE), in which the bacteria produce OXA-48 and similar carbapenemases, an enzyme conferring resistance to carbanem and similar β-lactam antibiotics. Such strains infected only about 43 U.S. patients between 2010 and 2015, according to Meghan M. Lyman and her CDC collaborators. Although transmissions of such strains occur in the U.S., they note, most such cases arose from exposures to CRE strains “outside the United States.” Details appeared 4 December 2015 in *Morbidity and Mortality Weekly Report*. Such findings suggest it is wise to continue monitoring for infections due to CRE strains, but they indicate no near-term need for drastic actions.

The situation in China with strains carrying mcr-1, however, appears to be more serious. “These are extremely worrying results,” says Shen’s collaborator, Jian-Hua Liu from South China Agricultural University in Guangzhou, China. Mcr-1 “is readily passed between common bacteria such as *Escherichia coli* and *K. pneumoniae*,” and its ready transmissibility suggests that “the progression from extensive drug resistance to pan-drug resistance is inevitable,” he adds. Until now, rare instances of polymyxin resistance were attributed to chromosomal mutations, not plasmid-borne horizontal gene transfers, which can greatly increase the speed with which such traits can be disseminated.

Cultured colonies of *K. pneumoniae*. Strains that are “hyper-virulent, multidrug-resistant, and transmissible” have been found by researchers in China. (Centers for Disease Control and Prevention photo.)
The *mcr*-1 gene was first detected several years ago in *E. coli* strains isolated from pigs being raised near Shanghai and, by 2014, was being found in pigs and chickens from four nearby provinces. More worrying, it also was detected among patients with either *E. coli* or *K. pneumoniae* infections in hospitals in Guangdong and Zhejiang provinces. “Because of the relatively low proportion of positive samples taken from humans compared with animals, it is likely that *mcr*-1-mediated colistin resistance originated in animals and subsequently spread to humans,” Shen says. “China is not the only country to use colistin in farming, but there are many countries, including in Europe, that use polymyxins in agriculture, and therefore the responsibility to acknowledge and address the use of antibiotics across human and veterinary sectors must be also global.”

Jeffrey L. Fox is the Microbe Current Topics and Features Editor.

NEW FROM ASM

**Enterococcal Plasmid Wars: Cycling from Harmless to Virulence, then Back**

Shannon Weiman

Transposons are largely responsible for the Dr.-Jekyll to-Mr.-Hyde switching that enables the enterococci to range from innocuous gut inhabitants to virulent, antibiotic-resistant pathogens—and then back again, according to several researchers who spoke during the 2015 ICAAC meeting held in San Diego last September. Those transposons can mobilize large genomic regions carrying multiple virulence, antibiotic, resistance, and metabolic genes, thereby contributing to the rampant spread of resistance and pathogenicity among clinically concerning strains such as vancomycin-resistant enterococci (VRE).

“The success of *Enterococcus faecium* and *E. faecalis*, evolving as multi-resistant nosocomial pathogens and leading hospital pathogens worldwide, is associated with their promiscuous nature in acquiring new genetic elements, including antimicrobial resistance genes encoded by mobile genetic elements,” says Guido Werner of the Robert Koch Institute in Berlin, Germany. Tn1546 is the main transposon that mobilizes vancomycin resistance genes, which may be marooned on large pathogenicity islands within “megaplasmids,” he says. These oversized, multifunctional plasmids confer survival advantages as they move rather freely among commensal bacteria and opportunistic pathogens, creating a dangerous ecology within the gut. One scenario raising fresh concerns is the shuttling of vancomycin resistance genes into *Staphylococcus aureus*, leading to more than a dozen confirmed cases of VRSA in the United States, he notes.

Antibiotics can help to drive transposon-mediated genetic transfers, according to Barbara Murray of the University of Texas Health Science Center in Houston. Referring to research by Kathryn Beabout of Rice University and her collaborators, Murray says that exposure to tigecycline, a tetracycline derivative, triggers Tn916 mobilization in *E. faecalis*, increasing transfer of the TetM resistance gene 1,000-fold. Thus, antibiotics not only select for resistant bacteria, but also accelerate transfers of...
resistance genes to formerly drug-susceptible strains.

Despite the multitude of virulence and drug resistance genes that some bacterial strains amass, commensal enterococci tend to outcompete and replace these clinical pathogens when pitted against each other in the mouse gastrointestinal (GI) tract, according to Maria Montealegre, a graduate student working with Murray. “This may explain the vast predominance of clade B commensal strains in humans in the community, and why antibiotic-resistant *E. faecium* strains are often replaced once patients leave the hospital,” Montealegre says.

Remarkably, commensal strains actively kill some of those pathogenic strains by turning their mobile elements against them, says Murray, citing research by Michael Gilmore of Harvard Medical School in Boston and his collaborators.

“We unexpectedly observed that the prototype clinical isolate strain V583 was actively killed by GI tract flora, whereas commensal enterococci flourished,” says Gilmore. Commensal strains secrete a heptapeptide pheromone, cOB1, that triggers virulent strains to self-destruct. This pheromone activates plasmid-based mobile elements, which are prevalent in virulent strains but not commensals, ultimately causing chromosomal genome instability that can prove lethal. “The accretion of mobile elements in *E. faecalis* V583 renders it incompatible with commensal strains,” he says. Thus, these critical mobile elements are responsible for both the rise and the downfall of this opportunistic pathogen.

Shannon Weiman is a freelance writer in San Francisco, Calif.

**RESEARCH ADVANCES**

**By Consuming Glycine, Gut Microbiota Control Glutathione Synthesis**

Carol Potera

The gut microbiota in mice consumes glycine, one of three amino acids needed by host animals to make the powerful antioxidant peptide glutathione, according to Adil Mardinoglu at the Royal Institute of Technology in Stockholm and Chalmers University of Technology, Gothenburg, both in Sweden, and his collaborators in Sweden and Denmark. He calls this
example of the gut microbiota exerting partial control over this host metabolic pathway “surprising,” and suggests that “imbalance in the composition of bacteria [within the microbiota] may lead to the progression of chronic diseases.” Details appeared 16 October 2015 in Molecular Systems Biology (doi: 10.15252/msb.20156487).

Mardinoglu and his collaborators compared metabolic differences between conventional mice—that is, host animals with a full complement of microorganisms in the gastrointestinal tract and other anatomic sites—and germ-free animals. Those comparisons drew on direct experiments with mice, analyses of gene expression data, some 28 tissue-specific genome-scale metabolic models, and a generic mouse metabolic reaction that the researchers developed, they note. Their approach combined proteomics, metabolomics, and transcriptomics, with computer modeling of organs such as the small intestine and liver.

By measuring levels in the hepatic portal vein of the three amino acids needed for making glutathione, the researchers determined that amounts of glycine shunted to the liver and glutathione production are lower in conventional mice than in germ-free mice. In other words, the microbiota within the gastrointestinal tract of the host mice consumed glycine, supporting their own growth while depriving their hosts of what they need to produce glutathione.

Moreover, expression of the gene encoding nicotinamide nucleotide transhydrogenase (NNT), an enzyme that is needed for making glutathione, is higher in mice with a full-fledged microbiota than it is in germ-free mice, Mardinoglu continues. Although the limited availability of glycine in such mice prevents them from making glutathione, they try to compensate by making more NNT, he says.

Lipid metabolism in such mice also is altered compared to germ-free animals. The small intestine of conventional mice produces lower levels of high-density lipoproteins and chylothromics. Overall, the gut microbiota regulates amino acids, glutathione, and lipid metabolism in mice.

These metabolic shifts could be clinically relevant for particular groups of
human patients, according to Mardinoglu. For example, individuals who are obese and patients with non-alcoholic fatty liver disease have low levels of glycine in plasma, he says. “The effect of glycine supplements should be investigated in these metabolic disorders.” More generally, deficiencies of glutathione contribute to oxidative stress, obesity, type 2 diabetes, and non-alcoholic fatty liver disease, he adds. “The link between gut bacteria and glutathione metabolism could lead to the development of probiotics that deliver beneficial bacteria to the gut.”

This research “introduces a novel methodological approach for inferring the impact of microbiome composition on metabolism in different tissues in mice,” says Costas Maranas at Pennsylvannia State University in State College, who was not involved in the work. “Their efforts open the door for more investigations that will link detailed descriptions of the gut microbiome with a mouse tissue model.”

Carol Potera is a freelance writer in Great Falls, Mont.

NEW FROM ASM

To Outcompete Others, S. pyogenes Clade Undergoes Transmissibility Upgrade

David C. Holzman

A Streptococcus pyogenes clade that emerged in Portugal during the past decade quickly outcompeted several other locally circulating lineages of this pathogen, according to Mario Ramirez and his collaborators at the University of Lisbon in Portugal. What happened in Portugal also apparently took place elsewhere in Northern Europe and in the United States, they note. “Taken together, these observations suggest that, in spite of the differences in the structures of the S. pyogenes emm89 populations previously circulating in different countries, the same clade disseminated and outcompeted other emm89 lineages over the first decade of the 21st century.” These findings carry implications for the design of diagnostic tests and vaccines aimed at detecting and controlling these pathogens.


Before being detected in Portugal, this same or other very similar S. pyogenes clades were being detected nearly simultaneously elsewhere in Europe, including the United Kingdom (UK), Iceland, and Finland, as well as in the United States (US). In the UK but particularly in Portugal, infections caused by this clade tend to be mild and non-invasive, but more persistent and more readily transmissible than are those caused by other strains of this same pathogen, Ramirez points out.

These clinical findings plus partial DNA sequencing data suggest that all these emergent versions of S. pyogenes are very close if not identical, according to Ramirez and his collaborators. “While virulence studies using animal models indicate an increased virulence of the emm89-new strains, other in vitro studies suggest that the novel emm89-new phenotype may be advantageous for environmental persistence and transmission, resulting in an increased number rather than severity of emm89 infections,” they note, adding that there may be multiple reasons for the success of this novel clade.

Enhanced production of secreted toxins is another way in which this pathogen shows “increased fitness in the upper respiratory tract, resulting in the ability to disseminate in a very short time frame and cause abundant human infections in susceptible persons,” notes James M. Musser of the Houston Methodist Research Institute in Houston, Tex., who commented on the analysis by Ramirez and his collaborators in the same issue of mBio. He also sees evidence for this version of S. pyogenes causing milder infections but being more readily transmissible than are strains belonging to other clades.

“Selection for transmission is frequently argued to be the most important outcome of the natural selective forces acting on . . . pathogens such as S. pyogenes that associate exclusively with humans,” Ramirez says. “The
Here in brief are findings from several recent reports of efforts to understand how microorganisms in the gut or elsewhere in the body affect the host:

- Depleting the gut microbiota helps to enhance type 2-cytokine signaling and convert M1 into M2 macrophages in host mice—in turn, stimulating development of beige from white fat, helping to keep such animals lean regardless of their food intake, according to Mirko Trajkovski of the University of Geneva, Switzerland, and his collaborators. Details appeared 16 November 2015 in *Nature Medicine* (doi:10.1038/nm.3994).

- Proteins produced by *Escherichia coli* in the gut of rodents may signal “fullness” to the host by activating “satiety pathways,” releasing hormones from the gut and also modulating sensory pathways in the brain, according to Serguei Fetissov of Rouen University in France and his collaborators at several French institutions and in England. Details appeared 24 November 2015 in *Cell Metabolism* (doi:10.1016/j.cmet.2015.10.017).

- Bacteria in the gut of German cockroaches release pheromones, including volatile carboxylic acids that play a major role in how the cockroaches socialize and communicate, according to Ayako Wada-Katsumata of North Carolina State University in Raleigh and her collaborators. Details appeared 7 December 2015 in *Proceedings of the National Academy of Sciences* (doi:10.1073/pnas.1504031112).

