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Last of the Great Potterers

Would it be possible today for one inspired individual to make major contributions across a range of different scientific specialties?

Bernard Dixon

As a swan song (goodbye, readers!), I thought this month I would discuss one of my little-known scientific heroes. In doing so, I shall be looking backwards but also forwards to 2020, the centenary of his richly deserved but rarely celebrated Nobel Prize.

The man’s name was August Krogh, one of the last of the great scientific potterers—that remarkable galaxy of men (yes, they were predominantly men) who poked about in numerous areas of science and, apparently effortlessly, made historic contributions in all of them. Krogh was a contemporary of the English geneticist J. B. S. Haldane, perhaps the best-known potter of all time. While Haldane was writing major papers on enzyme kinetics, blood groups, antigen-antibody reactions, population dynamics, evolution, and other often-unrelated topics, Krogh was pioneering important work in fields such as human physiology, marine biology, nutrition, botany, cell biology, histology, and biochemistry.

August Krogh seems to have been a competent but unremarkable schoolboy at Grenaa in Jutland (now comprising the continental part of Denmark and the northern portion of Germany), and said in later life that his real education took place outside of school time. He was a dedicated boy scientist, studying insects and spiders, making novel apparatus, and spending considerable time in the field botanizing and zoologizing. After a false start, when he enlisted in the navy, he went in 1893 to study physiology under Christian Bohr at the University of Copenhagen.

Immediately, Krogh began making important, original contributions to science. While studying the way in which mosquito larvae regulate their buoyancy, as a fish uses its swim bladder, he invented a new and highly sensitive method for analyzing air bubbles. He then applied the concepts and techniques of physics to a wide variety of biological problems—including the rising of sap in plant stems, the swelling of plant cells, and changes of pressure in animal body fluids. He soon became highly critical of other biologists who lacked the knowledge, dexterity, or inclination to apply physics in biological research. Krogh was, of course, right in his criticism. To a large extent, plant and animal physiology progressed by using just the sort of methods he was then pioneering.

Krogh gained his doctorate in 1903 for research in which he established that the frog takes up oxygen mainly through the lungs, but loses carbon dioxide by diffusion through the skin. In 1905, the year he married, he became interested in a controversy then raging as to whether human respiration was an active or passive process. He devised a micro-aerotonometer to measure gaseous exchange between a single bubble of air and the blood flowing around it. Using this device, he and his wife Marie discovered that arterial oxygen pressure was always below that in alveolar air, so that simple diffusion was sufficient to account for oxygen transfer.

Thus they demolished the prevailing theory—that lung cells actively secreted oxygen into the bloodstream. Until that time, the secretion theory had been supported enthusiastically by Krogh’s chief, Bohr, and in Britain by J. S. Haldane—J. B. S.’s father and an outstanding authority in the field.

Before starting this classical work, Krogh had taken time off to join a scientific expedition to northern Greenland, where he investigated the metabolism of Arctic animals. Now, having finished the research, he went back to the Isle of Disko to study the nutrition of Eskimos in relation to their metabolism. Despite the severe climate, and dismal facilities for research, he did important work and began to lay the foundations for a new experimental approach to the physiology of exercise. The methods he evolved were
adopted later for worldwide surveys by the Health Organization of the old League of Nations, forerunner of the WHO.

Polishing off the research for which he later received a Nobel prize—showing, by a unique blend of elegant experiment and ingenious mathematics, how the capillaries respond to a need for increased blood—he then moved on to a wide variety of other matters. He invented the electromagnetic bicycle ergometer for studying exercise, and a highly sensitive means of weighing the subject; the “tilting spirometer,” a uniquely sensitive apparatus for gas analysis; new techniques for observing living tissues under the microscope; histological methods; the nitrous oxide method of measuring circulation rate; equipment for measuring the osmotic pressure of human blood; a wristwatch-type “micro climatograph” measuring temperature and humidity; and an instrument for monitoring oxygen consumption by insects.

The extraordinarily polymathic Krogh was also the first researcher to suggest the “sodium pump” that carries ions across cell membranes. He discovered that living things obey van’t Hoff’s Law, used isotopes (as early as 1935) to investigate the permeability of skin in aquatic animals, established the relative amount of energy the body liberates from fat and carbohydrate, and pioneered studies on the metabolic role of insulin. Moreover, he wrote about his work in superb, economical prose.

As regards insulin, August Krogh, were he still alive today, would be fascinated to learn of successive developments over the decades in methods of producing ever more potent, safer, and more appropriate forms of the hormone for the treatment of diabetes, culminating in today’s manufacture of genetically modified human insulin in bacteria. Shortly after insulin was discovered, in 1922, he and his wife Marie obtained a small supply which they used in their own studies. Marie herself had type 2 diabetes, and one of her patients suffered from the type 1 version of the condition. Their work led to the foundation of Nordiskinsulin Laboratorium, which made the hormone by ethanol extraction from pig pancreas—at a cost lower than anywhere else in the world.

Since Krogh died in 1949, polymathic potterers have largely disappeared from the science scene. Why? Blameworthy on some occasions is premature specialization at school, which can place intelligent people on tramlines of increasingly narrow and irrevocable commitment. The chemistry teacher, mindful of a school’s greater glory, impels a young pupil with good marks in chemistry towards a degree course in chemistry. The teacher does so regardless of the student’s broader aptitudes and interests, which he or she tends not to notice, and regardless of the eventual utility of a degree in chemistry. Later, an equally well-meaning tutor assumes without question that because the graduate gained a good degree, with outstanding marks in physical chemistry, this must lead to research in physical chemistry. The cycle is complete 20 years later when a career is crowned with a chair of physical chemistry.

That is part of the story. Equal blame must attach to those grant-awarding bodies, heads of research departments, and the like, who invariably suspect the polymath and interpret versatility as shallowness of mind. Predictably, they will reject as a dilettante an individual with dozens of original but variegated ideas to their credit, and take on instead the plodder or single-minded enthusiast. Funding agencies that tend to favour “mission-oriented” rather than “curiosity-oriented” programs are especially suspect from this perspective.

All this, too, at a time when everyone acknowledges the importance of multi-, inter-, and cross-disciplinary research. We need to remember the ancient aphorism that “Talent does what it can. Genius does what it must.”
ASM MICROBE 2016

Virome Affects Host Immune Status, Susceptibility to Range of Diseases

Shannon Weiman

While the limelight shines on the bacterial microbiome for its role in shaping human health and disease, the virome remains more in the shadows. However, viruses associated with human hosts can have profound impacts on their health, according to several researchers who spoke during the ASM 2016 Microbe Conference held in Boston last June. Even though some chronic viral infections appear asymptomatic, the viral particles being generated during such latent periods can stimulate innate immune responses, dictating immune reactivity as well as susceptibility to infections and inflammatory and other diseases, including cancer.

Most humans chronically carry at least 10 different known persistent or latent viruses at any given time, including herpesviruses, noroviruses, and adenoviruses, according to Herbert “Skip” Virgin of Washington University in St. Louis, Mo., who spoke during the President’s Forum at ASM Microbe. “Herpesviruses persistently infect most humans, and exert significant effects on innate immunity in mice during experimental chronic infection, including inducing resistance to tumors and a range of pathogens,” he says. For example, herpesviruses stimulate interferon (IFN)-γ, macrophages, and natural killer cells—in effect, defining the immunophenotype of the host.

Such latent viruses can be mutual symbionts, benefitting the host by enhancing immunity and even compensating for immunodeficiencies. For example, when the RBCK1 gene is mutated in humans and mice, their cytokine and macrophage responses are impaired, leaving them unusually susceptible to some kinds of infections. However, latent herpesvirus infections in mice enhance their IFN-γ levels significantly, restoring the ability of macrophages to fight bacterial pathogens, according to Virgin. “The protective effect of chronic herpesvirus infection is due to the stimulation of innate immune functions that compensate for deficient early cytokine responses associated with multiple immunodeficiencies,” he says.

Other latent infections can prove detrimental, says Taylor Gray of the University of Massachusetts, Amherst. Adenovirus infection can increase the risk for obesity and possibly cancer. Latent human adenovirus 36 infections are more common in women with high rather than low body mass indices, and women in the former group also happen to be predisposed to breast cancer, she says. In animals such as rodents, obesogenic adenoviruses alter fat cell metabolism, leading to systemic inflammation, which might account for this predisposition to develop breast cancer.

By heightening immune reactivity, latent viruses can also exacerbate chronic inflammatory diseases. In mice with a syndrome resembling multiple sclerosis (MS) in humans, latent herpesvirus enhances production of inflammatory cytokines, inducing T-cell migration into the central nervous system and leading to neurodegenerative pathologies similar to what happens to humans with MS.
“Gene expression changes induced by latent or persistent viral infection may alter the course of chronic disease pathogenesis,” says Virgin. Thus, he suggests, viruses associated with the respiratory tract may influence diseases such as asthma, chronic obstructive pulmonary disease, and chronic bronchitis.

Latent infections also may induce inflammatory diseases in genetically predisposed individuals, according to Virgin. For example, Atg16L1 mutations associated with Crohn’s disease do not confer that disease to mice. However, when such mutations occur in mice with chronic norovirus infections, the animals develop blunted intestinal villi, abnormal Paneth cell morphology, and colitis that do not arise in mice infected with that virus but with normal Atg16L1 genes. “Virus-plus-susceptibility gene interactions determine Crohn’s disease gene phenotypes in the intestine,” he says. “Chronic infections can modify the clinical presentation of genetic variations, thereby opening a new avenue for the analysis and interpretation of human genotype-phenotype associations studies.”

Shannon Weiman is a freelance writer in Boulder, Colo.

RESEARCH ADVANCES
Analysis Suggests Habitat, Lifestyle for Last Universal Common Ancestor

Barry E. DiGregorio

The last universal common ancestor (LUCA) apparently was a thermophilic, anaerobic, nitrogen-fixing microorganism, according to William F. Martin from the Institute of Molecular Evolution at Heinrich Heine University Düsseldorf, in Düsseldorf, Germany, and his collaborators. Their findings support the theory of an autotrophic origin of life involving the Wood–Ljungdahl pathway in a hydrothermal setting. Details appeared July 25, 2016 in Nature Microbiology (doi: 10.1038/nmicrobiol.2016.116).

The researchers took a phylogenetic approach in their search for traces of LUCA genes. Specifically, among proteins encoded in prokaryotic genomes, they searched for those that fulfill two criteria: first, that the protein be present in at least two higher taxa of bacteria and archaea and, second, that its phylogenetic tree recapitulates bacterial and archaeal monophyly. Genes meeting both criteria are unlikely to have undergone transdomain lateral gene transfer, and thus were probably present in LUCA and inherited within domains since the time when LUCA lived, according to Martin.