- In mice lacking lymphocytes, the adaptation of *E. coli* to the gut environment is slowed compared to those bacteria in hosts with intact immune systems, according to Isabel Gordo and Jocelyne Demengeot of Instituto Gulbenkian de Ciencia in Oeiras, Portugal, and their collaborators. Details appeared 30 November 2015 in *Nature Communications* (doi:10.1038/ncomms9945).

- Analyses of the gut microbiomes of American Indians of Cheyenne and Arapaho ancestry indicate a reduced abundance of the anti-inflammatory bacterial genus *Faecalibacterium* and a fecal metabolite profile consistent with dysbiosis and metabolic disorders, according to Cecil M. Lewis, Jr., of the University of Oklahoma, Norman, and his collaborators. Details appeared 6 December 2015 in *Current Biology* (doi:http://dx.doi.org/10.1016/j.cub.2015.10.060).

- The gut microbial populations in patients with enteric infections change in similar ways regardless of the specific pathogen responsible for causing their disease, according to Shannon Manning of Michigan State University, Lansing, and her collaborators. Moreover, blocking increases in *E. coli* may be important for preventing those bouts of disease. Details appeared 22 September 2015 in *Microbiome* (doi:10.1186/s40168-015-0109-2).

- Microbes in the gut convert polyphenols in pomegranate juice into urolithins (6H-dibenzo[6,7]pyran-6-one derivatives), which can protect against Alzheimer’s disease, according to Navindra Seeram of the University of Rhode Island, Kingston, and his collaborators. Details appeared 11 November 2015 in *ACS Chemical Neuroscience* (doi:10.1021/acschemneuro.5b00260).

Identification of this clade raises the possibility of using the genomic information to search for candidate genes implicated in this higher transmission phenotype.”

The surprising degree of genetic plasticity within these emergent *S. pyogenes* clades could prove important for those designing diagnostic tests and vaccines to detect and control the infections that this pathogen is causing, note Claire Turner, Shiranee Sriskandan, and their collaborators of Imperial College London in the UK in the same issue of *mBio*. “The changes [this clade] had undergone are likely to impact on transmission and ability to spread through the population,” says Turner. “I would think that this is likely to happen with other bacteria as it is a fundamental part of the pathogen life cycle and is an important area for future research focus.”

David C. Holzman, who writes from Lexington Mass., is a contributing writer for Microbe.
were attached to the major coat pVIII protein of the virus. Because this virus can be genetically reprogrammed with slight differences in that protein, those attachment sites can be “tuned” by changing how they are spaced along the viral surface—“multiplying the possibilities for creating intricate chromophore networks and for controlling energy transfer,” the researchers note.

“Our original motivation was to be able to reproduce the quantum-enhanced energy transport occurring in natural photosynthesis by using an artificial, man-made device,” Scudo says. “At first, we did not think of industrial applications of our system. However, probably with a few more changes, these systems could be tested in dye-sensitized solar cells, chemical sensing, or medical diagnostics.”

“Our hypothesis was that we could select the spacing between amino acids to precisely control the distance between attached chromophores,” Belcher adds. “By changing the interaction between the chromophores, we are able to control the energy transport.” The two versions were designed and chosen to demonstrate two representative regimes of energy transport: classical and quantum, she points out. In one version of M13 phage, the chromophores were scattered in a rather diffuse grid, and while collecting light energy they behaved as a classical “hopping network” for energy transport. In the other, the chromophores were spaced closely enough to be “strongly coupled,” behaving more quantum-like in energy transport and thus enhancing by 68% their capacity to transfer the light energy that they collected.

“This [research] represents a new threshold for the development of solar cells,” says So Young Yoo of Pusan National University in Busan, Korea. “The authors proved that genetically engineered phages can be successfully utilized as ‘tunable light harvesting materials.’” This approach, he adds, is “an important energy-transfer design concept.”

What will it take to move from working concept to practical use? Viruses “can boost solar cell efficiency” in dye-sensitized solar cells, according to Belcher. “We are still in the early stages in terms of industry implementation,” she says. “We hope that within the next few years we will test cost-effective materials systems and will conduct research in the detailed implementation for solar cell technology.”

Barry E. DiGregorio is a freelance writer in Middleport, N.Y.

NEW FROM ASM

Physical Interaction Directs cyclic-di-GMP Signaling in Gram-Negative Bacteria

Second messenger cyclic-di-GMP controls many cellular behaviors in gram-negative bacteria, but it remains a mystery how the cell’s signaling networks, consisting of dozens of proteins that can make, break, or bind the molecule, correctly direct signaling output. Recent work from Dartmouth College in Hanover, N.H., in collaboration with Cornell University in Ithaca, N.Y., highlights physical interaction as one way to direct signaling. First author Kurt Dahlstrom looked at mutations in diguanylate cyclase enzymes that lead to biofilm defects in *Pseudomonas fluorescens*, focusing on interactions of one, GcbC, with its cyclic-di-GMP responsive protein, LapD. “Signaling specificity occurs at least in part through the ability of the DGC enzyme to physically interact with the protein that binds cyclic-di-GMP,” explains lead scientist George O’Toole. Using genetic, biochemical, and structural approaches, the team identified an alpha helix on the surface of GcbC and an alpha helix on the surface of LapD that interact with each other. “We think this is one mechanism by which specificity is conferred,” concludes O’Toole.

Dahlstrom KM, Giglio KM, Collins AJ, Sondermann H, and O’Toole GA. Contribution of physical interaction to signaling specificity between a diguanylate cyclase and its effector. Published online 15 December 2015; doi: 10.1128/mBio.01978-15

NEW FROM ASM

Whole-Genome Sequencing for *Listeria* Outbreak Surveillance

Foodborne outbreaks remain a major concern worldwide, and the number of *Listeria monocytogenes* outbreaks reported increased in the European Union in 2015. New research from the University of Melbourne in Australia suggests that whole-genome sequencing (WGS) may improve surveillance methods. A team lead by Benjamin Howden performed comparative studies of WGS against traditional surveillance methods used to type 423 *L. monocytogenes* isolates. Their results suggest WGS is not only in agreement with methods such as multilocus sequence typing and PCR-serotyping, but that WGS is able to further refine strain differences that traditional methods aren’t. Prospective studies using 97 additional strains were able to find a match between a human isolate and one found in food-industry surveillance, demonstrating the ability of this method to infer links between potential outbreaks and their source of origin.

Determining an effective drug dose for an infection means taking many factors into account, including nutrient levels, antimicrobial peptide production, and vascularization. Albumin concentration can now be added to factors that change the efficacy of caspofungin against Aspergillus growth, shows a research team including the University of Crete in Greece; Rutgers, The Statue University of New Jersey in New Jersey, and the University of Texas in Texas. The research team, led by Giorgios Chamilos, showed that caspofungin—but not other echinocandins—was able to inhibit germinating hyphae, possibly due to albumin’s ability to bind both germinating hyphae and albumin. The next step is to determine structural requirements that facilitate albumin-drug synergy for potential therapeutic applications.

As we continue to wage the war against drug-resistant infections, research is moving forward on alternative therapies to fight resistant microbes. Histatin-5 (Hst5) is an antimicrobial peptide with known antifungal properties, including against Candida albicans. Researchers working with lead scientist Mary Ann Jabra-Rizk at the University of Maryland in Baltimore, Md., are developing the means to apply Hst5 in an infected oral cavity. The research team developed a hydrogel embedded with Hst5 and tested it against a mouse model of candidiasis. Untreated mice uniformly developed white plaques of fungal growth on their tongues, while most treated mice did not develop visible growth, and those that did were successfully treated with subsequent Hst5-hydrogel therapy. Further testing is warranted to test Hst5-hydrogel activity against additional oral pathogens, such as Porphyromonas gingivalis.

Most probiotic treatments consist of ingesting bacteria known to have commensal relationships with their human hosts but that have undergone little manipulation themselves. Lab head Todd Klaenhammer has a different idea. With first author Evelyn Durmaz, he and his team at North Carolina State University have engineered a strain of Lactococcus lactis to express a known toxin. The toxin, cry5B from Bacillus thuringiensis, is known to act against nematodes and has no known effects against human cells. The team hope to produce an probiotic that can be used to make anthelmintic treatments in underdeveloped countries. Their latest research in Applied and Environmental Microbiology demonstrates that several versions of the cry5B gene can be expressed in L. lactis, and that L. lactis lysates have antinematode activities.

Antiviral compounds generally act at more virus-specific level than antibacterial compounds. Work from the David Geffen School of Medicine at UCLA in Los Angeles, Calif., is hoping to improve this situation. First author Jun Zuo, working in Paul Krogstad’s lab, conducted a high-throughput screening against the enterovirus coxsackievirus B3 (CVB3). The team identified several compounds that inhibited replication of viral RNA and viral proteins in infected cells. Further, they observed replication inhibition in several other common enteroviruses, including several coxsackieviruses and enterovirus A-71. These compounds show promise for development into a broad anti-enterovirus treatment.


Understanding how probiotic treatments work will help scientists better design pa-
tient therapies that involve probiotics. James Versalovic and his lab at Baylor College of Medicine in Houston, Tex., hope to do just that. The scientific team tested the hypothesis that *Lactobacillus reuteri*, a common gut microbiome member for many mammalian species, quiesces the immune response by release of histamine. They showed that *L. reuteri* convert dietary histidine into histamine in the gut, where it interacts with histamine H2 receptor. “The histamine type 2 receptor is the key receptor receiving the histamine signal and suppressing factors produced by immune cells that promote inflammation,” explains Versalovic. The researchers showed that bacteria unable to generate histamine were unable to suppress a mouse model of colitis. Conversely, they showed that this histamine was diet-dependent, and that mice fed a histidine-free diet were also unable to suppress inflammation. In the future, says Versalovic, “we may be able to select specific probiotic strains, coupled with diet including specific amino acids like histidine, and possibly prevent or treat disease.”

Bacterial Predators in Host Microbiomes

Halobacteriovorax bacteria are marine predators that drive the dynamics of their host microbiomes, in turn modulating the health of their animal hosts

Rory M. Welsh and Rebecca Vega Thurber

In macroecology, predators play major roles in structuring ecosystem function and community diversity. Yet relatively little is understood about the roles of bacterial predators in the community ecology of microorganisms and host-associated microbiomes. Host-associated microbial community dynamics are affected by extrinsic environmental factors such as resource availability, temperature, and salinity, as well as host diet, genetic background, and health. Cooperative symbioses, antagonisms, competition, and predation also occur within a microbiome.

Thus, microbiomes are complex ecologies where intrinsic interactions among the members of the community may also significantly alter the structure and function of the microbiome, benefiting or harming the host. For example, the host flora may act as barriers to pathogens, physically blocking attachment sites and consuming nutrients while depriving pathogens of habitat space and necessary resources. In such cases, microbiomes can prevent invasive pathogenic microbes from colonizing and infecting the host.

Similarly, predatory bacteria likely play a significant role in controlling pathogenic bacterial populations. While we understand a great deal about the impacts of predation by viruses and protists on bacterial mortality, diversity, and evolution, less is understood about microbially mediated predation shaping communities or host niches. Here we discuss recent evidence examining the hypothesis that predatory bacteria are keystone members of microbiomes that influence the health of their hosts by consuming pathogens.

Bacterial Predators

Diverse modes of predation evolved independently across taxonomically disparate bacteria. For example, the alphaproteobacteria Micavibrio aeruginosavorus and the Bacteroidetes Cytophaga hutchinsonii are epibiotic predators, while the deltaproteobacteria Myxococcus xanthus are facultative predators that employ a “wolf pack” strategy of swarming to consume prey. Meanwhile, another group of predators, the deltaproteobacteria Bdellovibrio and like organisms (BALOs), are primarily obligate periplasmic predators that consume a wide variety of bacteria (Fig. 1). They were discovered in 1962 by German microbiologists Heinz Stolp and H. Petzold, who found Bdellovibrio in soil samples. Yet, as with all nonviral predators, these clades of predatory bacteria tend to be in low relative abundance, typically accounting for only 1 to 10% of the population in their habitats, and thus have remained at the fringe of microbial ecology research.