The researchers examined 6,103,411 protein-coding genes from 1,847 bacterial and 134 archaeal genomes before sorting them into 286,514 protein families, 11,093 of which contained homologs from bacteria and archaea. Within this large set, only 355 clusters preserve domain monophyly, consis-

MINITOPIC
Microbiology Policy Bulletin Board

Recent developments involving microbiology and related science policy matters and including drug, vaccine, and diagnostic product approvals:

- During the United Nations General Assembly last September, world leaders vowed to take a coordinated approach to antimicrobial resistance problems in human and animal health—promising to develop national action plans based on the “Global Action Plan on Antimicrobial Resistance,” a 2015 report from officials of the World Health Organization.
- Late in September, members of the U.S. Congress agreed to provide $1.1 billion to study and control the Zika virus; these resources were issued as part of a continuing resolution needed to keep the government running through December 9.
- U.S. officials in September announced a competition, “the Antimicrobial Resistance Diagnostic Challenge,” promising $20 million in prizes covering “innovative and novel laboratory diagnostic tests.”
- The High-Risk, High-Reward Research program, supported by the National Institutes of Health Common Fund, in October issued 88 grants amounting to approximately $127 million to “highly creative and exceptional scientists with bold approaches to major challenges in biomedical research.”
- U.S. Food and Drug Administration (FDA) officials in September issued a final rule on the safety and effectiveness of antibacterial soaps, calling for removal of triclosan and triclocarban from over-the-counter antibacterial hand and body washes.
- Also in September, FDA officials sought comments on rules to slow antibiotic resistance that would restrict use of such drugs in livestock—specifically, by limiting the duration of the use of “antimicrobial drugs of importance to human medicine” when they are “administered in the feed or water of food-producing animals.”
- The Government Accountability Agency in September issued another report in a series, “High-Containment Laboratories: Actions Needed to Mitigate Risk of Potential Exposure and Release of Dangerous Pathogens,” which focuses on a Department of Defense laboratory that inadvertently distributed samples of live Bacillus anthracis during a 12-year period. The report questions whether there is adequate oversight for the federal Select Agent Program as well as high-containment laboratories.
Recent developments involving new means to detect microorganisms and to diagnose infectious diseases include:

- A new diagnostic platform being developed, called “universal microbial diagnostics,” first exposes microbial samples to randomly generated DNA probes and then uses “compression sensing” to detect microbial pathogens and estimate their concentrations, according to Richard G. Baraniuk of Rice University in Houston, Tex., and his collaborators. Details appeared 28 September 2016 in *Science Advances* (doi:10.1126/sciadv.1600025).
- A test to determine the switching on of two genes, called IFI44L and FAM89A, predicts whether sick children have a bacterial rather than a viral infection with 95–100% accuracy, according to Michael Levin at Imperial College London, United Kingdom, and his collaborators. Details appeared August 23, 2016 in the *Journal of the American Medical Association* (doi:10.1001/jama.2016.11236).
- A point-of-care test to determine levels of C-reactive protein, whose concentration rises in response to bacterial pathogens, provides a simple means for determining whether pediatric patients carry serious infections, according to Jan Verbakel of the University of Leuven in Leuven, Belgium, and his collaborators. Details appeared October 5, 2016 in *BMC Medicine* (doi:10.1186/s12916-016-0679-2).
- A phage-based assay provides a highly sensitive means for detecting bacterial pathogens such as *Escherichia coli* O157:H7 in foods—by using the phage to introduce a light-emitting enzyme into the bacteria, according to food scientist Bruce Applegate of Purdue University in West Lafayette, Ind., and his collaborators. Details appeared September 20, 2016 in *Scientific Reports* (doi.org/10.1038/srep33235).

“There is a problem” with this new analysis, says Massimo Di Giulio from the Institute of Biosciences and Biotechnology of CNR, in Naples, Italy. “The LUCA’s gene list reveals only nine nucleotide biosynthesis and five amino acid biosynthesis proteins. This is not expected ... at the evolutionary stage of LUCA and above all because the genetic code co-evolved with the biochemical pathways of amino acids.” Whether this apparent inconsistency is only marginal or a more central flaw in the analysis cannot be said for sure, he notes.

This new vision of LUCA sees it as being only “half-alive,” Martin says. “We think that the picture of LUCA presented by the data reflects a phase of evolution in the transition from geochemical reactions to biochemical reactions. Every theory for the origin of LUCA has to entail something like that, and we think that these genes provide a glimpse of it.” Put another way, he adds, “There is no way to get from carbon dioxide, rocks, and water to fully fledged prokaryotes without going through an intermediate that is not completely alive. The idea is not as radical as it seems. It’s actually a necessary element of all origin of life theories, whether the theory says so or not.”

*Barry E. DiGregorio is a freelance writer in Middleport, N.Y.*
When the researchers broadened their search to include all fungi, they found that fungi belonging to Basidiomycota, a completely different phylum from Ascomycota, express these fungal genes, according to Spribille. "It took a long time to convince myself that I wasn’t dealing with contamination,” he says. He and his collaborators also detected basidiomycetes yeasts in 52 other lichens that grow worldwide. “Once we found the yeast, it was everywhere.” These 52 genera show great diversity and cover "a lot of evolutionary time,” adds his UM collaborator John McCutcheon.

“This discovery overturns our long-standing assumptions about the best-studied symbiotic relationship on the planet,” says their collaborator Catherine Aime at Purdue University in West Lafayette, Ind. “These yeast comprise a whole lineage that no one knew existed, and yet they are in a variety of lichen on every continent as a third symbiotic partner,” she says.

Lichen long proved difficult to cultivate in the laboratory, McCutcheon points out. Perhaps the newly identified yeast component was the missing ingredient needed for laboratory propagation, he suggests, adding: Culturing lichen “could answer basic questions about what component makes what metabolite. Long term, there could be pharmaceutical or commercial applications.”

“This is a novel find that changes how we perceive lichen symbiosis,” says Robert Luecking at the Field Museum in Chicago, Ill., who was not involved in the research. “There currently is no example of a mutual relationship between two different fungi, and this first one is proposed with strong evidence.” It’s a good reminder, he adds, that “science is all about discovery, not methodology.” The researchers started with a small problem that led to questions, and they chose the best method to address a particular question during each step. “Many studies today put the method first and then consider what possible questions could be,” he says.

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

NEW FROM ASM

Zika Genome Sequences Set for Diagnostic, Vaccine Development Purposes

David C. Holzman

Zika virus strains fall into two major genetic lineages—one African, the other Asian—based on recent genome sequencing analysis, according to Young-Min Lee of Utah State University, Logan, and his collaborators. “Studies are currently underway at Utah State University to examine the functional importance of the genetic variation on viral replication and pathogenesis,” he says. Meanwhile, the World Health Organization (WHO) designated another Zika isolate as a reference strain for use in diagnosis. Its sequence was determined by Sally Baylis of the Paul-Ehrlich-Institut in Langen, Germany, and her collaborators. Details appeared online in Genome Announcements, August 18 and Septem-

MINITOPIC

Roundup of Microbiota Studies Involving the Gut or Other Anatomic Sites

Here in brief are findings from several recent reports describing how microorganisms in the gut or elsewhere in the body affect the host:

• SagA, an enzyme from the gut bacterium Enterococcus faecium that is critical to cell survival, can suppress infection by Salmonella enterica serovar Typhimurium in rodents as well as in Caenorhabditis elegans worms, according to Kavita Rangan of the Rockefeller University in New York, N.Y., and her collaborators. Details appeared 23 September 2016 in Science (doi:10.1126/science.aaf3552).

• Mice infected with gastroenteritis-causing Escherichia coli, which promotes inflammatory responses, appear to be at greater risk for Crohn’s disease than are uninfected animals, according to Brian Coombes at McMaster University in Hamilton, Ontario, Canada, and his collaborators. Details appeared October 6, 2016 in PLoS Pathogens (doi:10.1371/journal.ppat.1005907).

• A newly recognized protozoan parasite, Tritrichomonas musculis, protects host mice from intestinal bacterial infections, according to Miriam Merad at the Icahn School of Medicine at Mount Sinai in New York, N.Y., and her collaborators. Details appeared October 6, 2016 in Cell (doi:10.1016/j.cell.2016.08.076).

• There are no clear signatures or predictors of obesity across a substantial volume of microbiome data reported thus far and, if there is any signature at all related to diversity of microbes, it is not biologically useful, according to Marc Sze and Patrick Schloss at the University of Michigan, Ann Arbor, based on their analysis of 10 such studies. Details appeared 23 August 2016 in mBio (doi:10.1128/mBio.01018–16).

• When NOD2, a receptor protein that ordinarily recognizes microbial members of the gut flora, is absent, the host immune system makes more Th2 helper cells than usual, predisposing the host to make more immunoglobulin E and thus making that individual more likely to have allergies, according to Tilo Biedermann at Rechts der Isar Hospital in Munich, Germany, and his collaborators. They presented their findings during the 46th annual convention of the European Society for Dermatological Research, held in Munich last September.
Here are several new and noteworthy developments across several sectors of microbiology research:

- Bacteria rely on a set of previously unrecognized enzymes, which are responsible for shape, elongation, division, and spore formation—called SEDS proteins and distinct from penicillin-binding proteins—to produce their cell walls, according to David Rudner and Thomas Bernhardt of Harvard Medical School in Boston, Mass., and their collaborators. Details appeared August 15, 2016 in Nature (doi:10.1038/nature19331).

- Synthetic, tryptophan-infused nanowires that derive from Geobacter bacteria are 2,000 times more conductive than are their natural counterparts, according to Derek Lovley at the University of Massachusetts, Amherst, and his collaborators. Details appeared 13 July 2016 in Small (doi:10.1002/smll.201601112).

- A newly recognized multicomponent virus, called Guaico Culex that infects mosquitoes but not mammals, and another separate member of the Jingmen virus group found in the blood of a nonhuman primate taken together suggest that the host range of this virus group is “quite diverse,” extending beyond plants and fungi, “highlighting the potential relevance of these viruses to animal and human health,” according to Jason Ladner and Gustavo Palacios of the U.S. Army Medical Research Institute of Infectious Diseases at Fort Detrick, Md., and their collaborators there and at the University of Wisconsin, Madison. Details appeared 25 August 2016 in Cell Host & Microbe (doi:http://dx.doi.org/10.1016/j.chom.2016.07.011).

- Analysis of stromatolites—sedimentary remains of microbial colonies—from Greenland that date back 3.7 billion years suggests that life arose about 4 billion years ago, which is about 220 million years earlier than previously suspected, according to Allan R. Chivas of the University of Wollongong in Wollongong, Australia, and his collaborators. Details appeared 31 August 2016 in Nature (doi:10.1038/nature19355).

The first of the three viral strains sequenced by the Utah State researchers was isolated in 1947 from a rhesus monkey in Uganda. It was regarded as a “sentinel animal”—namely one that was “intentionally placed in a particular environment to detect the presence of an infectious agent in the area,” says Lee. The second sequenced strain was isolated in 1966 from Aedes aegypti mosquitoes in Malaysia. The third strain is the one considered responsible for the epidemic that recently swept parts of Brazil and other countries in the Caribbean and Latin America. Although first isolated in 2015 in Puerto Rico, it derived from an ancestor of the Asian lineage, according to Lee. In 2016 it reached southern Florida, from where it is spreading to other parts of North America.

The decision by WHO officials to begin using a reference Zika strain prior to its review by experts reflects the urgency of the epidemic, says Baylis. “This will facilitate the development of sensitive, better-performing tests to detect Zika in patients. Knowledge of the sequence of this and other virus strains is essential to design robust testing methods...and will help not only in diagnosis but in epidemiological studies.” Reference standards from WHO are used to harmonize assays for diagnostic testing, as well as screening assays for blood transfusions, and to define regulatory requirements for test sensitivity where screening is implemented.

WHO officials declared Zika a “public health emergency of international concern” because of complications that may arise for babies when pregnant women become infected with the virus. Microcephaly and other central nervous system abnormalities are being detected in large numbers of fetuses and newborn babies since the epidemic struck Latin America. Guillain-Barré syndrome, a disorder in which the body’s immune system attacks part of the peripheral nervous system, is also thought to be caused by Zika among some of the adults it infects.

These and other Zika viral genome sequences “will enable us not only to develop effective nucleic acid-based diagnostic tools, but also to study the viral evolution related to Zika virulence and pathogenicity,” Lee says. “The latter issue is critical to addressing a key question of whether the current American pandemic strains are more neurovirulent than the previously isolated strains.” It will also help determine which strain to use for vaccine development.

RESEARCH ADVANCES

Visualizing Bacteria as They Develop Antibiotic Resistance in Vitro

Marcia Stone

The development of antibiotic-resistant strains of bacteria depends on a dynamic growth process, involving a program that is far more complex than mere emergence of mutants with higher resistance than their predecessors, according to Roy Kishony of Technion-Israel Institute of Technology in Haifa and Harvard Medical School. ...
School in Boston, Mass., and his collaborators. This conclusion is based on viewing how cells change while growing on “microbial evolution and growth arena (MEGA)” plates, following those cells as they spread along large plates containing antibiotics as well as nutrients. Details appeared 9 September 2016 in *Science* (doi:10.1126/science.aag0822).