Nevertheless, the fascinating lifestyle of BALOs led some investigators to test them as broad-spectrum, living antibiotics. For instance, in 1973 BALOs were used as a biocontrol agent to prevent the bacterial blight of soybeans caused by Pseudomonas syringae (formerly P. glycinea). Unfortunately, the logistical obstacles inherent to

SUMMARY

➤ Predatory bacteria appear to be keystone members of microbiomes, and they can influence the health of their hosts by consuming pathogens.
➤ Little is yet known about the ecology of these predatory microorganisms, which occupy a wide range of habitats.
➤ Investigators began testing predatory bacteria, including Bdellovibrio, as biological control agents as early as the 1970s, and now with the ability to study community-wide effects such studies are gaining new emphasis.
➤ Following recent efforts to compile genomic sequence data for predatory bacteria, the next logical step is to assign them functional roles within their natural communities.
➤ Our recent time series, microbiome profiling studies, and coral microbiome manipulation experiments in laboratory settings focused on coral-associated Halobacteriovorax all suggest predatory bacteria regulate the structure of microbial communities.
growing and maintaining predators in the company of their prey prevented BALOs from becoming biocontrol agents. More recently, however, investigators made several noteworthy advances in characterizing BALO biology, including insights into their cell cycle, physiology, biochemistry, taxonomy, and utility as probiotics.

In 2004, details describing the first complete BALO genome were released, and since then the genomes of numerous freshwater and marine strains have been sequenced, providing additional information for researchers interested in BALO biology. For example, proteomic and transcriptomic analysis of the two phases of the BALO life cycle—attack phase and growth phase—revealed cell cycle-dependent expression and functions. However, little is yet known about the ecology of these predatory microorganisms.
and whether they truly act as the cheetahs of the microbiome.

**Isolating Predatory Bacteria from Hosts**

Predatory BALOs exert top-down forces—sometimes referred to as sideways control—in microbial community ecology. Because this top-down control involves consuming opportunistic copiotrophs and also preventing infections, it is hypothesized that these predators can contribute significantly to the health of some animals.

BALOs are among the smallest members of the rare microbiome, making it a challenge to isolate and culture these bacteria. To isolate individual strains of one group of marine BALO, the *Halobacteriovorax*, we used techniques developed by Henry William and his collaborators at Florida A&M in Tallahassee. That approach begins with a size-based filtration step, followed by an enrichment step before using the widely used double-layer plate technique to identify isolates from characteristic plaques.

Specifically, host samples are homogenized and passed through a 0.45-μm filter, which excludes larger cells and protozoan grazers, and thus separates out BALOs on the basis of their small size. The filtrate can then be applied directly to double-layer plates for enrichment culture. Because BALOs sometimes preferentially attack and kill one prey more readily than others, enrichment cultures can be made by adding nutrients to boost the levels of native prey when targeting a wide range of predators or by simply adding the target pathogen and then enriching for predators adapted to attack and kill that prey. Within three days plaques begin to develop on such double-layer lawns of prey bacteria, and these plaques continue to spread for approximately a week. Plaques are excised and examined under phase-contrast microscopy, and those containing highly motile bacteria (moving at speeds up to 160 μm/sec) are further purified and characterized.

Using such methods, we isolated *Halobacteriovorax* from a wide range of organisms and habitats (Fig 1). Although predatory bacteria occupy niches in almost every conceivable environment, we focused on collecting *Halobacteriovorax* from marine environments, ranging from the warm waters of Caribbean to the below-freezing waters and sea ice of Antarctica, where the water column is a constant -2°C year-round (Fig. 1).

We also isolated and characterized *Halobacteriovorax* strains from four different coral hosts in the Florida Keys (Fig. 1). *Halobacteriovorax* bacteria were routinely detected in these host-associated communities by means of gene amplicon and metagenome surveys. Using community-based data and additional experiments, we further evaluated the roles of these predators and their prey choices in ecologically important marine hosts.

**Characterizing *Halobacteriovorax* Interactions with One of Its Marine Hosts**

Using our *Halobacteriovorax* strains isolated from marine corals, we confirmed that these predators can prey upon some members of the coral microbiome in culture. However, whether they do so in nature and with what members of the host’s microbiome are two unresolved questions.

Although the wealth of sequence data emanating from microbiome studies has allowed for unprecedented detailed categorization and cataloging of individual members within host microbiomes, the ultimate goal is to begin to assign functional roles to those members. Exploring predator populations in amplicon and metagenomic datasets allowed us to generate hypotheses about potential interactions between these *Halobacteriovorax* strains and other members of the microbiome. Ideally predator-prey cycles in the microbiome will be studied by absolutely quantitative measures of abundance in future studies. But without a priori knowledge of which biological interactions to target among the hundreds of taxa present, truly quantitative approaches would be exceedingly costly and logistically infeasible.

However, our network analysis now offers exciting possibilities for evaluating such interactions in a complex microbial community. Specifically we applied co-occurrence network analysis to a set of 16S amplicon data from three coral species to evaluate the potential interactions of *Halobacteriovorax* with other members of the microbiomes associated with those three host species (Fig. 2). This three-year dataset of amplicon libraries revealed *Halobacteriovorax* species consistently associate with corals (79% prevalence) across the reef study site. Yet, as with all nonviral predators, these clades of predatory bacteria tend to be in low relative abundance, and their mean relative abundance across all libraries was only 0.40% (± 0.04 SEM).
However, this three-year monthly sampling time series combined with network analysis also revealed that corals harbor active bacterial predators that interact consistently with important heterotrophic coral microbes (Fig. 2). For example, on *Agaricia* spp. corals, *Halobacteriovorax* positively co-occur with eight members of the coral microbiome, including *Vibrionales*, *Cytophagales*, and *Atleramodadales*, each of which is considered a coral opportunist. This approach enabled us to condense our list of potential biological interactions, thus simplifying our future studies involving microbiome manipulation experiments and truly quantitative methods. We have now conducted addition experiments where we added these opportunists in the presence and absence of *Halobacteriovorax* and found evidence for similar interactions in situ.

**Studying Effects of Halobacteriovorax on Predation and Pathogenesis in Marine Hosts**

The predatory nature, broad prey range, and high grazing rates of *Halobacteriovorax* all lead to the intriguing possibility of using these and other predatory bacteria as “living antibiotics,” particularly against fast-growing pathogens such as vibrios. Alternatives to antibiotics are clearly needed due to the rise in antibiotic resistance among bacterial pathogens, and whether predatory bacteria prove to be a viable alternative remains to be seen.

Currently the usefulness of such predators as probiotics is being explored. For example, the U.S. Defense Advanced Research Projects Agency recently began studying whether predatory bacteria can eliminate pathogens such as...
Francisella tularensis, Bacillus anthracis, Burkholderia mallei, B. pseudomallei, and Yersinia pestis.

In aquaculture settings, Halobacteriovorax preys on a wide range of gram-negative bacteria, including many pathogens that infect oysters, crabs, and shrimp. Thus, Halobacteriovorax has the potential to regulate opportunistic pathogens by controlling their blooms, thereby reducing stress and increasing growth rates of hosts in aquaculture settings. For example, when shrimp were treated with BALOs as a probiotic before being challenged with vibrio pathogens, the survival rates of the shrimp significantly increased, according to Haipeng Cao and colleagues at the Shanghai Ocean University. Similarly, rapid decreases of pathogenic vibrios coincided with increases in native predatory bacteria populations in seawater containing shellfish, according to a 2012 study by U.S. Department of Agriculture researcher Gary Richards and his collaborators. These findings support the notion that predatory bacteria can modulate pathogenic vibrios in seawater in which the farming of aquatic organisms are being cultivated.

Although such findings are encouraging, there is a wide gap between what we know now and where our understanding needs to be before any use of predators to control pathogens becomes a commercially useful therapeutic or mitigation option. Before using predatory bacteria as biological control agents, several issues need to be considered, including the consequences: (i) when removal of target prey is incomplete (BALOs generally do not remove 100% of their prey), (ii) when unintended grazing lowers the populations of beneficial or commensal bacteria, (iii) side effects when predators persist, and (iv) when predator-resistant phenotypes or strains emerge.

Despite such uncertainties, however, predatory bacteria offer tremendous opportunities beyond their potential application as living antibi-
otics. Because both predatory and pathogenic bacteria are small and grow so rapidly, they provide unique communities for studying fundamental theories of ecology and evolution of predator-prey dynamics as well as the role of predators in structuring communities.

Moreover, as we and others have learned, adding pathogens to a microbiome can cause unexpected changes to that microbial community, and it is difficult to predict precisely what causes a healthy microbiome to shift to a disease state or, instead, maintain a healthy steady state. For example, with the coral Montastrea cavernosa and its microbiome, we explored how bacterial predators can protect that microbiome against single pathogens or how combinations of interacting predators and potential prey alter the structure of those host microbiomes. We found that adding predators to this host-microbiome ecosystem can alleviate some of the effects of pathogens on microbiome and host health. Yet we have only scratched the surface of this system, and building a better understanding of these cascading effects and how microbial predators drive microbiome structure and function need further exploration.

Rory M. Welsh is a recently graduated Ph.D. student advised by Rebecca Vega Thurber. Rebecca Vega Thurber is an assistant professor of microbiology at Oregon State University, Corvallis.

Suggested Reading
Cao, H., J. An, W. Zheng, and S. He. 2015. *Vibrio cholerae* pathogen from the freshwater-cultured...


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Transforming Laboratory Education in the Life Sciences

Erin R. Sanders, Jordan Moberg-Parker, Ann M. Hirsch, Pei Yun Lee, Casey Shapiro, Shannon Toma, and Marc Levis-Fitzgerald

Throughout college, students encounter experiences that influence their decisions to continue or leave their intended science, technology, engineering, and math (STEM) majors. All STEM faculty share in a responsibility to encourage undergraduates to persist in these studies. Evidence continues to support active learning as an equitable teaching practice that benefits diverse student populations, including women and underrepresented minority students most at risk for leaving STEM. The hope is that more STEM instructors will move away from the traditional lecture format as the primary mode of teaching undergraduates and that institutional leaders will reward those faculty who use inclusive, student-centered teaching practices effectively.

Also deserving reexamination are the ways in which laboratory instruction is being delivered to college students. As with alternatives to conventional lectures, student-centered teaching strategies can be tailored to undergraduate laboratory courses. For instance, inquiry-based learning experiences, when incorporated into undergraduate instructional laboratories, can help students apply the process of science by posing questions that require students to engage in scientific explorations of their natural world and that challenge their conceptions of scientific phenomena. This approach also better prepares students to tackle interdisciplinary problems that mirror those they will encounter outside universities and colleges.

One particular approach to inquiry—an authentic research experience—plays a critical role in capturing the imagination of undergraduate students. By sustaining their interest in science, students are more likely to complete degrees in their intended STEM majors. The positive outcomes associated with research engagement are prompting others to explore ways by which to scale this inquiry-based learning strategy to entire undergraduate classes. These course-based undergraduate research experiences, or CUREs, can be devised to support the participation of diverse groups of students, including directly admitted and transfer students as well as students with limited time for activities due to off-campus employment or housing that necessitates commuting long distances. Altogether, CUREs embody an inclusive teaching approach that helps to keep students on track for completing bachelor degrees in STEM majors.

Creating a Framework for Undergraduate Research Participation

In 2010, the University of California, Los Angeles (UCLA) implemented the competency-based research laboratory curriculum (CRLC), a framework that enables large numbers of upper-division undergraduate students pursuing a life sciences major to experience authentic research. After com-

SUMMARY

Course-based undergraduate research experiences (CUREs) and apprentice-based research experiences (AREs) represent inclusive, student-centered instructional strategies that can improve student learning and help to keep them on a scientific career pathway.

Using backwards course design ensures that educators and faculty align research activities with the learning outcomes and that selected assessments provide adequate evidence of student achievements, visualized via curriculum mapping.

Rubrics are suitable assessment tools for measuring how students perform in these research-based laboratory courses.