The MEGA-plate, which Kishony and his collaborators developed, consists of a 120-by-60-cm dish filled with agar containing nutrients and different concentrations of antibiotics. Its size enables an antibiotic gradient to be maintained for about 10 days, allowing drug-sensitive *Escherichia coli* cells to grow, evolve, and generate sufficient numbers of mutations to withstand and migrate into higher and higher concentrations of the specific antibiotic to which they are being exposed.

For example, an early set of MEGA-plates contained four-step gradients of either trimethoprim or ciprofloxacin. *E. coli* cells were inoculated onto drug-free regions of plates and allowed to spread. When the inoculant cells reached antibiotic concentrations at which they could no longer grow, resistant mutants emerged and their descendants migrated successively into regions containing stepped-up concentrations of the specific antibiotic to which they are being exposed.

“Importantly, access to intermediate regions of moderate selection enables a range of evolutionary pathways to high-level resistance,” Kishony says. When bacteria were inoculated onto variant MEGA-plates in which they were challenged to go directly from no-drug to high-drug areas, they were unable to adapt. By moving through regions of escalating antibiotic intensity, the *E. coli* ultimately developed high levels of resistance, but it invariably came at the expense of growth rate. Although subsequent mutations compensated, in the absence of sufficient nutrients these very fit mutants became trapped.

“Thus, even though more fit, the bacteria with compensatory mutations were usually spatially restricted from contributing to the ultimate evolutionary success of the population,” says Michael Baym at Harvard Medical School, the project’s lead scientist. “The fitness of a bacterial population confronted by increasing antibiotic levels in natural and clinical setting is not driven by the fittest bacteria but rather by those that are both sufficiently fit and sufficiently close to the advancing front,” adds his colleague Tami Lieberman, also at Harvard Medical School.

These experiments have really captivated people—scientists and regular folks alike—not only because they let people see evolution as it happens, but also because the “films they took of bacteria evolving are just plain cool to watch,” says James Jeffrey Morris at the University of Alabama at Birmingham, adding: “This isn’t the Kishony lab’s first ‘gee whiz’ experiment.” And says Harmit Malik from the Fred Hutchinson Cancer Research Center in Seattle, Washington, there is “amazing value watching evolution in action for students: just like a chemical reaction taking place, seeing is believing.”

Marcia Stone is a science journalist based in New York City.

**2016 SCIENCE AWARDS**

**One 2016 Nobel: Yeast-Based Autophagy Work; 3 MacArthurs: Microbiology**

Jeffrey L. Fox

The 2016 Nobel Prize in Physiology or Medicine, about $936,000 this year, recognizes Yoshinori Ohsumi of Japan for his efforts to understand autophagy, a fundamental process for degrading and recycling cellular components, research that he began by studying yeast. Separately, among the 2016 MacArthur Foundation Fellows, who receive $625,000 “genius awards,” are microbiologist Dianne Newman, who studies bacteria that played roles in shaping the Earth as well as in modern biomedical contexts; geobiologist Victoria Orphan, whose focus is on microbial communities in extreme environments; and physical biologist Manu Prakash, who invented several devices that can be used for diagnostic work in microbiology. Also noteworthy, the 2016 LaskerDeBakey Clinical Medical Research Award is shared by three scientists whose research on hepatitis C virus (HCV) led to development of drugs for treating HCV infections.

During the 1990s, Ohsumi, who is now a professor at the Tokyo Institute of Technology, identified genes in the yeast *Saccharomyces cerevisiae* that are essential for autophagy, determined its underlying mechanism, and later showed that similar mechanisms are at work in human and other mammalian cells. These studies led to insights about autophagy in mammalian cells, where mutations contribute to various diseases, including type 2 diabetes, cancer, and neurological diseases such as Parkinson’s.

Among the 2016 MacArthur Foundation fellows whose work touches on microbiology, both Newman and Orphan are faculty members at California Institute of Technology in Pasadena, Calif., while Prakash is on the faculty at Stanford University in Stanford, Calif. Both Newman and Orphan are studying microorganisms in extreme or exotic environments, while Prakash works on nanoscale inventions.

Some bacteria use metals such as arsenic and iron instead of oxygen in electron-transfer reactions that are necessary for their metabolism. Indeed, some ancient bacteria depended on iron rather than water for a form of photosynthesis.
sis, consistent with this type of anoxygenic metabolism catalyzing deposition of early banded-iron geologic formations, according to Newman and her collaborators. They also are studying the pathogen *Pseudomonas aeruginosa*, which can use electron-shuttling phenazines as a means for surviving within lungs.

Similar to Newman, Orphan studies microorganisms in places where oxygen is scarce—in this case, deep-sea beds. Some of these microbes depend on anaerobic oxidation of methane, a process that helps to prevent this greenhouse gas, which is being released from underwater seeps, from reaching the atmosphere. Another line of her research focuses on an oxidative, extracellular electron transfer process that couples methane-consuming archaea with sulfate-reducing bacteria.

Among other projects, Prakash recently invented several “frugal science” devices that may prove useful for diagnosing infectious diseases in field settings. For example, he incorporated an origami-based folding design into a lightweight optical microscope that is being field-tested for use in public health and biomedical settings. Meanwhile, a specialized microfluidic chip is being developed to collect nanoliter-scale samples of saliva from mosquito bites to screen for pathogens. Such a device might be used, for example, to collect surveillance data during mosquito-borne disease outbreaks such as the one now involving the Zika virus.

Finally, the 2016 LaskerDeBakey award recognizes three scientists for their research on HCV. Specifically, Ralf F. W. Bartenschlager of the University of Heidelberg in Germany and Charles M. Rice at Rockefeller University in New York, N.Y., developed a means for growing this virus in cells in vitro. The third recipient, Michael J. Sofia, who now is at Arbutus Biopharma, headquartered in Burnaby, British Columbia, Canada, used this in vitro system to evaluate candidate drugs for treating HCV infections. That drug development work was done at Pharmasset, a company acquired by Gilead Sciences of Foster City, Calif.

Jeffery L. Fox is the Microbe Current Topics and Features Editor.
Different Strokes: Blending Microbiology and Art

Microbiologists collaborating with artists uncover new ways to find beauty and importance in microbes and to make them into art

Jeffrey Maloy

Although Michele Banks is not a microbiologist, she found herself speaking to a packed room of microbiologists at the 2016 ASM Microbe meeting in Boston last June. “It all started with the paint,” she says. “I was working with wet-in-wet watercolor, making abstract paintings with a kind of bleeding look and fuzzy edges. I had a show at Children’s National Medical Center in Washington, D.C., and the art coordinator told me that . . . my work looked like ‘friendly little things under a microscope.’”

The idea was intriguing to Banks, and as she began to look at microscopic images she discovered a new subject for her art: microbes. “[They] appealed to me at the visual level, but I was also really attracted to the idea that there’s this whole microscopic world that we can’t see just with our eyes, that is happening all around us and even inside us all the time.”

Nowadays, Banks is a fixture in the world of microbiology and runs an online store selling her microbe art, Artologica, which was featured prominently in scientific venues such as Scientific American, Wired, and Microbe, among others. And her message to microbiologists during the first microbial art symposium at ASM Microbe is emphatic. “They don’t build museums because art is pretty. They build them because art is important.” Like science, Banks explains, art is a way of understanding the world around us, and microbe art uses microbiology to help us make sense of our humanity.

To illustrate her point, Banks refers to an iconic photograph of an AIDS patient named David Kirby on his deathbed with his mourning family surrounding him. The black-and-white photograph, taken by a young photographer named Therese Frare during the height of the AIDS epidemic in 1990, is devastating. And although the casual observer may not look at the photograph and see the virus, to Banks this photo is a portrait of HIV. “A scientific or clinical view of what a virus can do—replicate, cause infection, eventually kill their host—is not the full view. In the artist’s view, that tiny virus just devastated a whole family.”

Similarly, Banks uses her own microbial art to connect the study of microbiology with the human experience of microbes. In one of her projects, Banks gleaned inspiration from data collected by the Home Microbiome Project, which analyzes microbes on smart phones. The result was a painting she calls “Phonome,” in which Banks depicted microbes as different, brightly colored application icons on a smart phone screen. “Art’s key role in the dissemination of microbiology is to draw people in, to intrigue them,” she says. In this case, by depicting giant colorful microbes on a screen, she hopes to make the science more salient to smartphone users. Her larger goal is that the emotion and sense of wonder experienced by those who view works like Phonome may be harnessed for science advocacy.

SUMMARY
➤ Art, a way of understanding the world around us, can use microbiology to help us make sense of our humanity.
➤ Conversely, the artful use of microorganisms can make the science of microbiology more accessible to the lay public.
➤ Bioluminescent and brilliantly colored microbial species are being used as media for making works of art.
➤ Microbially based artworks can help to interest members of the public in science, giving them fresh opportunities to reflect on scientific issues.
From the Bench to the Kiln: Microbial Pottery as an Elevator Pitch for Science

Peggy Muddles might be considered a living embodiment of Michele Banks’ ambitious vision for microbial art. “I don’t think I ever really spoke to a nonscientist about science before my first art show that featured my microbial ceramic work,” Muddles says. Unlike Banks, Muddles works by day as a laboratory scientist at the University of Toronto Centre for the Analysis of Genome Evolution and Function. But like Banks, she discovered an aesthetic appreciation for microbes early on in her career as a scientist.

“When I started my undergraduate degree in biology, I needed some kind of creative outlet—my brain doesn’t do well with a rigid schedule—but I didn’t have space for an art studio. I discovered a local pottery studio, took a few classes, and fell deeply in love with clay,” says Muddles of her beginnings in microbial art. “When I took my first microbiology class in third year, it was like I had found my spirit animal. Suddenly all I wanted to create was bacteria and viruses and microscopic structures rendered at a relatively massive scale.”

Muddles’ fascination with recreating microbes in clay form has led her on a thrilling journey of science communication and advocacy that she hadn’t entirely expected. “Art shows were my first introduction to the whole notion of science communication, and there was a steep learning curve,” she says. “I quickly learned that sharing my excitement, and the reasons for it, were the keys to engagement. I had to toss out all the jargon and Latin names, and focus on connecting with the public through things they already had some basic knowledge about.”

Muddles’ commitment to public engagement has paid off. “As I’ve become better at explaining my art, I’ve gotten a lot more nonscientist customers,” she says. “I love that it’s possible to convince the lay public to wear a virus around their neck by getting them excited about something incredibly technical like capsid self-assembly. I love that they learn enough about it to explain it to their friends. It’s incredibly gratifying to see their eyes light up when they grab the person they came with and proudly explain what they just learned through my art.”

Bioluminescent Bacteria in Research and Art

While artists like Michele Banks and Peggy Muddles use microbes as their inspiration, others are beginning to explore the use of microbes as the medium for their art. Consider Siouxsie Wiles, head of the Bioluminescent Superbugs Lab at the University of Auckland in New Zealand. Her research focuses on bioluminescent bacteria as a potential source for antibiotics and as a means for developing bioluminescence-based animal models of bacterial infection. However, a few years ago Wiles realized that bioluminescent microbes readily pique the interest of non-scientists.

When a friend asked Wiles to participate in a local art show called Art in the Dark, Wiles collaborated with an artist to prepare a three-dimensional vessel in the shape of a Hawaiian bobtail squid, which forms a symbiotic relationship with bioluminescent bacteria, *Vibrio fischeri*. She filled the squid-shaped vessel with *V. fischeri* and let Art in the Dark participants handle it.

Their response was phenomenal. “When peo-
people find out the light is being made by living microbes, their interest takes on a whole different dimension and the questions start!” Wiles says. “Are the works really made of living bacteria? How do the bacteria make light? Why do the bacteria glow? Where do the bacteria normally live?” Another upshot is this art display enabled Wiles to share her research with the public in a curiosity-driven manner. “Chatting with people about the artwork usually leads on to further questions about the research my lab does, which is using bacteria like *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Mycobacterium tuberculosis*, which we engineered to produce the same kind of light, to find new antibiotics, and to understand how nasty bacteria cause disease.”