Faculty benefit from teaching CUREs and mentoring students in AREs in ways that enhance both their teaching portfolios and research productivity.
pleting requisite lower-division core courses, students fulfill departmental major laboratory requirements by following one of two paths. Path 1 engages students in CUREs as a laboratory option, while path 2 embraces apprentice-based research experiences, or AREs (Fig. 1). These two laboratory options offer third- and fourth-year life sciences students comparable research experiences that account for varied levels of academic preparedness, confidence and proficiency in laboratory skills, and commitment to or interest in research. Both paths support student learning as well as the development of skills and abilities that align with desired learning outcomes. Development of this program relied on a strategy called backwards design.

Overview of the Competency-Based Research Laboratory Curriculum

When entering the CRLC at UCLA, path 1 students enroll in one of four 10-week laboratory courses, termed Research Immersion Labs (Path 1, Course AL), followed by a second 10-week course called Advanced Research Analysis & Report (Path 1, Course BL). Throughout both terms, students work together in teams to collect data, analyze preliminary results, read and evaluate items in the scientific literature, give oral presentations, and document their research discoveries and accomplishments. Each pair of path 1 AL and BL courses make up a CURE.

Among four options, each CURE focuses on a different research project (Fig. 1). Briefly, in the microbiology CURE, students explore microbial diversity in plant rhizospheres; in the plant-microbe ecology CURE, they examine the effects of inoculating plants with bacteria from the rhizosphere; in the virology CURE, they isolate bacteriophage, and characterize their genome compositions and structures; and in the cell and molecular biology CURE, they investigate the expression patterns and evolutionary history of genes in the sea urchin genome.
Path 2 of the CRLC engages students in two consecutive 10-week terms of independent research, courses AR and BR. This path requires their concurrent participation in sequential research seminars, courses AS and BS, where students read and discuss relevant scientific literature, as well as give presentations about their individual research projects. Despite involving more than 80 different path 2 faculty mentors since its implementation in 2010, the CRLC achieves consistency across AREs by having the AS and BS seminars taught as a series with the same instructors both terms.

Curriculum Design as an Intentional Practice

Backwards design involves three key stages: (1) identify the desired results by formulating student learning outcomes, (2) determine acceptable evidence of learning to be collected and evaluated during the course, and (3) plan the learning experiences to ensure students achieve the desired results (Fig. 2). We employed this design strategy in the development of the CRLC.

Common to the two paths in the laboratory curriculum are 10 student learning outcomes (SLOs). For instance, students completing the CRLC are expected to develop problem-solving skills associated with conducting experiments (SLO 4 in Fig. 2). Research products and embedded course assignments were identified for each SLO and evaluated to determine the extent to which students achieved the desired learning outcomes. For SLO 4, laboratory notebooks were collected and subjected to assessment for evidence of learning.

CRLC faculty subsequently designed research and learning activities to support students in their development of the knowledge, skills, and abilities reflected in the SLOs. In the case of SLO 4, faculty asked students to use decision trees to rationalize unexpected experimental results and
to troubleshoot and repeat failed experiments. These activities were logged and explained in their laboratory notebooks. Alignment of learning outcomes, assessments, and CRLC project activities was all part of this backwards design process.

**Making Performance Standards Explicit Using Rubrics**

The CRLC learning outcomes require students to exercise lower- and higher-order cognitive skills (LOCS or HOCS, respectively), as defined by Bloom’s Taxonomy. This hierarchy comprises six levels, with each level connected to action verbs that are appropriate for learning at that level. More importantly, the verbs describe a type of competency or conceptual understanding that can be directly measured by evaluating embedded course assignments and research products.

Research-based laboratory investigations enlist benchmarks of student progress not readily captured by, say, multiple-choice exams. Thus, CRLC student performance standards are formulated using rubrics—evaluation tools that scale levels of ability and conceptual proficiency. One set of such rubrics was generated by using action verbs to describe what CRLC students are expected to do on an assignment shared by CURE and ARE students. These rubrics were then used to evaluate and compare student learning in each path.

The analysis suggests that course-based research experiences gradually reduce the achievement gap between high-performing ARE students and their peers in CUREs. We might not have recognized this result had we relied entirely on self-reported data generated through surveys. Furthermore, we could not readily compare CUREs to AREs without having shared student learning outcomes (SLOs) for all our student participants.

Our rubric creation process involve categorizing items as LOCS or HOCS, and, when finer distinctions are preferred, at one of the six levels of Bloom’s Taxonomy. Rubric items, in turn, can be translated into a list of learning objectives, which serve as explicit statements about the performance expectations of a “successful student” who engages in a particular research or learning activity. Learning objectives represent measurable instructional goals that are not as broad as student learning outcomes (SLOs). A list of learning objectives can be given to students to guide them in building skillsets while making explicit the performance criteria, which they are expected to meet on a given assignment or research product.

Plotting the learning objectives for various project activities and course assignments over time produces a visual representation of a CURE learning experience (Fig. 3). This visualization, referred to as a curriculum map, shows that successful execution of the research projects by students in all four CUREs of the CRLC requires cognitive skills spanning the six levels of Bloom’s Taxonomy. Curriculum maps are excellent tools for promoting discussions among faculty about how to align learning outcomes in ways that meet program, departmental, and college accreditation goals.

**Research-Based Laboratory Courses Engage Research Faculty**

By integrating research into the undergraduate curriculum, the CRLC benefits a broad range of students. Moreover, this approach benefits faculty members, providing them with teaching and mentoring opportunities that make them better teachers and also can help with their own research programs. For instance, several students who studied under Ann Hirsch, a CRLC instructor, later joined her laboratory research group and contributed to several peer-reviewed publications. “Becoming involved in a research-based course helped me transform my teaching in ways that clearly benefited students, was much more fun for me to teach, and even enhanced my research portfolio,” she says.

Since UCLA implemented the CRLC in 2010, many participating faculty mentors report increases in productivity in their own research programs. Collectively, across more than 80 research laboratories, faculty have published at least 65 peer-reviewed research articles with ARE students as contributing authors. During this period, hundreds of CURE students were coauthors of Genbank submissions based on their analyses of 16S rRNA gene sequences and bacteriophage genomes as part of this program. Additionally, a cohort of CURE students was acknowledged as coauthors on a 2013 ASM Genome Announcements report by Graham Hatfull of the University
of Pittsburgh and his collaborators, and another 46 CURE students were cited as collaborators in other reports, one in 2014 in the *Journal of Virology* and another in 2015 in *eLife*.

Participating in the CRLC also led instructors to develop and publish innovative instructional materials and make other scholarly contributions to STEM education research. They include five video protocols describing laboratory techniques common to several of our CUREs (four published in the *Journal of Visualized Experiments* and one recently submitted to MicrobeLibrary), an opinion piece in *Frontiers in Plant Science* describing the merits of CUREs that engage civic-mindedness among STEM undergraduates, a research article in *Biochemistry and Molecular Biology Education* describing a peer-assisted learning strategy used in one of the CUREs, and a research article in the *Journal of Microbiology and Biology Education* comparing the impact of CUREs and AREs within the context of the CRLC.

**Conclusion**

More than 1,000 UCLA students participated in the CRLC since 2010. Each year, this research-based curriculum trains hundreds of diverse, talented, and ambitious undergraduates, many of them headed for careers in science. Not only do students gain from this program, but also the faculty teaching and mentoring CRLC students benefit from this approach by leveraging the opportunity to balance, intertwine, and enhance teaching effectiveness with increased research productivity. Moreover, this framework for integrating research into the life sciences curriculum is scalable, providing large public research uni-
iversities a means for engaging undergraduates in authentic scientific inquiry, thus increasing the likelihood of those students persisting in STEM majors, and, in turn, STEM careers.

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Suggested Reading


Analyzing Evolvability To Anticipate New Pathogens

Fusing the study of microbial pathogens with evolutionary biology potentially provides a means for predicting emergent pathogens

Meghan A. May

Scientists working on infectious diseases wonder about the evolution of virulence. Indeed, people want to know why new diseases appear, where they come from, and, perhaps most interesting of all, what is coming next. Many researchers are working hard to answer those questions, particularly the last one. Figuring out what comes next depends on understanding what makes infectious agents change to become more successful at infecting hosts, transmitting between hosts, and avoiding a host’s immune system.

Once we understand the factors involved in conferring virulence, can we use that information to predict and possibly prevent the emergence of novel disease-causing pathogens? An approach to understanding those issues that fuses the study of microbial pathogens with evolutionary biology provides an exciting way of tackling these questions. Studying how disease-associated traits evolve holds the potential of enabling us to predict accurately the emergence of infectious diseases.

Evolvability—the Capacity to Respond to Evolutionary Pressures

From the standpoint of natural selection, the evolvability of a trait is its capacity to change in response to evolutionary pressures. In terms of evolvability, it is not enough that a trait changes transiently in response to a stimulus. Changes must become permanent and transmissible from one generation to the next.

Evolvability was conceived and first studied by examining information processing in the human brain, and was first tested in the fruit fly Drosophila melanogaster. Those early studies focused mainly on physiology or developmental biology, and the traits were measured by studying inbred or outcrossed populations. Later, analyses included genetic diversity in the form of specific point mutations in DNA and introduced evolutionary drivers, traits that change in direct response to selective pressure, and evolutionary passengers, traits that change in response to selection introduced by changes in their drivers.

Tumor cells are also used for characterizing evolutionary drivers and passengers as well as their evolvability. Some investigators are designing therapeutics to target traits that are presumed to be evolutionary drivers, while others are considering the value of targeting evolutionary passengers.

Other factors such as changes in gene expression, dominant and recessive forces, alternative gene splicing, and redundant functions add further complexity to the study of evolvability. However, by using bacterial systems, many of these potentially confounding factors can be more readily controlled.

Examining Evolvability in Bacteria

Describing bacterial evolvability begins with considering selection outcomes. Selection can be

SUMMARY

➤ Pathogens adapting to new hosts or constantly shifting to escape the defenses of their natural hosts are subject to measurable evolutionary forces.

➤ The evolvability of a trait is its capacity to change permanently, most notably in response to diversifying natural selection.

➤ Mycoplasma synoviae and Mycoplasma gallisepticum share a horizontally transferred sialidase that is subject to distinct selective pressures and evolves at different rates in each species.

➤ Because genomic context can drive the evolvability of genes, it should be included when modeling emerging pathogens.
thought of as exerting either a “purifying” or “diversifying” force. When that force is purifying, the DNA and protein sequences that determine the trait change very little, indicating that the population is at its fittest because the trait in question does not change much. However, when that selective force is diversifying, there is marked variation in the DNA and protein sequences that determine a trait, indicating that the population of organisms is at its fittest when the trait in question varies extensively. A background of random genetic drift, also known as neutral selection, falls between these two extremes.

Examples of proteins under purifying versus diversifying selection are the replication initiation factor DnaA and the variable surface antigen VlsE, respectively. Little variation can be tolerated in DnaA because the function of this enzyme is so critically important to every cell. In other words, DnaA has a low potential for evolvability. However, the situation for VlsE is nearly opposite. Thus, it is advantageous for individual cells within a population to express slightly different antigens along their surfaces, enabling at least some of them to escape when they are all exposed to a host immune surveillance system. Therefore, VlsE is said to have a high potential for evolvability.

The selective force acting on individual amino acid residues can be recognized by aligning homologous DNA codon sequences from multiple isolates within a population of bacteria. Nucleotide changes that do not result in major structural or functional changes in the protein sequence are termed synonymous mutations, whereas changes that do lead to such changes are termed nonsynonymous.

The ratio of nonsynonymous to synonymous mutations ($K_a/K_s$ or $d_a/d_s$, abbreviated as $\omega$) reveals the type of selective force acting on a particular trait. Neutral selection should result in an $\omega$ ratio close to 1. Thus, values less than 1 indicate purifying selection, while $\omega$ ratios greater than 1 indicate diversifying selection. Statistical significance can be determined across an entire protein sequence by performing a likelihood ratio test between the native measurements to allow for diversifying selection, and a null model that artificially caps the $\omega$ ratio at 1 and thus does not. While inferring selection based on $\omega$ ratios allows consideration only of changes in protein sequence rather than changes in gene expression level or timing, in true instances of diversifying selection this limitation would err on the side of false-negative findings rather than false-positive. Any statistically significant diversifying selection is considered remarkable.