Later, Wiles harnessed this public enthusiasm for this artwork to further her research goals. “All of the artists who I have worked with allow me to sell merchandise made from photos taken of their works to support my research lab,” she says. For instance, Wiles uses a website called RedBubble to sell t-shirts, phone cases, notebooks, and more items that are based on the bioluminescent artwork she produced with her collaborators. About 10–15% of the sales revenue from those products goes directly to support her research. “We don’t make a lot of money,” she says. “But every little bit counts.”

Wiles continues to produce a variety of living bioluminescent art pieces, including “sculptures” and a photo booth. “I love all of the works [I have produced] in different ways,” she says. “But I think my favorite project was the very first exhibition I curated, as part of Think Science Day at the Auckland Arts Festival. I brought together seven different artists and challenged them to ‘paint’ with bacteria, giving them a collection of square petri dishes so that their ‘canvas’ was about 1 meter high and 1 meter wide. Just seeing what they produced was fantastic.”

**C-MOULD: Bacteria Collected for Use in Art**

Like Wiles, Simon Park, a bacterial geneticist, recognizes the power of microbial art to engage
the public. His journey began 10 years ago, while teaching a first-year undergraduate microbiology lab course at the University of Surrey in the United Kingdom (UK). As a fun side project, Park had his students make simple drawings on agar plates using pigmented bacteria. Out of the blue, he received a call from an artist named Jo-Wonder, who told him that she wanted to try working with bacteria in her art. The two applied and received funding from the Wellcome Trust to make a version of John Millais’s painting “Ophelia” entirely from bacteria. The ambitious project required Park to curate a library of pigmented bacteria, with about 20 different types to provide different hues. The Park and Jo-Wonder collaboration was a hit, receiving plenty of press in and outside the UK.

“I was inspired by the way that the beauty of the painting drew people in, and then by peoples’ reaction as they discovered it was made entirely by bacteria and thus things that normally invoke disgust,” says Park. “This was when I became really interested in art and biology and its ability to engage people in ways that more formal scientific processes often don’t.”

Following his first experiment with microbial art, Park continued to explore the diversity of bacteria through art. “Bacteria are important for many other reasons than just producing color,” he says. These interests led him to curate the world’s largest collection of microbes, called C-MOULD, for use in the arts. In this collection, Park maintains more than 50 different types of bacteria with properties that make them intriguing for artistic purposes. “In the C-MOULD collection, I have bacteria that can generate gold (from gold salts), make nanocellulose (for textiles/paper), form electrically conductive nanowires, and detect quorum-sensing signals.” Park and others are using these microorganisms for a variety of projects, ranging from microbial paintings to a new book cover for an edition of The Origin of Species. That cover is based on pigmented bacteria drawn onto a cellulose canvas made entirely from a hyper-cellulose producing variant of Gluconoacetobacter xylinus.

Through his microbial art, Park discovered a means for engaging the public in microbiology that often is overlooked. One larger aim, he says, “is to change the perception that bacteria are primitive and simple, and to reveal their complex social lives and amazing abilities.” Acclaim for these artistic collaborations as well as for his art blog (www.exploringtheinvisible.com) helps him in furthering this goal.

Moreover, like Siouxsie Wiles, Park finds that his involvement in artistic endeavors leads him along new avenues of research. Earlier, he focused on the molecular biology of Campylobacter jejuni and other organisms involved in foodborne illness. Some of his new research directions include “pattern formation in liquid cultures of bioluminescent bacteria and the characterization of bacteria that detect and respond to physical forces in their growth environment,” he says. Although his interest in foodborne illness continues, “working with bacteria through art has given me now a much broader perspective of the microbial world.”

From Micro to Macro: Cultural Implications of Microbial Art

“Both art and science can be ways of exploring the world,” says microbiologist T. Ryan Gregory of the University of Guelph in Ontario, Canada. “For me, BioArt is a fascinating way to connect
As an evolutionary biologist, Gregory got his start in microbial art when he set out to create an exhibit honoring Darwin in 2009, the 200th anniversary of Darwin’s birth and the 150th anniversary of *The Origin of Species*. “I wanted my lab to contribute something living that would change over time,” he says. “Painting with microbes turned out to be perfect for this.”

After the exhibit, Gregory remained interested in microbial art, and began curating an online collection of many of the best examples (www.microbialart.com). Although he agrees that microbial art is an important tool for outreach, Gregory maintains that it has a deeper role in shaping the collective scientific culture.

“BioArt can be used not just as a way to get the public interested in science, but also to give them an opportunity to reflect on issues raised by science, such as our place in nature, the diversity of life (much of it unseen), our interactions with microbes (both positive and negative), and so on,” says Gregory. “BioArt provides a very useful venue for exploring issues related to ethics, the human condition, the impact of science on our lives, and the way people understand what science is and what it does and does not do. As with any high-level artistic endeavor, BioArt can elicit emotions and stimulate reflection about the current state of society. Given how prominent biology is in modern societal issues, I think that BioArt could have a very important role to play in this regard.”

To underscore his view of the cultural impact of microbial art, Gregory cites leading BioArtist Eduardo Kac, who described BioArt as the first artistic movement of the 21st century. To hear him discuss BioArt, one gets the impression that Gregory sees it as the “Wild West” of microbiology. And like generations of microbiologists before him, from Anton van Leeuwenhoek to Robert Koch, its mysteries draw him in.

“I don’t think the BioArt movement is sufficiently well developed or defined yet to draw clear boundaries of what is and isn’t ‘legitimate’ art in

**FIGURE 4**

‘Salmonella’ by Hope Sutherland in collaboration with Siouxsie Wiles. Photo by Benj Brooking.
that domain,” Gregory says. He points to the variety of artistic mediums employed by others, including Banks, Muddles, Wiles, and Park, as examples of the incredible diversity of microbial art. “BioArt continues to evolve, and having a diversity of explorations out there is, in my view, a good thing.”

Jeffrey Maloy is a graduate student at the University of California, Los Angeles.

**Artists**

Michele Banks: artologica.blogspot.com  
Peggy Muddles: thevexedmuddler.com  
Siouxsie Wiles: www.redbubble.com/people/siouxsiew  
Simon Park: www.exploringtheinvisible.com  
T. Ryan Gregory: www.microbialart.com

**ASM Agar Art**

No discussion of microbial art would be complete without a mention of ASM’s own Agar Art contest, in which submitters can express their creativity through cultures grown on agar plates. See the 2016 winners on the Microbe World site:

Approximately 70% of the Earth’s surface is covered by ocean—on average, under 3,700 m of water. At the seafloor is a blanket of unconsolidated sediment consisting of continental detritus; particulate organic matter; silica- and carbonate-rich, biologically produced hard materials; and void spaces filled with saline fluids of wide-ranging chemistries. Near the continents, especially where relief is high and physical weathering is prominent, the sediment thickness can measure more than 10 km. However, underneath the oligotrophic open ocean gyres, it can be less than 0.1 km, even on seafloor that is tens of millions of years old, and parts of the ocean floor, especially the mid-ocean ridges, young ridge flanks, and ubiquitous seamounts, are naked or covered by only a thin veneer of sediment.

Globally, there are about $3 \times 10^8$ km$^3$ of ocean sediment saturated with $8 \times 10^7$ km$^3$ of porewater that is inhabited by an estimated $3 \times 10^{29}$ microbial cells. Our understanding of these intraterrestrial microbes and their host environments, especially beyond the near-coastal regimes, remains limited and reliant on the analysis of relatively few samples. When, as in this case, data are sparse and the environment is vast, modeling efforts can facilitate our understanding of the biogeochemical drivers that govern deep life.

**Uncertainty whether Microbes Are Active, Dormant, or Dead**

In a low-energy environment where metabolic strategies are honed for long-term persistence, it can be difficult to determine if a microbe is dead or alive. An intact cell may be inactive, possibly for thousands of years or longer, even though it is still viable. Assessing the viability of cells typically relies on our ability to culture them. However, environmental microbes are notoriously difficult to culture, with recent estimates claiming that perhaps 0.1–1% can be grown in vitro.

Moreover, dormancy or an extreme form of endospore formation can be observed in some bacteria. Even in million-year-old sediments, the numbers of spores can equal that of vegetative cells, according to Tori Hoehler of NASA Ames and Bo Barker Jørgensen of Aarhus University in Denmark. They assert that, in very stable, low-energy environments such as deep-sea sediments, sporulation appears to be a strategy akin to suicide. Although endospores can survive periods of environmental stress, to flourish, such cells would need to invest considerable energy to germinate and return to vegetative activity. However, energy tends to be in very short supply in these settings.

**Archaea and Bacteria Are in Near-Equal Abundance**

Life in deep-sea sediments consists mainly of archaea and bacteria, but which domain dominates? The first long sediment cores that were...
targeted specifically for microbiology analyses were obtained by the Ocean Drilling Program (ODP) during Leg 201 to the Peru Margin in 2002. Those early excursions plus several dozen more recent ocean sediment studies to quantify the archaea and bacteria yield conflicting results, according to a review by Karen Lloyd of the University of Tennessee.

For example, taxa-specific cell counting techniques (CARD-FISH) and quantitative PCR data point to a preponderance of bacteria over archaea, whereas evidence from analyzing intact polar lipids suggests the opposite. Yet a third assessment, combining FISH, CARD-FISH, metagenomics, and qPCR data, shows that archaeal and bacterial numbers are roughly equal.

Subsequent studies showed that lipid analyses can overestimate archaea but that specific qPCR bias can underestimate them. Meanwhile, some methods accurately determine the ratios of archaea to bacteria, but vastly undercount the total number of cells. Despite these methodological uncertainties, it appears that archaea and bacteria exist in similar abundances in deep-sea sediments. However, culture-dependent and culture-independent techniques are almost exclusively designed for and tested with bacteria, not archaea. This limitation is particularly relevant where archaeal and/or bacterial dark matter—phyla that consist only of uncultured members—makes up a significant fraction of the biomass identified in sedimentary samples.

**Anaerobes Dominate Aerobes in Sediment Ecosystems**

Oxygen levels in most ocean sediments drop below detection limits within a few centimeters of the seafloor. Aerobic respiration of easily degradable organic matter is mostly responsible for this steep decline. However, microbial life in ocean sediments extends to at least 2.5 km below the seafloor, with organic-rich layers extending to such depths near the Shimokita Peninsula of Japan, according to Fumio Inagaki of the Japan Agency for Marine-Earth Science and Technology, Kai-Uwe Hinrichs of the University of Bremen in Germany, and their collaborators.

Thus, anaerobic metabolisms dominate in these sediments, especially those in which sulfate reduction is coupled to organic matter oxidation. In fact, geochemical analysis and modeling techniques demonstrate that, globally, sulfate reduction accounts for three-fourths of carbon mineralization—that is, conversion of organic carbon to carbon dioxide in these ecosystems, according to Martin Thullner of the Helmholtz Centre for Environmental Research in Leipzig, Germany, and his collaborators. Their finding is supported by the first transcriptional analysis of sub-seafloor sulfate-reducing bacteria that was conducted by William Orsi from the Ludwig-Maximilians University in Munich, Germany, and his colleagues.

Aerobic respiration follows far behind sulfate reduction, accounting for a mere 15% of organic matter that is degraded in the top 50 cm of sediments. How does this jibe with the claims of Steve D’Hondt of the University of Rhode Island (URI) that perhaps as much as 40% of the ocean floor is covered by sediments that are oxic all the way through the sediment packet, from the sediment-water interface to the underlying basement rock? One plausible answer is that this 40% is restricted to material that is found below oligotrophic, open-ocean gyres, where little sediment accumulates, little organic matter is deposited, and, consequently, limited oxygen is consumed.

In some ocean sediments, oxygen levels first decrease with depth before increasing as the underlying rocky crust is approached. This change in pattern is due to upward diffusion from oxic aqueous solutions that flow through the upper basement. In these oxic-anoxic-oxic sandwiches, aerobes dominate near the sediment-bottom water interface and perhaps again near the sediment-basement interface, but anaerobes call the shots in between.

**Modeling Helps To Describe Sedimentary Ecosystems**

Cell counts and sequencing efforts are helping to describe the numbers, viability, and variety of microorganisms in marine sediment. However, the relative inaccessibility of these environments, the difficulty of cultivating representative microorganisms, and the long timescales associated with some of their lifestyles are major impediments to obtaining a comprehensive understanding of the complex marine sediment ecosystem. Hence, we turn to modeling, using additional datasets and other approaches to connect microorganisms to their appropriate geochemical environments. Energy availability, temperature, and
metabolic reaction rates are three key factors that shape sedimentary microbial ecosystems.

All living things depend on redox reactions to obtain energy. In ocean sediments, many different minerals, aqueous solutes, and organic matter serve as the electron donors and acceptors in such reactions. Moreover, in the absence of light energy, the identities and concentrations of these ingredients, together with temperature and pressure, determine how much energy is available from redox reactions. The calculated Gibbs energies of these reactions reveal which metabolic strategies are thermodynamically possible and which environmental variables, including temperature, pressure, pH, salinity, organic matter content, and oxygen levels, control or at least influence microbial activity.

For example, in oxic sediments with ample organic matter, aerobic respiration typically yields the most energy at 100–120 kJ per mole of electrons transferred, and aerobic heterotrophs typically dominate the microbial communities. However, with increasing temperature or other environmental stressors, the energy required for cellular maintenance increases, so the energy available for growth and other cellular functions becomes a smaller and smaller fraction of the total used by organisms. An additional energetic challenge results from the low energy yields associated with most anaerobic metabolisms in deep-sea sediments, including globally dominant sulfate reduction, which has peak yields of about 20 kJ, but more commonly yields about 10 kJ per mole of electrons transferred, or less.

Energy calculations can be coupled with other modeling approaches to infer rates of microbial processes in marine sediments. For example, to determine such rates for microbes in the extremely low-energy sediment packet below the South Pacific Gyre, we used a continuum model to quantify particulate organic matter degradation rates and combined these with thermodynamic calculations and cell counts to infer microbial power usage. Based on that analysis, the resident cells could be persisting on as little as a few hundred zeptowatts (zW or 10⁻²¹ W). For comparison, sulfate reduction in deep sediments translates to about 100 zW, based on values from Hoehler and Jørgensen, while numbers from Hans Røy of Aarhus University and colleagues

**FIGURE 1**

Global sediment thickness [km]

Thickness (in km) of marine sediments. Note that the top of the scale (dark red) corresponds to ≥8 km, with the thickest sediments >18 km.
for deep sediment aerobes equate to about 5,000 zW. Meanwhile, typical maintenance power measured in the laboratory for aerobic heterotrophs is several orders of magnitude higher, about one picowatt (or 10^9 zW).

Modeling approaches can also be used to predict under what environmental conditions specific metabolic processes occur and at what rates they proceed. Sandra Arndt at Bristol University in the United Kingdom and colleagues constructed a reaction transport model to identify what, if any, biogeochemical processes are operating in sediments that were investigated as part of ODP Leg 207 on the Demerara Rise in the equatorial Atlantic. They determined that 100 million-year-old black shales, which are hundreds of meters beneath the sediment-water interface, produce methane that is then oxidized anaerobically (AOM) higher up in the sediment column by consortia of sulfate-reducing and methane-oxidizing microorganisms. Further, these AOM rates are much slower than those nearer the sediment-water interface, but in line with metabolic rates of organisms living in the deep biosphere.

To expand such metabolism modeling from site-specific to the global sub-seafloor sediment ecosystem requires large-scale quantitative assessments of particular sediment properties. However, the requisite data on global ocean sediment volume and corresponding pore water volume and temperatures are poorly known. To remedy this, we recently integrated and reevaluated seismic survey, bathymetry, and heat flow data to generate detailed global maps of sediment thickness and temperature. One such map depicts the distribution of the 3 × 10^9 km^3 of ocean sediment which, if spread out evenly across the ocean floor, would average 720 m in depth (Fig. 1). Viewed in this way, 23.5% of the ocean floor is covered by less than 100 m of sediment, yet more than 10 km of sediment have accumulated in the Bay of Bengal, the Gulf of Mexico, in Arctic regions, and elsewhere.

Another result of recent efforts to combine global datasets with modeling approaches can be seen in Fig. 2. Here, maps depict the three-dimensional distribution of temperature in marine sediments, which influences the types of microbial groups in a given region (thermophiles, mesophiles, or psychrophiles), their levels of metabolic activity, the thermodynamic tendency of reactions to happen, the rates of these reactions, and the diffusion of metabolic reactants and products. The temperature in about 1/4 of global sediment is less than 20°C (Fig. 2A), conditions most preferred by cold-loving psychrophiles. However, about 75% of global sediment is less than 80°C, a temperature range suitable for extensive biological activity, including that of mesophiles and thermophiles (Fig. 2B). Although some archaea and bacteria grow in the laboratory at temperatures higher than 100°C, even to as high as about 120°C, biotic processes in natural environments appear to be nearly inconsequential above about 80°C.

Prospects for Probing Microbial Ecosystems in Sediments and Rocks on and off Earth

In 1955, Richard Morita and Claude ZoBell of the Scripps Institute of Oceanography in San Diego reported the bottom of the open ocean biosphere to be 7.5 meters below the seafloor (mbsf). With access to far more advanced cell-counting techniques, D’Hondt of URI and colleagues more recently analyzed similar sedimentary environments below the Pacific Ocean gyres, extending this limit to at least 75 mbsf. Meanwhile, by integrating available microbial cell counts from marine sediments—those from oligotrophic ocean gyres as well as those from nutrient- and carbon-rich near-shore settings—Jens Kallmeyer of the Helmholtz Centre in Potsdam, Germany, and his colleagues determined a global total of 3 × 10^29 microbial cells in marine sediments—a figure that is now widely accepted.

What about the porous basement rocks that lie below these sediments? A modest sampling of rocky outcrops on the seafloor and cores retrieved from targeted ocean drilling into basement rock hint at another intriguing microbial habitat, one that may be even larger and is certainly even less understood than the enormous, little-understood ocean sediments discussed here.

Why limit these investigations to planet Earth? Mars, our second-nearest neighbor planet, was once warm and wet, with a large ocean likely having occupied much of its northern hemisphere about 4 billion years ago. Recent and planned missions to the Red Planet tend to focus on sedimentary features and evidence of past life, but surface oceans and, hence, the water-saturated sediments, are long gone. Perhaps not surprisingly, the oceanographic and planetary science communities are now joining forces to develop mission concepts for exploring other extraterrestrial worlds, ones with present-day...
oceans at or near the surface. These relatively near-term extraterrestrial missions include ones to Europa (a moon of Jupiter) and to Enceladus and Titan (two moons of Saturn). Nevertheless, even the most optimistic among us realizes that it will take at least several decades before extraterrestrial ocean sediments on Europa or elsewhere can be investigated directly. Until then, the micro-

**FIGURE 2**

A. Sediment thickness [m] for temperature range <20°C

B. Sediment thickness [m] for temperature range <80°C

Thickness (in m) of marine sediments that are (a) <20°C and (b) <80°C. Note that the top of the scales (dark red) correspond to ≥1,400 m and ≥6,000 m, respectively.
bial secrets that are buried in the sediments and rocks below the Arctic, Pacific, Atlantic, Indian, and Southern Oceans on Earth will have to do.

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Suggested Reading


Clinical Virology, Fourth Edition

Presents the diverse agents and diseases associated with human viral infections and provides the critical information scientists and health care professionals need to stay current.

Editors: Douglas D. Richman, University of California, San Diego; Richard J. Whitley, University of Alabama at Birmingham; Frederick G. Hayden, University of Virginia Health System

Clinical Virology covers broad topics in virology, including immune responses, vaccinology, laboratory diagnosis, and principles of antiviral therapy, as well as detailed considerations of significant organ system syndromes caused by viral infections. This book provides overviews of specific etiologic agents, including discussions of their molecular virology, epidemiology, pathogenesis, clinical manifestations, laboratory diagnosis, management, and prevention.

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Universal Influenza Vaccine: Quest in Sight?

Several efforts to develop a vaccine that might work against all or most flu virus strains fortify hopes for fulfilling this one-time “flight of fancy”

Marlene Cimons

“Over a glass of wine, we infectious diseases specialists and public health officials often have allowed ourselves these flights of fancy about how effective a universal influenza vaccine would be. We imagine how we could control or perhaps eliminate the most feared infectious disease plague on the planet. . .”

William Schaffner, professor of medicine at Vanderbilt University in Nashville, Tenn., and medical director of the National Foundation for Infectious Diseases, remembers the countless times he and other flu experts mused about the possibilities of a universal vaccine, one that would not need modifying each year. These days, however, thanks to modern molecular technology, this dream no longer appears so improbable. “Now or very soon, these may no longer be flights of fancy,” he says. “There are some very impressive scientific efforts underway to make this real.”

Several groups of scientists report significant gains toward developing an influenza vaccine that could yield lifelong protection to an individual following a single injection, or one every 5 to 10 years. Even that latter approach would be a major advance over the current approach that depends on individuals receiving annual injections of a vaccine whose components need painstaking adjustment each year. Indeed, every year public health officials scramble as they try to predict nine months in advance what the common circulating flu virus strains will be, relying on careful analysis plus hope that they are right.

Ideal Flu Vaccine Would Protect against both Seasonal Outbreaks and Pandemics

“We wouldn’t have to worry about that, and manufacturers would not have to reconstitute the vaccine on an annual basis,” Schaffner says, referring to the annual challenge of reconfiguring the flu vaccine. “Each year we have to vaccinate everybody. If we had a universal or long-lasting vaccine, each year we could go after people who hadn’t been vaccinated before. It could be a year-long, daily vaccination activity, not just focused in the fall anymore.”

The truly game-changing flu vaccine would also protect against influenza pandemics, the even bigger nightmare that public health experts face. Pandemics occur irregularly and unpredictably when a new strain of flu virus appears abruptly—one to which few or none in the population carries immunity. “It would be the single most important thing we can do in public health today,” says Michael Osterholm, professor of public health and director of Center for Infectious Disease Research and Policy at the University of Minnesota in Minneapolis, alluding to such a vaccine. “A severe pandemic. . .could kill up to 300 million people.”

Three types of seasonal influenza viruses are circulating among humans, and those strains are designated A, B, and C. Type A influenza viruses are further classified into subtypes according to the combinations of their two main surface pro-

SUMMARY

➤ Modern molecular technologies are helping researchers to overcome obstacles in the path to developing a universal influenza virus vaccine.

➤ A major near-term goal of flu vaccine researchers is to learn how to elicit a reliable immune response to many or all varieties of the hemagglutinin, or H, protein on the surface of the virus.

➤ Several research teams found ways to anchor the residual stem after removing part of the H protein—an important technical breakthrough en route to a universal flu vaccine.

➤ Other approaches seek site-specific mutations in one case, or subtype-specific versions of a flu vaccine that would prove superior to the now-standard vaccine, which requires annual reformulation to adjust its efficacy and coverage.
proteins, hemagglutinin (H) and neuraminidase (N). Among many subtypes of influenza A viruses, influenza A (H1N1) and A (H3N2) subtypes are now the major types circulating among humans. Seasonal flu is riskiest for the very young, the elderly, or the chronically ill. Worldwide, annual epidemics cause an estimated 3 to 5 million cases of serious illness and from 250,000 to 500,000 deaths, according to the World Health Organization.

Several Distinctive Research Efforts To Develop Versions of a Universal Vaccine

Such a universal and long-lasting vaccine will be capable of provoking antibody responses against conserved regions of the virus—that is, those common to a broad spectrum of influenza virus strains. Several groups of scientists are trying to do just that, but they differ in their approaches. A major near-term goal of these flu vaccine researchers is to find the means for eliciting a reliable immune response to most or all forms of the hemagglutinin, or H, protein on the surface of the virus. One major challenge is that the amino acid composition of part of this protein, its head, is highly variable, while its stem is not.

Two teams of researchers, in separate efforts, removed its head segment, but found that lopping it off caused the stem to become unstable and fall apart, making it impossible for antibodies to bind to it. However, each team found a way to anchor the stem after beheading the protein.