Looking More Deeply for Evolutionary Drivers

It is possible to observe diversity either by phenotype or by genotype. For example, experiments that focus on the VlsE proteins of Borrelia burgdorferi, which causes Lyme disease, indicate that these variable antigens are evolvable and diversify in order to escape host immune responses during infection. Further, even unexpressed $vlsE$ gene cassettes, which would presumably not be subject to evolutionary pressure from host antibodies, can contribute significant diversity. This unexpected finding provides key evidence that evolvability—in the form of elevated mutation rates in unexpressed genes—is itself an evolvable trait.

Further understanding comes from measuring the sialidase enzymes of the avian parasites Mycoplasma synoviae and Mycoplasma gallisepticum while they adhere to sialic acid residues along the surfaces of host cells. The diversity in enzymatic activity and corresponding genetic diversity for the sialidase ($nanI$) of $M. synoviae$ significantly correlates with strain virulence. In other words, the more sialic acid a strain cleaves, the more likely it causes severe disease.

The genetic variation in gene $nanI$ arises from significant ($P < 0.001$) diversifying selection. Like the influenza virus, $M. synoviae$ adheres to host cells by attaching to sialic acid residues along the host cell surface while retaining the ability to cleave those residues. Indeed, there is a coordinated interplay between the pathogen attaching to those sialic acid residues, and then detaching from them because of sialidase activity. When these two antagonistic phenotypes are not properly balanced, the pathogen becomes less virulent. In other words, extremes of either too strong attachment or detachment lead to less-efficient infection or transmission, respectively. For an obligate parasite, “unbalanced” variants would likely be lost from the population.

Knowing that $nanI$ sialidase is under diversifying selection in $M. synoviae$, we predicted that the organism’s adherence mechanism would also be subject to diversifying selection. $M. synoviae$ attaches to host cells primarily through its immunogenic lipoprotein, called VlhA. Although it,
too, diversifies to escape host immune responses, unlike VlsE of B. burgdorferi, this specific adhesive function of VlhA is well known.

Moreover, the strength with which M. synoviae binds host cells depends on which variants of VlhA are being expressed. Some variants cling tenaciously, while others bind only weakly. Because of the predicted functional balance between sialidase activity and attachment, we assessed both the level of diversifying selection acting on VlhA and the mathematical relationship between the two traits. Not only is VlhA also under significant ($P < 0.01$) diversifying selection, but there is also a striking, statistically significant ($P < 0.001$) correlation between sialidase activity level and adherence (Fig. 1).

Evolvability Is Not Universally Favored

These traits and the genes encoding them do not make their evolvability universally favorable. To address the broader question of evolvability, we measured selection acting on analogous instead of homologous sialidases of two distantly related bacterial species, Streptococcus pneumoniae and Clostridium perfringens.

This distinction is critical: a homologous gene comes from the same common ancestor, whereas an analogous gene is not related by descent, but performs the same function. We found that the analogous sialidases of S. pneumoniae and C. perfringens are largely conserved, and under global purifying selection, suggesting that selection does not always act to diversify bacterial sialidases.

Meanwhile, another question arises. Is there something unique about the nanI gene of M. synoviae that makes it particularly prone to evolve? To address this question, we examined another species of Mycoplasma that parasitizes birds, M. gallisepticum. These two species frequently coinfect the same animal, creating opportunities to share genes by horizontal transfer and enabling the same gene to be in two different species simultaneously. nanI is one such shared gene, but the $\omega$ value for nanI in M. gallisepticum clearly indicates that it is under purifying rather than diversifying selection.

**FIGURE 1**

Spearman rank correlation between host cell adherence and sialidase activity in 12 clinical isolates of Mycoplasma synoviae. Shading indicates the 90% confidence interval. (Adapted from M. May and D. R. Brown, J. Bacteriol. 193:2116–2121, 2011.)
This critically important finding suggests that no feature of the gene itself makes it evolvable. Rather, genomic context determines its fate. In other words, nanI is evolvable even though, in the context of the M. gallisepticum genome, the gene and trait remain stable.

**Genomic Context Can Determine Evolvability of Traits**

When diversity in nanI and sialidase activity is favored in M. synoviae, why is the same trait encoded by the same gene so stable in M. gallisepticum? It comes down to pressure to perform. Selective pressures can be either direct or indirect, and the affected traits can thus be thought of as either drivers or passengers of evolution.

In nature, the M. synoviae VlhA proteins perform an indispensible function: host cell attachment. For a parasitic organism that attaches to its host surface, this capacity is tantamount to survival. But as variants of parasitic organisms may differ in their capacities to escape the responses of the host immune system, the avidity with which they adhere to the host consequently varies, too. And because sialidase activity is necessarily coordinated with avidity of adherence, direct selection on VlhA indirectly drives diversity in the evolutionary passenger gene, nanI.

However, this relationship is not the case for M. gallisepticum because it has a distinctly different primary mechanism of adherence to its host by means of a complex, multimeric attachment organelle (Fig. 2). This structure is stable, constitutive, and completely absent from M. synoviae. Even though nanI is an evolvable gene, against
the biological backdrop of the attachment organelle, it lacks a driver of diversification and, thus, remains stable.

Mycoplasmas are parasitic bacteria with minimal, streamlined genomes. By their very nature, these organisms avoid introducing potentially confounding variables in evolutionary studies such as co-dominance, inheritance, redundant functions, alternative gene splicing, and environmental survival. Thus, for the first time, we can see markedly different selective forces acting on homologous genes in two distinct species occupying the same niche in a shared habitat. These forces can be measured and phenotypically verified, tying together informatics, mathematical, and biological data.

In short, this system demonstrates that evolvability is not necessarily inherent to a particular trait, but is heavily influenced by the genomic context in which that trait is found. Determining the evolutionary pressures acting on disease-associated traits, along with the evolvability in context of the genes encoding those traits, creates the exciting potential for forecasting infectious disease. In other words, by thinking about infectious diseases in the same manner as evolutionary biologists consider this subject more broadly, we can come a bit closer to answering that critical question: “what is coming next?”

Acknowledgments

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Suggested Reading


University of Michigan Department of Microbiology and Immunology Recognized as a “Milestones in Microbiology” Site

On 22 October 2015, the University of Michigan Department of Microbiology and Immunology became the twelfth Milestones in Microbiology site designated by ASM. The Milestones program, established to promote greater awareness and appreciation of microbiology, recognizes institutions with a strong history of significant contributions advancing the field of microbiology.

The University of Michigan Department of Microbiology and Immunology (UM M&I)’s distinguished history began in 1881 with one of the first bacteriology courses in the United States, Sanitary Science, taught by Victor Vaughan. In 1902, Professor Frederick G. Novy became chair of the Department of Bacteriology at UM, where he brought his training under Robert Koch and Louis Pasteur to bear, developing some of the earliest techniques for the study of anaerobes, spirochetes, and trypanosomes. Novy became the fifth president of the Society of American Bacteriologists, which later became ASM. Other distinguished UM microbiologists include Paul De Kruif, author of Microbe Hunters; former ASM president and proteomics innovator Frederick Neidhardt; Rolf Freter, a pioneer of microbiome research; and Thomas Francis, Jr., a leader in research on influenza and epidemiology and mentor to Jonas Salk during development of the polio vaccine.

Kicking off a three-day celebration of the Milestones in Microbiology designation, Powel Kazajian, M.D., Ph.D., Professor of Internal Medicine, outlined the history and accomplishments of Frederick Novy. This subject is of special interest to Kazajian, as Novy was the topic for Kazajian’s doctoral dissertation in history. Harry Mobley, Ph.D., current Frederick G. Novy Distinguished University Professor and Department Chair, then spoke at the “plaquing” ceremony, highlighting M&I’s ongoing contributions to microbiology. Mobley also noted that a descendent of Frederick Novy, Heather Smith, also a microbiologist, was in attendance. Smith, Novy’s great-great-granddaughter, commented that she was thrilled to learn firsthand how his work laid the foundations for microbiology research in the United States. M&I faculty were honored to have the University of Michigan President, Mark Schlissel (also a Professor of M&I), attend and give congratulatory remarks. Reflecting on his background in virology, Schlissel joked that he is one of only a few university presidents who would catch Mobley’s earlier “plaquing” reference. The president is “proud of our [UM M&I’s] historical role in this field” of microbiology and emphasized microbiology’s role in the evolution of molecular biology and contributions to precision medicine.

Douglas Eveleigh, Ph.D., Chair of the ASM Milestones in Microbiology Committee, described the role of ASM’s Center for the History of Microbiology and some specific contributions by UM M&I faculty. He then introduced former ASM president Moselio Schaechter, Ph.D., who expressed his own fond remembrance of UM M&I’s contribution to the history of microbiology. Schaechter made special mention of Neidhardt’s influence, remarking, “in addition to his powerful scientific discoveries, his chairmanship of the department is celebrated for his introduction of participatory management, an operating mode then unique in medical schools; the current chair, Harry Mobley, has successfully continued it.” Schaechter also noted that although Neidhardt was unable to attend the Milestones event in person, he was surely there “in spirit.” Schaechter then presented the ASM Milestones in Microbiology plaque to the Department. The plaque, detailing key UM historical figures, was later installed at the entrance to M&I’s office, serving to achieve ASM’s objective of increasing professional and public recognition of the significance of microbiology.

A live podcast recording of This Week in Mi-
crobiology (TWiM) immediately followed the plaque unveiling ceremony. In TWiM episode #114, host Vincent Racaniello and co-hosts Michele Swanson and Moselio Schaechter highlighted research by UM’s Vincent Young, Mary O’Riordan, and Harry Mobley. The Department’s annual Neidhardt-Freter Symposium concluded Thursday’s events. UM M&I established the symposium, now in its fifth year, as a venue for leading bacterial physiology and pathogenesis researchers to share their research with UM while honoring esteemed former colleagues Neidhardt and Freter. Manuela Raffatellu, Ph.D., from the University of California, Irvine, and Sam Miller, M.D., of the University of Washington, shared their work on Salmonella. Raffatellu recounted that a parting gift from her postdoctoral mentor had been a copy of Neidhardt’s text *Escherichia coli and Salmonella (EcoSal)*, and selection for the lectureship meant a lot to her. Miller recounted that during a previous visit in 1992, he interacted with both Freter and Neidhardt, and thus it was a special honor to return for the Symposium.

Friday featured the live recording of Vincent Racaniello’s *This Week in Virology* (TWiV) episode #360 with co-host Kathy Spindler and featured guests Adam Laureng, Akira Ono, and Mike Imperiale. The *Milestones in Microbiology* celebration concluded on Saturday with the Michigan Branch of ASM Fall 2015 meeting, hosted at the University of Michigan Union. With a “Spotlight on Bacterial Pathogenicity,” three UM alumni, Andrew Camilli, Melody Neely, and Neal Hammer, were plenary speakers at the Branch meeting. Students and faculty from schools throughout Michigan, including Michigan Tech, more than 500 miles away on the Upper Peninsula, participated in the meeting with posters, oral presentations, and networking.

For the schedule of Milestone events and links to video recordings of Powel Kazanjian’s talk, the plaquing ceremony, TWiM, and TWiV, see http://umhealth.me/M-in-M. For more information on the Milestones program, see www.asm.org/milestones-in-microbiology.