One approach entailed combining a set of mutations to realign the subunits of the stem at the top, enough to keep its structure for the vaccine, according to Antonietta Impagliazzo of Janssen Pharmaceutical Companies of Johnson & Johnson in Leiden, the Netherlands, Ian Wilson of the Scripps Research Institute in La Jolla, Calif., and their collaborators.

The other approach also involves introducing mutations into the viral H gene to stabilize the stem, which then is bound to a bacteria-based nanoparticle to hold it in the right position, according to Barney Graham, deputy director of the vaccine research center at the National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Md., and his collaborators from there, nearby BioQual, Inc., in Rockville, Md., and Osaka University in Japan.

“Our group’s goal, which is an intermediate goal—before we get to one vaccination for life—is to have a group-specific vaccine that covers either group 1 or group 2 of influenza A,” Graham says, referring to viral groups based on the sequence and characteristics of the viral hemagglutinin protein. (H1, H2, and H5 are examples of group 1 viral subtypes, while H3, H7, and H10 are examples of group 2.) “What we are working on is to find a way to cover all the viruses in a group. It might be possible to cover both groups of A. Even if we could have an H1 construct that would cover current and future H1s, that would be a major advance. It just wouldn’t cover pandemic H5.”

Both these constructs can protect mice against the potentially lethal H5N1 influenza strain, according to Graham. “We made a vaccine against H1 that protected against H5,” he says. “Getting protection against subtypes hasn’t been done before. So this was exciting to see a vaccine against H1 protect against H5. The goal was to have antibodies that were cross neutralizing. We got antibodies that bound to the viruses, but didn’t necessarily neutralize—but still protected. We’re not giving up the goal of having cross neutralization, because that would protect better.”

Other Strategies for Developing Universal Flu as well as Other Antiviral Vaccines

Yet another strategy for developing a universal-type vaccine against the influenza virus first applies reverse genetics to this negative-strand RNA virus, according to Peter Palese, who chairs the microbiology department at the Icahn School of Medicine at Mt. Sinai Hospital in New York, N.Y. Site-specific mutations are introduced into the genomes of these viruses, a step that proves critical for studying the structure and function relationships of viral genes and viral pathogenicity as well as in developing novel vaccines. Thus, he and his colleagues took this approach to reconstruct and study the highly virulent but extinct 1918 pandemic influenza virus.

“We are changing the head of the hemagglutinin to one which we have not experienced in terms of human infections,” Palese says. He and his collaborators then designed a vaccine aimed against “a [flu] virus we made in the lab that is an entirely new virus,” he says. “We hope that, by doing that, our immune system will remember the conserved regions—meaning the stalk and the neuraminidase—so that changes in the head won’t matter. The immune system will redirect
itself to recognize the stalk and the neuraminidase.”

Thus far, this experimental vaccine “works wonderfully in mice and it works wonderfully in ferrets and guinea pigs, but these are not humans,” Palese continues. The experimental vaccine, although ready to test in humans, awaits major financial backing—an estimated $1 billion—before a clinical trial can be launched, he says. In addition to receiving development money from GlaxoSmithKline in England, additional support is being sought from that company as well as the Bill & Melinda Gates Foundation.

Palese is confident that this kind of vaccine will work and that the reverse genetics approach could also be effective for developing vaccines against other viruses with variable regions

Recent Concerns over FluMist: Yet Another Reason for Seeking Universal Vaccine

Having access to a universal or even long-acting influenza vaccine would surely help to overcome other peculiar public health issues that arise through reliance on available flu vaccines. For example, officials at the Centers for Disease Control and Prevention (CDC) in June 2016 recommended against using the live-attenuated influenza vaccine (LAIV) during the 2016–2017 flu season, saying data from the last three years indicate that it works poorly, or not at all.

In August, however, a Canadian study challenged the findings that are the basis for that CDC recommendation, saying the LAIV, which is administered as a nasal spray, is as effective as the standard inactivated flu vaccine, which is administered by injection. The Food and Drug Administration (FDA) has not withdrawn FluMist’s license, and the CDC said that this decision applies only to the current flu season. FDA officials first approved this vaccine in 2003 for use among US adults, and later extended that approval to children aged 2 to 5 in 2007.

According to CDC officials, data from the previous flu season show that efficacy for LAIV for young people from ages 2 through 17 was only 3%—in effect, it provided little, if any, protective benefit. This conclusion is based on an analysis conducted by members of the CDC advisory committee on immunization practices (ACIP). Moreover, this version of the flu vaccine fared equally poorly during the two previous flu seasons, the ACIP said. In contrast, use of the injectable vaccine proved about 63% effective among young people in the same age group.

Meanwhile, an evaluation of a similar version of the nasally administered flu vaccine in Canada shows just the opposite—that it was effective, according to Mark Loeb at McMaster University in Hamilton, Ontario, Eleanor Pullenayegum at the Hospital for Sick Children in Toronto, Ontario, and their collaborators there and elsewhere in Canada. Their study was based on use of that vaccine among children in 52 Hutterite colonies in Alberta and Saskatchewan, Canada. Its use led to levels of protection from flu similar to that of the standard vaccine administered by inoculation. Thus, overall vaccine protection among children in the nasal spray group was 76.9% versus 72.3% for children who received the injectable flu vaccine.

However, a difference between versions of LAIV used in treating the two different groups of children might help to explain this discrepancy. The Canadian group, which conducted its study for three years beginning in 2012, used a trivalent formulation of the nasal spray vaccine, while the children in the US group were treated with a quadrivalent product, which became available in 2013.

“ACIP has no plans to revisit [this] decision regarding the use of LAIV during the 2016–2017 season at this time,” says Kristen Nordlund from CDC. “However, the decision was an interim one meant to apply only to 2016–2017, so the issue will be brought up for deliberation before the 2017–2018 influenza season. And while the quadrivalent nasal spray vaccine is still FDA-approved, CDC and other organizations do not recommend its use because of concerns about how well it works.”

“It’s a bit complicated, but the bottom line is that when FluMist went from trivalent to quadrivalent, something happened to substantially reduce its effectiveness,” says William Schaffner of Vanderbilt University School of Medicine in Nashville, Tenn. “The ‘something’ remains a scientific mystery.”

This mystery becomes a bit more confusing when one considers a recent recommendation from public health officials in the United Kingdom (UK), according to Peter Palese from Mt. Sinai Hospital in New York, N.Y. “The UK National Health Care system [declared recently] that they only will pay for LAIV, the quadrivalent version,” he says. “Go figure!”

Marlene Cimons
in their respective genomes, including HIV, hepatitis C (HCV), and rhinoviruses. Moreover, even if the flu vaccine, the first in this anticipated set, proves imperfect, it might well prove useful from a public health standpoint, he says. However, the approach will require considerable improvement before it can be applied to other viruses.

“If I reduce the amount of flu virus 10-fold, we won’t get sick, but that’s not good enough for HIV,” Palese explains. “With HIV, you have to get sterile, or neutralizing, immunity. With hepatitis C virus, a 10-fold reduction might be a viable vaccine, although it might not be enough to avoid the most deadly consequences of the virus, like liver cancer. Rhinoviruses should be similar to flu.”

In yet another strategy, one whose focus is on developing a longer-lasting flu vaccine, researchers at the University of Georgia (UG) and Sanofi Pasteur have developed an experimental vaccine against multiple strains of both seasonal and pandemic flu H1N1 using a technique called computationally optimized broadly reactive antigen, or COBRA, according to Ted Ross, director of the University of Georgia Center for Vaccines and Immunology in Athens. He and his collaborators made nine prototype synthetic compound vaccines whose compositions were based on genetic sequences from multiple influenza virus strains. The same type of COBRA programs also might prove promising in developing vaccines against HIV, dengue, and even Ebola, he notes. “I think it could work in any pathogen with a variety of diversity.”

The initial COBRA flu-targeting vaccines specifically recognize H1N1 viruses isolated within the last 100 years, but many of the experimental vaccines tested in mice produced immunity against flu strains not included in the design, according to Ross. “We’ve demonstrated that we can go back in history and make vaccines that protect against all the variants for the last 100 years,” he says. “That doesn’t mean we can do 100 years in the future, but we still can prevent a lot of disease.” The researchers hope to begin clinical trials of their candidate vaccines near the beginning of 2018.

The UG-Sanofi vaccine is not aimed for being universal against flu, but to be long-lasting while protecting recipients against a variety of flu strains, Ross says. Comparing this approach to the one that Palese and his collaborators are following, Ross invokes a baseball metaphor. “Peter’s approach is a homerun or a strikeout. We’re trying to get on base,” he says.

The UG-Sanofi vaccine is subtype specific, “the next layer down,” from a type-specific product, such as Palese’s, Ross continues. “If we could go 5 or 10 years or even longer, it means you won’t have to change it every season. But you can continuously do surveillance and make adjustments. We don’t know how long it will be. It might be 5 years. It might be 20.”

In yet another effort, researchers at the Dana-Farber Cancer Institute in Boston, Mass., led by Wayne A. Marasco, a cancer immunologist and virologist, report finding a type of antibody that can rapidly adapt to and neutralize a wide array of influenza virus strains—including some that have not yet been encountered. The antibody protein, called 3I14 mAb, is a “broadly neutralizing antibody,” that can identify and disable a diverse group of flu strains, according to Marasco and his collaborators. More specifically, it can neutralize the two main types of influenza A virus, group 1 and 2, and protects mice against otherwise lethal doses of flu virus.

**Perspective**

The prospect of a universal flu vaccine, or even a long-lasting one, makes public health experts almost giddy. “Influenza is at the very top of the list of pathogens feared by public health specialists because it has the capacity to create pandemics that run around the world,” Schaffner says. “It staggered the mind how much illness and mortality it creates. If we had an effective universal vaccine, it would take a huge dent out of health care costs, disruption of work, school attendance and social activities. Even if you had to be revaccinated every 5 or 10 years, it could still change the entire way we prevent influenza.”

Marlene Cimons lives and writes in Bethesda, Md.

**Suggested Reading**


Merck Research Laboratories Designated as “Milestones in Microbiology” Site

On October 17, 2016, Merck Research Laboratories (MRL) was officially designated as a Milestones in Microbiology site by ASM for contributions made by its Rahway, N.J., and West Point, Pa., facilities to anti-infectives and vaccines, respectively. This was the first time an industrial site received Milestones recognition. The Milestones in Microbiology program recognizes institutions and scientists that have made significant contributions toward advancing the science of microbiology.

Rahway, N.J. Site. Since the opening of MRL’s Rahway facility in 1903, Merck scientists have conducted pioneering work in the development of a number of antimicrobial agents including penicillin, streptomycin, imipenem/cilastatin, ivermectin and caspofungin. Merck researchers are credited with advancing a method of deep tank fermentation, which increased yields substantially and paved the way for the mass production of penicillin. In addition, Merck leaders worked with Nobel Prize winner Selman Waksman (Rutgers University, New Jersey) to secure one of the earliest formal collaborations between a business and a university, which ultimately led to the demonstration that streptomycin was effective for the treatment of tuberculosis.

Merck researchers established a natural product screening program that enabled the development of several new antibiotic medicines by culturing and screening organisms sampled from sites all over the world. Notably, the discovery of *Streptomyces cattleya* and the subsequent isolation of thienamycin from it formed the basis for the first clinically used carbapenem antibiotic, which, at the time, was the most complex total chemical synthesis that the industry had known.

Further, Merck researchers developed ivermectin for the treatment of onchocerciasis, also known as river blindness. The development of ivermectin coupled with Merck’s commitment to donate it worldwide has led to the elimination of river blindness in several countries. For his role in this research, long time Rahway-based Merck scientist William Campbell shared the 2015 Nobel Prize in Physiology or Medicine.

West Point, Pa. Site. MRL’s facility in West Point has been the site of multiple breakthroughs in vaccine research and development since its opening in 1952. In 1956, Maurice R. Hilleman became the facility’s director of virus and cell biology research. During his tenure, Hilleman and his team developed many life-saving vaccines, including those to prevent *Haemophilus influenzae* infection, hepatitis A, hepatitis B, measles, meningitis, pneumonia and rubella.

The Commemoration Ceremony. To commemorate the Milestones designation, Merck hosted a ceremony featuring remarks from Roger M. Perlmutter, M.D., Ph.D., President, MRL, Daria Hazuda, Ph.D., Vice President, Infectious Diseases Discovery, MRL and Douglas Eveleigh, Ph.D., Chair of the ASM Milestones in Microbiology Committee. MRL alumni Arnold Demain, Ph.D., Ed Grabowski, Ph.D., Dennis Schmatz, Ph.D., and Mervyn Turner, Ph.D., also took the

Roger M. Perlmutter, President, Merck Research Laboratories, and Susan E. Sharp, President, American Society for Microbiology (photo courtesy of Merck Creative Studios).
stage to share their personal stories from their tenures at the company.

ASM President Susan E. Sharp, Ph.D., presented the commemorative Milestones plaques to Roger M. Perlmutter. Sharp remarked, “Merck has met and certainly has unequivocally exceeded the criteria required for recognition as a Milestone in Microbiology. And we’re especially pleased to recognize Merck as our first industrial site.”

The event was attended by Merck leadership and employees, as well as ASM representatives. Following the ceremony, Merck held its 125th anniversary celebration in Rahway, which began with remarks from Kenneth C. Frazier, Chairman of the Board and Chief Executive Officer, Merck. Attendees then viewed the company’s traveling exhibition titled, “Celebrating Our Legacy.”

The Milestones in Microbiology Program. The Milestones in Microbiology program, administered by the Center for the History of Microbiology/ASM Archives (CHOMA), promotes greater awareness and appreciation of microbiology and inspires interest in our microbiological heritage. By placing plaques at Milestones sites, ASM aims to increase professional and public recognition of the significance of the science of microbiology. MRL is the 14th recognized Milestones site. For more information on the MRL designation, for a list of previously designated Milestones in Microbiology sites, and to learn how to nominate a future Milestones site, visit www.asm.org/milestones-in-microbiology.

2016 Career Development Grants for Postdoctoral Women Recipients

The ASM Membership Board is pleased to announce the recipients of the 2016 Career Development Grants for Postdoctoral Women:

Cheryl P. Andam, Harvard T. H. Chan School of Public Health (William P. Hanage’s Laboratory)

Elizabeth N. Bess, University of California, San Francisco (Peter Turnbaugh’s Laboratory)

Tera Levin, Fred Hutchinson Cancer Research Center (Harmit Malik’s Laboratory)

Laura Mike, University of Michigan (Harry Mobley’s and David Sherman’s Laboratories)

Mary M. Weber, NIH/NIAID Rocky Mountain Laboratories (Ted Hackstadt’s Laboratory)

Cheryl P. Andam, after earning a Ph.D. at the University of Connecticut and doing a postdoctoral fellowship at Cornell University, moved into a postdoctoral position at Harvard T. H. Chan School of Public Health in the laboratory of William P. Hanage, where she researches the population structure and evolution of Streptococcus pneumoniae and examines how clinical interventions such as vaccination have influenced its population structure, dynamics and genome evolution. Through sequencing and analysis of 900 pneumococcal genomes, she has demonstrated that changes in their population structure are driven mainly by both the expansion of variants existing at low frequencies prior to vaccine introduction and highly variable rates and patterns of recombination across the population. The process of serotype replacement allows non-vaccine serotypes to occupy the ecological niche left behind by those eliminated by the vaccine, consequently undermining the benefits of the vaccine. Andam used the CDGPW award to attend the 10th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD-10) in Glasgow, Scotland.

Elizabeth N. Bess earned a Ph.D. in Organic Chemistry from the University of Utah, and is now a postdoctoral fellow in Peter Turnbaugh’s laboratory at the University of California, where she employs an interdisciplinary approach to study enterolignans, microbial metabolites which are thought to protect against breast cancer. The precursors to these compounds, lignans, are found in many commonly consumed foods, but their activation requires gut microbes, suggesting that differences between individuals’ gut microbiomes may shape the lignans’ beneficial effects. Bess’s research focuses on identifying microbial genes responsible for lignin metabolism, determining if other components of the diet alter their function, and testing the ability of the microbiome to prevent breast cancer in animal models. Bess will use the CDGPW award to attend the Microbiome in Health and Disease Keystone Symposium in Keystone, Colo.
Tera Levin, a postdoctoral fellow in Harmit Malik’s laboratory at Fred Hutchinson Cancer Research Center, earned a Ph.D. in Molecular and Cell Biology from the University of California, Berkeley. Currently, she studies the biology of Legionella bacteria within their natural hosts, environmental amoebae, and examines what genetic changes occur when Legionella evolves between symbiotic and pathogenic states within amoebae, and if the symbiotic Legionella strains serve as a genetic reservoir of host-adaptation genes that can then be transferred to pathogens. She explores how Legionella species have acquired their enormous repertoires of eukaryote-manipulating effectors, as well as the evolutionary steps that have shaped this class of pathogens. Levin plans to use the award to visit the laboratory of Howard Shuman (University of Chicago, Ill.), a leading expert in the field of Legionella biology.

Laura Mike earned a Bachelor’s degree in chemistry from Duke University, followed by a Ph.D. in Microbiology from Vanderbilt University. She is currently a postdoctoral fellow at the University of Michigan in Harry Mobley’s and David Sherman’s laboratories, pursuing research that bridges bacterial pathogenesis and natural product chemistry. Her work includes the development of a novel vaccine strategy that protects against urinary tract infections (UTI) caused by uropathogenic Escherichia coli (UPEC), accomplished by attaching iron-chelating compounds called siderophores to immunogenic carrier proteins thereby eliciting a B cell-mediated immune response that protects against UTI. Complementary to the vaccine project, she conducted a high-throughput screen that identified several Streptomyces species that secrete natural products which subvert UPEC growth in low iron, and she has successfully isolated a novel antimicrobial compound (nicoyamycin) that inhibits UPEC iron acquisition. Mike used the CDGPW award to attend the American Chemical Society’s shortcourse on 1-D and 2-D NMR Spectroscopy in Philadelphia, Pa.

Mary M. Weber, a postdoctoral fellow in Ted Hackstadt’s laboratory at NIH/NIAID Rocky Mountain Laboratories, earned a Ph.D. in Biomedical Sciences from Texas A&M Health Science Center. Her research uses biochemical and molecular techniques to elucidate effector mechanisms for virulence factors. Specifically, she studies mechanisms by which Chlamydia trachomatis inclusion membrane proteins (Incs) modulate the host response and facilitate chlamydial development. Employing a variety of genetic approaches to express 50 predicted Incs, she demonstrated that ten previously undefined Incs localize to the C. trachomatis inclusion membrane. Using site-specific mutagenesis and a complementation system that she implemented, she has identified several Incs that are required to subvert the host response and promote normal inclusion development. (Due to NIH/NIAID regulations governing the acceptance of cash awards, Weber was named an awardee, but no cash award was or will be provided.)

Call for nominations. The 2017 Career Development Grants for Postdoctoral Women program is currently accepting nominations. Up to five grants ($1,500 each) are given annually to postdoctoral women with outstanding scientific accomplishments and potential for additional significant research or study in the area of microbiology. For more information on the program and the application process, go to http://www.asm.org/index.php/career-development-grant-postdoctoral-women on the ASM website or contact adempsey@asmusa.org.

Inspiring Bench Scientist Careers at ASM Microbe 2016

Ten young clinical laboratory scientists were recognized for their enthusiasm and commitment to the clinical microbiology profession and given a chance to gain valuable insight into career advancement. The recipients were awarded professional development grants to help facilitate their attendance at ASM Microbe 2016. Funding was generously provided by Accelerate Diagnostics, Alere North America, Applied Maths, Beckman Coulter, BioFire Diagnostics, Bruker Daltonics, Cepheid, GenMark Diagnostics, Hardy Diagnostics, Medical Chemical Corporation, Nano-
The American Society for Microbiology Distinguished Lecturer Committee Is Pleased to Announce Its 2016–2017 Roster:

- **Niaz Banaei** (Stanford University, Palo Alto, Calif.)
- **Briana M. Burton** (University of Wisconsin–Madison)
- **Kelly S. Doran** (San Diego State University, Calif.)
- **Ferric Fang** (University of Washington School of Medicine, Seattle)
- **Ramon Gonzalez** (Rice University, Houston, Tex.)
- **D. Jay Grimes** (University of Southern Mississippi, Ocean Springs)
- **Michael Ibba** (Ohio State University, Columbus)
- **Karl Klose** (University of Texas at San Antonio)
- **Pamela A. Marshall** (Arizona State University, Glendale)
- **Nancy S. Miller** (Boston Medical Center; Boston University School of Medicine, Mass.)
- **Melanie R. Mormile** (Missouri University of Science and Technology, Rolla)
- **Steven C. Ricke** (University of Arkansas, Fayetteville)
- **David H. Sherman** (University of Michigan, Ann Arbor)
- **Tara C. Smith** (Kent State University, Ohio)
- **Christine White-Ziegler** (Smith College, Northampton, Mass.)
- **Henry Neal Williams** (Florida A&M University, Tallahassee)
- **Daniel J. Wozniak** (Ohio State University, Columbus)
- **Vincent B. Young** (University of Michigan Medical School, Ann Arbor)

A list of topic areas covered by each individual Lecturer can be found on the ASM website at http://www.asm.org/distinguished-lecturer. For a list of upcoming ASM Branch meetings, go to www.asm.org/branches.

The American Society for Microbiology Distinguished Lecturer (ASMDL) Program annually selects a scientifically diverse group of lecturers who are available to speak at local ASM Branch meetings throughout the country. Lecturers are chosen through a competitive nomination process, and only the most distinguished lecturers and researchers are chosen to participate in the program.

Since its founding over 50 years ago, the ASMDL program has been a mainstay of Branch programming, and has enhanced the scientific content available at the local level. The program reaches thousands of microbiologists, including students, every year and extends the reach and impact of ASM throughout the United States.

sphere, Quest Diagnostics, Quidel, TECHLAB, TIB MOLBIOL, and ASM.

The awardees for 2016 are:

- **Maria Bui**, Children’s Hospital Los Angeles, Calif.
- **Raymond Chow**, Kaiser Permanente Regional Laboratory, Berkeley, Calif.
- **Tyrell Cox**, Banner University Medical Center, Tucson, Ariz.
- **Lara Crossthwaite**, University of California San Diego Health System, Calif.
- **Lisa Hernandez**, Children’s Medical Center, Dallas, Tex.
- **Leeann Korprapun**, University of California Irvine Medical Center, Arcadia, Calif.
- **Alex Lawler**, Durham VA Medical Center, N.C.
- **Charlotte Lea**, Regional Medical Laboratory of St. John Health System, Tulsa, Okla.
- **Allison Tsan**, Huntington Memorial Hospital, San Gabriel, Calif.
Some of the awardees shared their impressions of the award. Rachel Hissong commented, “Attending my first ASM conference through the New Tech Professional Grant Program was an incredible and inspiring experience. The information gained through attending sessions and perusing the exhibit hall only skimmed the surface of what I walked away with. I believe that the heart of my experience was in the opportunity to network with the fellow grant recipients and mentors. The chance to talk with fellow micro techs and listen to the mentors’ stories of their progress in the field left me feeling very optimistic about my future in microbiology. Attending this conference made me realize that ASM is truly for people like me, and I cannot wait to get more involved.”

Raymond Chow: “I am truly grateful to be given the opportunity to attend ASM Microbe 2016 through this grant. I gained a lot of insight from fellow mentees and mentors about local ASM branch meetings, other laboratories’ operations, and online resources.”

Charlotte Lea: “I have never been more excited for my profession. Attending ASM Microbe 2016 was an invaluable experience. Not only did I get to see vendors showing the latest technology and attend lectures about the latest microbiology research, I got to meet other clinical microbiologists like myself at different stages in their careers. The world of microbiology is incredibly large and diverse, something that’s easy to forget, working day after day on the bench. I am incredibly grateful to ASM for awarding me a professional development grant. I now have better ideas on where I would like to take my career. And another highlight? I was able to bring Ebola back to my lab—as a stuffed animal.”