ASM Public Affairs

ASM Comments on Fast-Track Action Report on Mapping the Microbiome

In December, the Life Sciences Subcommittee of the National Science and Technology Council (NSTC) released the Report of the Fast-Track Action Committee on Mapping the Microbiome. The full report, which can be found at https://www.whitehouse.gov/sites/default/files/microsites/ostp/NSTC/ftac-mm_report_final_112015_0.pdf, recognizes that doing diverse scientific research on the world’s ubiquitous communities of microorganisms offers “vast potential to improve plant, animal, and human health, to mitigate climate change, and to promote industrial innovation.” ASM sent an advisory to ASM members asking for comments on the report. On 2 December, ASM sent letters to John P. Holdren, Ph.D., Director, Office of Science and Technology Policy, and Shaun Donovan, Director of the Office of Management and Budget, in support of the recommendations in the report. ASM cautioned that new funding for the microbiome should not be at the expense of basic research and noted that the field of mycology should be included in any initiative.

On 4 December, Ronald Atlas, Chair of the ASM’s Public and Scientific Affairs Board; Timothy Donohue, Past President of ASM; and Janet Shoemaker, Director, ASM Office of Public Affairs, had meetings with Anthony Fauci, Director, National Institutes of Allergy and Infectious Diseases, National Institutes of Health; Sharlene Weatherwax, Associate Director of Science for Biological and Environmental Research; and Todd Anderson, Director, Biological Systems Science Division of the Department of Energy, to discuss microbiome research. To read the ASM letter and advisory, go to http://www.asm.org/index.php/public-policy/137-policy/documents/statements-and-testimony/93869-microbiome-12-15.

ASM Participates in Antibiotic Resistance Working Group Meeting

ASM President-Elect Susan Sharp was invited as an ASM representative to participate in a teleconference with the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) Working Group on One Health Surveillance on 8 December. Sharp presented responses to questions submitted by the Working Group on optimization of the interactions between Federal laboratories to address the continued problem of antimicrobial-resistant bacteria, utilization of governmental repositories of antimicrobial-resistant organisms, and ways to tie data from human and veterinary sources together to assess resistance organisms in a holistic manner. See the comments at http://www.asm.org/index.php/public-policy/98-policy/issues/93873-paccarb-12-16.

ASM Comments on Proposed Changes to Human Subject Protection Regulations


ASM Comments on Identifying Sources of Agricultural Innovation

In December, the Public and Scientific Affairs Board (PSAB) Committee on Agricultural and Food Microbiology responded to a Request for Information from the Office of Science and Technology Policy about identifying sources of agricultural innovation. The committee identified a number of research gaps and recommended that the administration focus efforts on funding R&D in areas including antigenically variable viruses, microbiome, antimicrobial resistance, and climate variability. A copy of the letter can be found on the ASM public policy website at http://www.asm.org/index.php/public-policy/137-policy/documents/statements-and-testimony/93872-ag-rfi-11-15.

ASM Participates in Unifying Message Discussion

ASM participated in a December meeting convened by the Charles Valentine Riley Memorial Foundation (RMF) at the American Association for the Advancement of Science in Washington, D.C., as one of 27 invited U.S. scientific societies active in food, agricultural, and natural researches research. The meeting resulted from a 2014 report produced by RMF, Iowa State University, Mississippi State University, Soil and Water Conservation Society, Texas Tech University, and Colorado State University that identified the need for a unified message to support increased funding for food and agricultural research.

ASM Attends House Hearing on Lab-Developed Test Regulation

On 17 November, ASM staff attended the House Energy and Commerce Health subcommittee hearing “Examining the Regulation of Diagnostic Tests and Laboratory Operations.” Jeffrey Shuren, Director of the Center for Devices and Radiological Health, Food and Drug Administration (FDA), and Patrick Conway, Deputy Administrator for Innovation and Quality & Chief Medical Officer, Centers for Medicare and Medicaid Services, served as witnesses on the topic of FDA’s Proposal for Oversight of Laboratory Developed Tests (LDTs). LDTs are in vitro diagnostic tests intended for clinical use and designed, manufactured, and used within a
single clinical laboratory; the FDA is expected to issue final guidance on the regulation of these tests in 2016. The availability of LDTs, especially molecular tests to identify infectious agents, may be affected by what is included in the final guidance. You can view the full hearing at http://energycommerce.house.gov/hearing/%E2%80%9Cexamining-regulation-diagnostic-tests-and-laboratory-operations.

**ASM Attends CLIAC Meeting on LDTs**

The Clinical Laboratory Improvement Advisory Committee (CLIAC) met 18–19 November and discussed the Interoperability of Laboratory Data, non-invasive prenatal testing, and the Food and Drug Administration Laboratory Developed Test Guidance. Additionally, new CLIAC members were introduced, including former ASM Division C Chair Sheldon Campbell. CLIAC provides scientific and technical advice and guidance to the Department of Health and Human Services and includes diverse membership across laboratory specialties, professional roles, and practice settings, and includes a consumer representative. To read more about the meeting and CLIAC, see http://www.cdc.gov/cliac/.

**National Institutes of Health NIH-Wide Strategic Plan Preview**

In December, the National Institutes of Health (NIH) previewed a revised NIH-Wide Strategic Plan, presented at the Advisory Committee to the Director meeting by Lawrence A. Tabak, DDS, Ph.D., principal deputy director of the NIH. The plan includes a new objective, “Excel as a federal science agency by managing for results,” which involves evaluating scientific outputs, creating a dynamic model of the biomedical workforce, and tracking the effectiveness of decision making, among others. The document is a preview of a final version of the plan, which will be presented to Congress. ASM sent comments on the framework for the strategic plan in August. To read those comments, go to http://www.asm.org/index.php/publicpolicy-2/statements-testimony/137-policy/documents/statements-and-testimony/93633-nih-sp-8-17-15. To read the preview of the plan, go to http://acd.od.nih.gov/presentations/NIH-Wide-Strategic-Plan-12082015.pdf.

**ASM Meetings and Conferences**

**ASM Microbe 2016: Register Now and Save**

Secure your seat before 5 May for the inaugural ASM Microbe 2016 (16–20 June 2016, Boston, Mass.) and take advantage of the early bird rates! Featuring the robust scientific program you’d expect at ASM’s General Meeting and ICAAC, as well as transdisciplinary scientific sessions, dynamic networking opportunities, and an integrated, expanded Poster and Exhibit Hall, the all-new ASM Microbe 2016 presents a unique opportunity to explore the complete spectrum of microbiology. To review the program by day, browse the list of exhibitors, and review all of the new opportunities this meeting offers, visit www.asm.org/microbe2016.

**32nd Clinical Virology Symposium: Submit Your Abstract Today**

Time is running out to submit your abstract for the 32nd Clinical Virology Symposium (19–22 May 2016, Daytona Beach, Fla.). Submit yours before 17 March and showcase your latest research findings in front of nearly 1,000 esteemed researchers and primary care physicians from around the world. New for 2016: the Symposium will take place from Thursday through Sunday, and will include increased networking opportunities for you to expand your connections. To learn more, visit www.asm.org/cvs2016.

**Upcoming ASM Conferences**

ASM Conferences address the needs of the diverse scientific interests of microbiologists by providing a forum for international groups of scientists to discuss their specific area of concentration. Mark your calendar for these upcoming ASM Conferences. For more information, visit www.asm.org/conferences.

-13th ASM Conference on Candida and Candidiasis (13–17 April 2016, Seattle, Wash.)
-ASM Conference on Streptococcal Genetics (31 July–3 August 2016, Washington, D.C.)
-5th ASM Conference on Salmonella (29 August–1 September 2016, Potsdam, Germany)
-6th ASM Conference on Beneficial Microbes (9–12 September 2016, Seattle, Wash.)

**Education Board**

ASM Represented at Fall 2015 Student and Educator Meetings

The strategic directions of the ASM Education Board include collaborating with national organizations to promote microbiology education at all levels. In fall 2015, the Board sponsored the Society’s participation in the following conferences for science students and educators.

- **SACNAS National Conference.** The Education Student Programs team—Irene Hulede, Leah Gibbons, Tiffani Fonseca, and Ronica Rodela—represented ASM at the Society for the Advancement of Chicanos and Native Americans in Science (SACNAS) National Conference held 29–31 October
in National Harbor, Md. The conference featured career workshops, scientific symposia, exhibits, and student research presentations, along with speakers highlighting resources designed to help Chicano/Latino and Native American students pursue advanced degrees in the sciences. During the exhibits program, the ASM team shared information about ASM education resources and student programs.

**BMES Annual Meeting.** Education staff member Irene Hulede represented ASM at the Biomedical Engineering Society (BMES) Annual Meeting held 7–10 October in Tampa, Fla. The BMES serves to promote and enhance the world’s knowledge of and education in biomedical engineering and bioengineering. It also serves to promote the utilization of this knowledge for human health and well-being. The BMES annual meeting draws more than 2,000 attendees and offers scientific presentations, a career fair, exhibits, and numerous networking and professional development sessions. During the meeting’s exhibits program, Hulede shared information about ASM education resources and programs.

**NABT Annual Meeting.** Communications staff member Emily Dilger and Education staff member Kari Wester represented the Society at the National Association of Biology Teachers Annual Meeting (NABT) held 12–15 November in Providence, R.I. The ASM-sponsored talks at the conference included “A Constructive Approach to Biology,” led by Kristala Prather and Natalie Kuldell of the Massachusetts Institute of Technology, and “Lab Biosafety,” led by Ruth Gyure of Western Connecticut State University. In the exhibits program, Dilger and Wester shared information about the Society’s K-12 outreach activities, along with other ASM career, curriculum, faculty, and student resources.

**NIAID Workshop.** Education Staff member Tiffani Fonseca was an invited speaker at the 12th Biennial “Bridging the Career Gap for Underrepresented Minority Scientists” Workshop, an event sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) on 8–9 October 2015. Attendees of the workshop are young researchers funded by NIAID diversity supplements initiatives, a group the institute has identified as among the future principal investigators of NIH grants. The workshop served to provide information on applying for research project grants, acquaint attendees with the opportunities and options open to them in biomedical research, and introduce them to NIAID intramural and extramural staff members (for the purpose of establishing mentoring relationships). Fonseca’s presentation focused on the funding resources available to graduate students, postdoctoral fellows, and junior faculty through ASM. She also addressed the benefits of being a member of a disciplinary society.

**ABRCMS 2015: 15 Years of Supporting Minority Student Excellence in STEM**

Presented by ASM since 2001, the Annual Biomedical Research Conference for Minority Students (ABRCMS) is a key conference for undergraduates in pursuit of advanced training in the biomedical and behavioral sciences, including STEM. The meeting offers opportunities for students to present research findings and receive professional skills training. It also provides faculty mentors, advisors, and program leaders with resources for facilitating student success. While the conference focus is on undergraduates, ABRCMS includes numerous post-baccalaureates, graduate students, postdoctoral scientists, faculty, and administrators as participants. In addition, the conference places a special emphasis on individuals from underrepresented minority groups and on persons with disabilities.

Under the theme “Strength in Diversity! Fifteen Years of Enhancing Minority Student Excellence in STEM Research,” ABRCMS 2015 was held 11–14 November in Seattle, Wash. The conference attracted over 4,000 participants (a 17% increase), including approximately 2,400 students, 550 faculty and program directors, and 700 recruiters for graduate and summer research programs.

Attendees took part in a four-day program of scientific symposia, panel discussions, mentoring and skill-building sessions, professional development, and networking events.

Keynote addresses on diversity, tolerance, and inclusion were given by Nontombi Naomi Tutu, human rights activist and daughter of Archbishop Desmond Tutu, and Hannah Valantine, Chief Officer for Scientific Workforce Diversity at the National Institutes of Health. Insightful plenary lecturers included:

- **Linda B. Buck,** Ph.D., Nobel Laureate, Howard Hughes Medical Institute investigator and researcher at the Fred Hutchinson Cancer Research Center
- **Jon R. Lorsch,** Ph.D., Director of the National Institute of General Medical Sciences at the National Institutes of Health
- **Patricia E. Molina,** M.D., Ph.D., president of the American Physiological Society and a professor and department head at the Louisiana State University Health Sciences Center-New Orleans
- **David Quammen,** B.A., B.Litt., author of 12 books and three-time recipient of the National Magazine Award

The conference offered numerous additional presentations by accomplished scientists selected for their scientific knowledge, ability to explain complex concepts to students, exemplification of diversity in science, and availability to mentor students throughout ABRCMS.

With nearly 1,900 abstracts accepted for presentation—a record high—student poster and oral presentations were a major highlight of ABRCMS 2015. Each undergraduate
and postbaccalaureate presentation was judged by three research scientists, and at the closing banquet, 243 students were recognized with awards for outstanding research presentations.

Other highlights included the conference’s exhibit and career development programs. In the ABRCMS Exhibits Program, students met with representatives from more than 350 academic institutions, government agencies, foundations, or professional societies to discuss graduate and research programs and other opportunities. Towards career development, ABRCMS offered “Gateway to the Future: Career Paths in the Biomedical Sciences, STEM Disciplines, and Behavioral Sciences,” a session where scientists from a variety of sectors shared their career pathways and educational backgrounds and led small group discussions focused on “a day in the life of a research scientist.” Additionally, many conferees sought out the ABRCMS Professional Skills Cafe, an interactive, participatory area where students and experts discussed strategies for preparing admissions documents, securing summer research internships, finishing dissertations, and other topics important for beginning scientists.

ABRCMS also held a special recognition ceremony for Clifford W. Houston, Ph.D., of the University of Texas Medical Branch, who retired as founding ABRCMS chair after 15 years. The new conference chair is Avery August, Ph.D., of Cornell University.

Organized and managed by ASM, ABRCMS is supported in part by award no. T36GM07377 from the Division of Training, Workforce Development and Diversity of the NIH National Institute of General Medical Sciences. ABRCMS 2016 will be held 9–12 November in Tampa, Fla. Learn more at www.abrcms.org.

**PRINCIPLES OF VIROLOGY**

**FOURTH EDITION**

Authors: Jane Flint, Vincent Racaniello, Glenn Rall, Anna Marie Skalka

*Principles of Virology* is the leading virology textbook because it does more than collect and present facts about individual viruses. Instead, it facilitates an understanding of basic virology by examining the shared processes and capabilities of viruses. This fully updated edition represents the rapidly changing field of virology.


“*Principles of Virology* is an extremely valuable and highly informative textbook that describes virology at the interface of modern cell biology. As a teacher of graduate students in Biosciences and in human medicine, I highly recommend this textbook.”

- Ralf Bartenschlager, Department Head and Professor, Molecular Virology, University of Heidelberg

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Publishing in August 2015; Full-color illustrations, Glossary, Index

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Microbe Mentor

Advice for Graduate School Applications

The decision to attend graduate school has huge implications on any young microbiologist. It can determine lifelong colleagues and friends, impact future research directions, and build business opportunities. It is no wonder, then, that the ultimate goal of any applicant is to find a university, program, and ultimately an advisor, that will satisfy the student’s current and future needs. Once the applicant has identified where he or she would like to spend the next few years of their lives, either as a Master’s student or a Ph.D. candidate, the next challenge is to convince this university/program/advisor to accept the responsibility of taking on this new student. Similar to that of a job, this application process can be very competitive.

Knowing this, one person asked Microbe Mentor, “What can students do to make graduate school applications stand out?” In other words, if you could give one or two pieces of advice to somebody preparing themselves to apply to graduate school, what would that advice be? Microbe Mentor reached out to three distinguished faculty members for their advice on this topic. Here’s what they had to say:

In regard to the application, Michael McInerney of the University of Oklahoma suggested that the applicant “tailor the application so that it is specific to the institution and a particular laboratory/faculty member if possible.” McInerney admitted that, “when I look at applications, I ask why is this person applying to the University of Oklahoma, and if the person indicates interest in my laboratory, why are they interested in working with me? They should show some knowledge about the areas of interest in the department and why the applicant is interested in these areas. I understand that students may not know exactly what they want to study. I did not know exactly what I wanted to do (when I started), but I was interested in microbiology and tried to emphasize my interest in learning more about microbiology. We want to make sure that we can meet the applicant’s interests.”

Graduate training in the microbial sciences emphasizes achievements in the laboratory as well as in the classroom, so having experience in the lab and an appreciation for the sort of commitment required to succeed there is widely viewed as a critical element to the applicant’s background. Therefore, McInerney also suggested that applicants “emphasize any laboratory or other experiences that allowed them to work independently. M.S. students and undergraduate students that did research projects should describe what research they did. Undergraduates that did not do research projects can describe experiences that they had in laboratory or other courses that allowed them to work independently. I would highlight the challenges that they faced and how they overcame them. The challenges could be technical, e.g., a difficult assay that needed optimization, or personal, developing the confidence that they can work on their own or persevere and keep going when the work does not turn out as expected. I would emphasize their ability to solve problems, overcome challenges, and work independently.”

Finally, McInerney said, “I would discuss anything that sets them (the applicant) apart from other students. Maybe they took more mathematics than required for their degree or volunteered in a laboratory, etc. Also, any leadership positions that they had should be mentioned. The application should bring out the excitement that the person has for microbiology, why they are interested in a particular topic, and what they plan to do in the future when they are done. Success in graduate school requires motivation and perseverance. These traits should also be brought out in the application.”

Elizabeth Edwards of the University of Toronto advised that “for a graduate student to be successful, . . . first and foremost there has to be keen passion for knowledge, and a belief that this quest for knowledge and deep understanding will make the world a better place. For a grad school application to be successful, this passion needs to
be evident.” She followed with, “Passion can be manifested in many different ways, but it has to be real, driven by some motivation to work for a better future, fueled by personal experiences and prior work. But it can’t be naïve either. There has to be understanding of existing constraints, recognition of the tough slog ahead, and of the importance of listening to and learning from others and building knowledge in partnerships. I like to hear a student’s story, and then get some independent corroboration of the story and their abilities. In reality, a bit of relevant experience in undergrad, say in a lab, or a similar testing ground, is a huge bonus.”

Edwards stressed that a successful “candidate needs to demonstrate a record of ability or a few proven relevant skills, and then bingo, they jump to the top of the pile.” In addition, “there also has to be a good “ﬁt” between the grad program, the supervisor, and the student - an alignment of interests and ethics.”

Lily Young of Rutgers University continued with these themes. In her opinion, when it comes to a graduate school application, demonstrating “experience in a lab is, of course, an important factor. It may or may not be a paid position; it may or may not be an independent research project; it may have been in the summer or during the semester. Some students have more opportunities than others to do research as an undergrad. Regardless, any kind of lab experience is helpful as it teaches routine, how to handle chemicals and reagents, how to organize an experiment, the preparation that is required before an experiment is carried out, how to clean up after a procedure, how to repeat and repeat and repeat and repeat, how there can be a lot of tedium, but once the data comes in and looks good, the excitement and satisfaction that is experienced.”

Young also suggested that applicants “show passion for the material. When putting together an application for grad school, more important than straight As or high GREs is a personal statement that shows passion for the subject. Show commitment and purpose. What did you do during the summers? Did you volunteer for a good cause, did you volunteer for a professor to gain experience, did you have to work in order to help cover [the] cost of college? All that shows character.”

In summary, these experienced faculty and mentors feel that a graduate school application should be seen as an opportunity to demonstrate:

- Technical laboratory skills
- Independent research skills
- Communication skills
- Passion for knowledge and the subject matter
- The ability to overcome challenges
- Perseverance and commitment
- Teamwork
- Alignment between the students’ interests and the university, program, and faculty strengths
- Why the applicant is special, unique, and worth the investment that the graduate program and faculty will be committing to

If these items are clearly outlined in a graduate school application, an applicant’s chances of being noticed and positively reviewed are significantly increased.

Our Microbe Mentor, Eleanor Jennings, would like to thank the following for taking the time to provide such helpful guidance to ASM’s early-career microbiologists:

- Michael J. McInerney
  Chair and Professor of Microbiology
  Department of Microbiology and Plant Biology
  University of Oklahoma

- Elizabeth A. Edwards
  Professor, Department of Chemical Engineering and Applied Chemistry
  Director, BioZone
  University of Toronto

- Lily Young
  Distinguished Professor, Environmental Sciences
  Provost
  Rutgers University

Want to know more about Microbe Mentor and ASM career offerings? Sign up for the monthly notification list at microbementor@asmusa.org. Each message will include a sneak peek at the upcoming column, career and mentoring news, and more!
Reviews and Resources

BOOK

The Art of Fermentation: An In-depth Exploration of Essential Concepts and Processes from Around the World

Microbes nourished humans for millennia before humans realized what microbes are. Today we have the good fortune of being able to enjoy traditional fermentation practices and delight in our knowledge of the microbial alchemists doing the work. The current revival in home, restaurant, and small-scale commercial production of fermented foods and beverages has been fueled, in part, by two books by Sandor Katz. Published in 2003, Wild Fermentation offered practical instructions that inspired many to try their hand in their own kitchens. His subsequent book published in 2012, The Art of Fermentation, is a well-researched and documented reference covering diverse global practices that employ microbes (including fungi) to transform and preserve just about everything edible: fruits, vegetables, grains, milk, meat, and honey, to name a few of the most familiar ingredients. Organisms and their metabolic products are named, where pertinent. References are abundant.

Warning! The attractive pages are liberally spiced with Katz’s enthusiasm and his own hands-on experimentation—a combination apt to inspire you to jump in yourself. And an experimentalist he is. He unearths traditional methods from Asia, Europe, or Africa, then brings them into his kitchen, improvises as needed, and shares his observations. Here are general methods, along with their underlying rationales, for partnering with microbes to safely produce sauerkraut, kimchi, sourdough breads, kefir, kombucha, yogurts, pickles, vinegar, and a host of less familiar foods. And yes, of course, mead, cider, beer, and wine. The use of these practices by countless generations under nonsterile conditions attests to their safety. Cleanliness is called for, but not sterility. Beneficent microbes belong in every kitchen. Here we, as microbiologists, observe processes that manifest symbiosis, coevolution, syntrophy, adaptation, and succession. We can experiment by tweaking variables. And we can eat, distribute for peer review, and enjoy our results.

Merry Youle
ASM-CDC Postdoctoral Research Fellowship. Postdoctoral scientists are encouraged to submit applications for 2015 ASM-CDC Postdoctoral Research Fellowships. Offered through the ASM-CDC Program in Infectious Disease and Public Health Microbiology, each fellowship is a two-year research experience under the mentorship of CDC scientists. The goal of the fellowship is to support the development of new approaches, methodologies, and knowledge in infectious disease prevention and control in areas within the public health mission of the CDC. All fellows in areas within the public health mission of the CDC. All fellows d mycotic diseases, viral and rickettsial infections, and HIV/AIDS. Learn more at http://www.asm.org/cdcfellowship

Deadline: 15 February 2016.

Undergraduate Faculty Research Initiative Fellowships. Early-career (and future) undergraduate STEM educators are encouraged to apply for a 2016 ASM LINK Undergraduate Faculty Research Initiative (UFRI) Fellowship. This new professional development resource trains STEM faculty to develop undergraduate research programs by initiating successful research partnerships. As part of the fellowship, ASM LINK will provide travel subsidies of up to $2,000 to (i) increase participation of undergraduate STEM educators at eight eligible ASM-sponsored research conferences, (ii) encourage networking and collaborations with potential research partners, and (iii) access resources and mentoring to advance undergraduate research programs. Fellowship applications are accepted on a rolling basis for each of the eight conferences. The deadline is 4 April to be considered for a UFRI fellowship for the ASM Microbe 2016 meeting (Boston, MA).


Deadline: 4 April 2016.

ASM Robert D. Watkins Graduate Research Fellowship. Senior-level graduate students are invited to apply for a 2016 ASM Robert D. Watkins Graduate Research Fellowship. With an aim to increase the number of students from underrepresented minority groups who complete doctoral degrees in the microbial sciences, the Watkins fellowship provides students with support to complete and present their microbiology research. Fellows attend the ASM Kadner Institute for Graduate Students and Postdoctoral Scientists in Preparation for Careers in Microbiology (http://www.asmgap.org/kadner) or the ASM Scientific Writing and Publishing Institute (http://www.asmgap.org/swpi) and – dependent on abstract submission and acceptance – are supported to present their research at the ASM Microbe Meeting.

WWW: http://www.asm.org/watkins.

Deadline: 1 May 2016.

American Board of Medical Laboratory Immunology (ABMLI) Certification. Certifies the expertise of doctoral-level scientists seeking to direct laboratories engaged in the immunological diagnosis of human disease. ABMLI certification is the highest credential available to practicing medical laboratory immunologists and is recognized under CLIA ’88 as one of the acceptable personnel requirements for high complexity laboratory directors. ABMLI certification is achieved by passing an online multiple-choice exam that is offered daily in the month of August at testing centers worldwide.

WWW: www.asm.org/abmli

Deadline: 1 June 2016.
ASM Meetings Calendar

8–10 February 2016.
ASM Biodefense and Emerging Diseases Research Meeting.
Arlington, Va.

@ASM Conference on The Individual Microbe: Single-Cell Analysis and Agent-Based Modeling.
Washington, D.C.
http://conferences.asm.org/

13–17 April 2016.
13th ASM Conference on Candida and Candidiasis.
Seattle, Wash.
WWW, http://conferences.asm.org/

19–22 May 2016.
32nd Clinical Virology Symposium.
Daytona Beach, Fla.
WWW, www.clinicalvirologysymposium.org

ASM Microbe 2016.
Boston, Mass.

31 July–3 August 2016.
ASM Conference on Streptococcal Genetics.
Washington, D.C.
WWW, http://conferences.asm.org/

4–7 August 2016.
2nd ASM Conference on Experimental Microbial Evolution.
Washington, D.C.
WWW, http://conferences.asm.org/

29 August–1 September 2016.
5th ASM Conference on Salmonella.
Potsdam, Germany.
http://conferences.asm.org/

9–12 September 2016.
6th ASM Conference on Beneficial Microbes.
Seattle, Wash.
WWW, http://conferences.asm.org/

ASM Conference on Infection and Cancer.
Washington, D.C.
WWW, http://conferences.asm.org/

11–14 December 2016.
ASM Conference on Antibacterial Development.
Washington, D.C.
WWW, http://conferences.asm.org/

About the Calendar

The ASM Meetings Calendar is provided as a service to readers of Microbe. It includes annual meetings and conferences organized by the Society. Detailed information for these events is published in the ASM Meetings and Conferences insert, which appears bimonthly in the center of Microbe.

As an added benefit of membership in ASM, an online calendar of microbiology-related meetings hosted by ASM and by other organizations is available through the ASM website. Any organization may submit items for the online calendar provided that submissions are of obvious interest to microbiologists. ASM will not permit announcements to appear in the calendar when the subject matter and dates conflict with ASM meetings or workshops. The calendar is located at https://info.asm.org/index.php/meeting-and-event-calendar. All entries in the online calendar are limited to conference name, dates, location, website, and contact information (person, address, telephone, fax, and/or e-mail). When websites and e-mail addresses are provided, links to them will be established. Because of the volume of submissions received, ASM staff is unable to provide proofs or other confirmation of receipt of each listing. Submit items for the online calendar through the “Add a new event/deadline” link on the Meeting and Event Calendar page.
Employment

POSITIONS AVAILABLE

Professor, Associate Professor, or Assistant Professor without Tenure

The Department of Laboratory Medicine, University of Washington, is recruiting a full-time Professor, Associate Professor, or Assistant Professor without tenure in clinical microbiology on the Clinician-Educator or Physician-Scientist pathway. This would be a 12-month, multi-year appointment. University of Washington faculty engage in teaching, research and service. The primary service responsibility will be to participate in the direction of one or more of the Department’s clinical microbiology laboratories. Additional responsibilities include the teaching of residents, fellows, medical students, and medical laboratory scientist program undergraduates, and development of a suitable area of research or scholarship. Documented experience is required directing clinical laboratories and in the clinical interpretation of microbiological testing results. Applicants must have an M.D., D.O., Ph.D. or foreign equivalent and be board-certified or board-eligible in clinical or anatomic pathology by the American Board of Pathology, in clinical microbiology by the American Board of Medical Microbiology, or in infectious diseases by the American Boards of Internal Medicine or Pediatrics. In order to be eligible for University sponsorship for an H-1B visa, graduates of non-U.S. medical schools must show successful completion of all three steps of the U.S. Medical Licensing Exam (USMLE), or equivalent as determined by the Secretary of Health and Human Services. Salary will be commensurate with qualifications and experience. Applicants should submit CV, contact information for five references, and a brief statement of professional goals to Brad T. Cookson, M.D., Ph.D., c/o Karen Walter, Box 357110, University of Washington, Seattle, WA 98195-7110 (kwalter@uw.edu). The University of Washington is an affirmative action and equal opportunity employer. All qualified applicants will receive consideration for employment without regard to race, color, religion, sex, sexual orientation, gender identity, national origin, age, protected veteran or disabled status, or genetic information.

Employment Advertising

Microbe is published monthly and available to nearly 40,000 ASM members and institutional subscribers. Lead time for employment ads is about 3 weeks. Microbe is mailed around the 8th of the month of issue, but the delivery date is not guaranteed. Please consider delivery dates when setting application deadlines.

ASM does not accept classified advertisements that indicate a limitation, specification, or discrimination on the basis of race, religion, national origin, sex, mental or physical disability, age, or any other matters which may not be lawfully considered in making employment decisions. Employment notices that discriminate against microbiologists on the basis of a particular board certification or doctoral degree will not be accepted. Such advertisements will be rejected unless it can be established that the position by state or federal law or regulation requires a specific board certification or doctoral degree.

Classified

Classified ads must be typed, double spaced, with normal sentence capitalization (capital and lowercase letters). Microbe cannot accommodate requests for extra capitalization, boldface type, or other text or layout enhancements in classified ads.

Include the name and telephone and fax numbers of a contact person for questions about your ad copy. Incorrectly typed ads or ads with application deadlines earlier than the 15th of the publication month requested cannot be guaranteed placement in that issue.

Deadlines: Your ad must be received by the 1st of the month before the publication month to ensure timely publication (e.g., to appear in the April 2016 issue, your ad must be received by 1 March 2016).

Classified ads should be sent (with payment) to Walchi-Tauber Group, 2225 Old Emmorton Road, Suite 201, Bel Air, MD 21015, attn: Rhonda Beamer, tel. (443) 512-8899x106; fax, (443) 512-8909; e-mail, rhonda.beamer@wt-group.com.

Rates:

1–50 words $185
50–100 words $350
101–150 words $535
151–200 words $720
201–250 words $910
251–300 words $1,070
301 words $3.45 per word

Internet posting: All classified line advertising printed in Microbe also appears on the ASM website. Ads are posted to the website shortly before the issue mailing date and remain on the site for approximately 1 month. Hence, line ads placed for an issue of Microbe will be available to ASM website browsers around the beginning of the month and will overlap their print appearance in the magazine. All ads are replaced with the close of the next issue.

For display ad Internet posting costs, please contact Rhonda Beamer at the address given above.

Display

Display advertising closes the 1st of the month preceding publication. For specifications, rates, and deadlines for display ads, contact Rhonda Beamer at the address given above.
Small Things Considered

Autoendoliths: Architects of the Deep
http://schaechter.asmblog.org/schaechter/2015/06/autoendoliths-the-architects-of-the-deep.html
by Jeffrey Marlow

The submersible’s headlights shine brightly into the water, illuminating a patch of the seafloor with a hazy glow, like a car moving tentatively over a snowy mountain pass. In front of us, white patches of craggy rock extend upward, decorated with hardy corals and colorful microbial mats. In the distance, we spot a column of rising bubbles and move in for a closer look, the robotic arm poised and ready for some geobiological prospecting.

The outcrop we’re investigating is Hydrate Ridge, a mound of carbonate rock 100 m tall that is one of the best-studied methane seeps in the world. Formed by the breakdown of organic goo deep beneath the seafloor or microbial reactions closer to the surface, methane percolates upward and into the shallow subsurface. There, roughly 80% of it is consumed through the anaerobic oxidation of methane (AOM), an intricate metabolic coupling between archaean and bacterial partners that operates at the edge of energetic feasibility. Methane and sulfate are biologically converted to bicarbonate, much of which is incorporated into carbonate rock, and these precipitation products form solid mounds that house their creators. Remarkably, the microbes remain metabolically active, at least in the cases we’ve studied at Hydrate Ridge.

Endoliths have traditionally been viewed in one of two contexts. Active rock degraders (“euendoliths”) adjust localized chemical equilibria to dissolve rock. Alternatively, passive inhabitants (“chasmooendoliths” or “cryptooendoliths”) seek energy or environmental stability from the rock-bound lifestyle. But microbes that build the rock structures in which they live? That seemed to be something else altogether.

Using the carbonate-hosted methanotrophic microbes of Hydrate Ridge as a type case, we have defined a fourth flavor of endolith—the “autoendolith”—whose members fulfill three criteria: (1) metabolic activity must directly or indirectly lead to mineralization; (2) mineralization must lead to a structurally coherent rock rather than loose mineral crusts; and (3) metabolic activity must continue within the rock. (Of course, the organisms responsible for biological AOM and seafloor carbonate architecture have been known for years; it is the functional categorization that is new here.)

Autoendolithic life is in some ways a confounding long-term strategy. With unchecked methanotrophy and mineral precipitation, conduits in the rock become occluded, potentially entombing the microbes and starving them of energy and nutrients. However, a sustainable existence may be possible. Properly balance the metabolic rate against seep fluid flow, and products could be swept away from the microbes to precipitate elsewhere. Alternatively, excreted metabolites could maintain sufficient permeability by discouraging mineral nucleation or dissolving previously formed structures.

Remarkably, evidence of autoendolithic activity may be preserved over millions of years. In the Marmorito limestone collected in northern Italy, Jörn Peckmann, a Professor at the University of Vienna, identified distinct carbonate phases that bear the isotopic signatures of methane-derived carbon. Mineralogical and biomarker evidence suggests that the limestone is attributable to autoendoliths and that this rock-building phenomenon is not a new development. The full extent of the autoendolithic lifestyle remains to be seen, but it does broaden our appreciation for geobiological possibilities, signifying yet another example of how unseen life may shape the world in ways we rarely consider.

THE FACULTY OF BIOLOGY AND MEDICINE OF THE UNIVERSITY OF LAUSANNE, SWITZERLAND AND THE UNIVERSITY MEDICAL CENTRE OF LAUSANNE (CHUV) INVITE APPLICATIONS FOR THE POSITION OF

FULL PROFESSOR OR ASSOCIATE PROFESSOR OF BACTERIOLOGY (METAGENOMICS AND/OR BACTERIAL GENOMICS)

Starting date: to be agreed

Your activities:
The successful candidate will lead the bacterial genomics and metagenomics unit, which is one of the 4 diagnostic unit of the institute of microbiology. He will provide undergraduate, postgraduate and further teaching in Bacteriology, with a specific focus in bacterial genomics, functional genomics and/or metagenomics. The successful candidate will also lead a high-level research program in bacteriology and will participate to the life of the Institute.

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Your application:
The applications, in English, will include a motivation letter, the curriculum vitae, the list of publications with a copy of the five most significant ones, a brief statement of the research programme and teaching experience and a copy of diplomas. They should be sent by April 1st, 2016 as a single pdf file to www.unil.ch/iafbm/application.

The job description as well as a description of the Division are also available on the Web at the address www.unil.ch/emplois «Postes académiques». For further information, please contact Prof. Gilbert Greub (Gilbert.Greub@chuv.ch), Director and Head of Service.

Seeking to promote an equitable representation of women and men among their staff, the University and the University Medical Centre encourage applications from women.
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www.asm.org/microbe2016