Alex Lawler: “This grant allowed me to learn far more than I expected to learn about the field of microbiology—beyond the scope of my current position. I thoroughly enjoyed meeting others at various facets of the profession and hear their journeys to their present line of work.”

Lara Crosthwaite: “This opportunity to attend ASM Microbe through the professional development grant couldn’t have come at a better time for me. I learned more than I anticipated about where I can go with my career and I met some wonderful people that were happy to share their thoughts and experiences. I felt encouraged to take the steps I had been hesitant to pursue in order to advance my career.”

Established by the Clinical Microbiology Mentoring Committee (CMMC), the ASM 2016 New Tech Professional Development Grant Program provides an opportunity for the awardees to interact with pre-assigned mentors, attend symposia, and visit poster sessions. Awardees also get the chance to network with fellow bench scientists and mentors, peruse industry-sponsored exhibits featuring the latest technological advances, and learn more about the profession of microbiology.

To be eligible for the grant, applicants must be ASM members, have less than five years of clinical laboratory experience, are non-doctoral bench-level clinical microbiologists, never attended an ASM General Meeting, and not presenting a poster or talk at ASM Microbe 2017. Information on the 2017 application process will be available in January 2017. Visit the Clinical Microbiology Portal, http://clinmicro.asm.org/index.php/explore-the-profession, for specifics.
ASM Public Affairs

ASM President Attends UN Meeting on Combating Antimicrobial Resistance

On September 21, ASM President Susan Sharp attended the United Nations General Assembly High Level meeting on antimicrobial resistance in New York. This was only the fourth time in the history of the UN that a health topic was discussed at the General Assembly (HIV, noncommunicable diseases, and Ebola were the others). Prior to the meeting, the ASM sent a letter to Samantha J. Power, the US Ambassador to the UN, urging that UN Member States unite to increase attention to the AMR challenge globally. The UN General Assembly reaffirmed its commitment to develop national action plans on AMR based on the WHO Global Action Plan on AMR (http://www.wpro.who.int/entity/drug_resistance/resources/global_action_plan_eng.pdf). The UN issued the following resolution (http://www.un.org/pga/70/wp-content/uploads/sites/10/2015/08/Antimicrobial-resistance-informal-consultations-8-September-2016.pdf) at the meeting on September 21.

The UN also released a report in conjunction with the resolution, “The United Nations Secretary-General’s High-Level Panel on Access to Medicines Report,” which is available online at http://www.unsgaccessmeds.org/final-report/. ASM continues its involvement in activities and programs to combat antimicrobial resistance. To see the history of ASM’s antimicrobial policy work, go to http://www.asm.org/index.php/issues-we-follow/98-policy/issues/2637-antimicrobial-resistance.

Congress Passes Continuing Resolution and Funds Zika Response

On September 28, the House passed H.R. 5325 a 10-week continuing resolution (CR) that funds the federal government through December 9, 2016, at a rate of operation that is 0.496% below the FY 2016 level. H.R. 5325 or the Continuing Appropriations and Military Construction, Veterans Affairs, and Related Agencies Appropriations Act, 2017, and Zika Response and Preparedness Act, funds the Department of Veterans Affairs and related Agencies through the end of FY 2017. The remaining federal government programs are funded at FY 2016 levels, minus the 0.5% across-the-board cut to remain within the sequestration caps. The bill also includes $1.1 billion in emergency supplemental funding to combat the Zika virus. Specific funding programs include:

- The National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID) will receive $152 million for “research on the virology, natural history, and pathogenesis of the Zika virus infection and preclinical and clinical development of vaccines and other medical countermeasures for the Zika virus and other vector-borne diseases, domestically and internationally.”
- The Public Health and Social Services Emergency Fund (PHSSEF) will receive $387 million to “prevent, prepare for, and respond to Zika virus, health conditions related to such virus, and other vector-borne diseases. ..develop necessary countermeasures and vaccines, including the development and purchase of vaccines, therapeutics, diagnostics, necessary medical supplies. . .”
- The Centers for Disease Control and Prevention (CDC) will receive $394 million for CDC-Wide Activities and Program Support “to prevent, prepare for, and respond to Zika virus, health conditions related to such virus, and other vector-borne diseases.” Of the $394 million, $44 million will be returned to the Public Health Emergency Preparedness cooperative agreement program which has funded Zika outbreak activities so far.

ASM has been working to fund the federal response to the Zika virus outbreak by urging Congressional passage of a supplemental funding bill at the requested level of $1.9 billion. Since February, ASM has communicated with Congress, met with appropriators and staff, collaborated with other public health and scientific organizations, and engaged the ASM membership through a legislative action alert campaign in August. The ASM also held a one-day conference on June 1 at ASM headquarters in Washington, D.C., to stimulate basic research and bring together Zika researchers and scientists. For more information on the ASM effort to combat Zika, go to http://www.asm.org/index.php/issues-we-follow/137-policy/documents/statements-and-testimony/94499-zika-8-17-16.

Congress is expected to return after the November 8 election and will have until December 9 to complete the remaining eleven FY 2017 appropriations bills. For more information about ASM’s Public Policy efforts go to: http://www.asm.org/index.php/public-policy.

ASM Authors Document on mcr-1 Colistin Resistance

The PSAB Committee on Laboratory Practices in Microbiology has authored a white paper on the emergence of mcr-1 plasmid-mediated colistin resistance in gram-negative pathogens. The document includes a discussion of polymyxin antibiotics, mcr-1 and mcr-2, epidemiology, and infection control. Particularly of interest to clinical microbiologists is the section on laboratory testing which discusses pitfalls to be expected when trying to perform accurate minimum inhibitory concentration (MICs). To read the document, go to http://www.asm.org/index.php/public-policy/93-policy/94613-colistinres-10-16.

ASM Participates in FDA Public Workshop on Antimicrobial Issues

PSAB Laboratory Practices Committee Chair Melissa Miller attended the Sep-
Laura E. Lasiter, Ph. D., ASM’s 2016-2017 Congressional Science Fellow has found a placement in the office of Senator Al Franken (D-MN). Lasiter will be working as one of three Health Policy Fellows in the Office and will work on issues like the Affordable Care Act, Centers for Medicare and Medicaid, Children’s Health Insurance Program (CHIP) reauthorization, and FDA user fees that expire in 2017. She will primarily focus on the One Health Initiative and the renewal of the Pandemic and All-Hazards Preparedness Act (PAHPA) which expires in 2018. The American Society for Microbiology has supported Congressional Fellows since 1977. The ASM Congressional Science Fellowship Selection Committee selects a postdoctoral to mid-career microbiologist to spend one year on the staff of an individual member of congress, congressional committee, or with some other appropriate organizational unit of Congress. Prospective Fellows must be citizens of the United States, members of ASM for at least one year at the time they apply and must have completed their Ph.D. by the time the fellowship begins in September. The Congressional Science Fellowship is supported in part by the Frobisher Fund, a bequest made to ASM by Martin Frobisher. Contact the Office of Public Affairs at publicaffairs@asmusa.org for more information on the ASM fellowship or go to the ASM web page for a program description: http://www.asm.org/index.php/congressional-science-fellowship. The deadline for applications for the 2017–2018 fellowship is February 17, 2017.

ASM Meetings and Conferences

2017 Meetings

2017 ASM Biothreats: Research, Response, and Policy. Introducing an added focus on emergency response, the former ASM Biodefense and Emerging Disease Research Meeting—newly named 2017 ASM Biothreats: Research, Response, and Policy meeting (February 6–8, 2017, Washington, D.C.)—will discuss a wide-range of biological threats and emerging infectious diseases to stimulate knowledge-sharing among stakeholders in academia, industry, and government. To learn more and register, visit www.asm.org/biothreats.

Clinical Virology Symposium. Now in its 33rd year, the ASM Clinical Virology Symposium (May 7–10, 2017, Savannah, Ga.) will provide an engaging forum to discuss key topics on viral infections. Abstract submission closes March 1, 2017. Get yours in today to share your virology research at this leading event. For more information, visit www.asm.org/cvs.

ASM Microbe 2017. Exploring the complete spectrum of microbiology and showcasing the best in the microbial sciences, ASM Microbe 2017 (June 1–5, 2017, New Orleans, La.) is the premier event in the field that you can’t afford to miss. With nearly 50% more oral abstract presentation slots, this is your opportunity to get cutting-edge research findings and recent discoveries front and center among your peers from around the world. Abstract submission closes on January 9, 2017. Submit your abstract today at www.asm.org/microbe.

Upcoming ASM Conferences. ASM conferences address the needs of the diverse scientific interests of microbiologists by providing a forum for international groups of scientists, ranging from 100 to 400 participants, to discuss their specific area of concentration. Mark your calendar for these upcoming ASM conferences. For more information, visit www.asm.org/conferences.


ASM Conference on Innovative Microbial Ecology for Mitigation of Antibiotic Resistance and Bacterial Diseases (March 22–25, 2017, Crystal City, Va.)


ASM–ASV Conference on Interplay of Viral and Bacterial Pathogens—"Living as a Threesome in the Gut: Viruses, Bacteria and the Host" (May 1–4, 2017, Bethesda, Md.)

2nd ASM Conference on Rapid Applied Microbial Next-Generation Sequencing and Bioinformatic Pipelines (October 8–11, 2017, Washington, D.C.)

6th ASM Conference on Cell-Cell Communication in Bacteria (October 16–19, 2017, Athens, Ga.)


4th ASM Conference on Viral Manipulation of Nuclear Processes (December 3–6, 2017, Charleston, S.C.)
Education Board

Fellowship Opportunities for Undergraduates, Graduate Students, and Postdocs

To promote access, excellence, professional development, and advancement in the microbial sciences, the ASM Education Board offers a variety of fellowship programs supporting research by trainees. In 2017, fellowships are expected to be available for undergraduates, graduate students, and postdocs. Learn more at http://bit.ly/asmfellows hips17nl.

Save the Date! ASMCUE 2017 Heads to Denver, Colorado Area

We are excited to share the new dates and location for the ASM Conference for Undergraduate Educators (ASMCUE). Next year’s Conference will take place on July 27–30, 2017 at the Sheraton Denver Downtown Hotel in Denver Colorado. ASMCUE gathers over 350 microbiology and biology educators for an interactive four-day conference. Educators come from colleges, universities, and international institutions to learn and share the latest information in the biological sciences and education research. The conference program includes plenary, concurrent, poster, and exhibit sessions. Participants engage in formal and informal small group discussions between colleagues, all focused on the same goal: to improve teaching and learning in the biological sciences.

The deadline to submit abstracts for poster presentation is February 15, 2017. The poster abstracts are organized by both content and pedagogy. The content themes are evolution, cell structure and function, metabolic pathways, information flow and genetics, microbial systems, and impact of microorganisms. For the purposes of ASMCUE, a seventh concept, advancing STEM education and research has been added to the abstract in order to identify authors working in this broader-scoped area. We look forward to another successful Conference next summer in Denver, Colorado. Keep checking for updates to the preliminary program and important deadlines at www.asmcue.org.

JMBE: New Journal Issue Available—Microbiology as a Nursing Curriculum Staple

The editors of ASM’s Journal of Microbiology & Biology Education (JMBE)—the premier journal for microbiology and biology education research—are pleased to announce the publication of the December 2016 issue (volume 17, issue 3) of the journal. It will feature 35 articles available via 9 sections.

The issue is introduced by an editorial from JMBE’s editor-in-chief, Dr. Samantha L. Elliott of St. Mary’s College of Maryland. The editorial seeks support from the community to keep microbiology as a mandatory component of the nursing curriculum. Some other highlights of the new issue include: late-breaking abstracts from the 2016 ASM Conference for Undergraduate Educators, research on student misconceptions, a guide for assessing a CURE, and a vetted statistics module for the classroom. There are over ten innovative, easily-implemented classroom and laboratory activities on topics such as quantitative modeling and using Twitter as a teaching tool. The December issue will also include a discussion of ASM’s Science Teaching Fellows online course structure and its impact on participants.

JMBE content, including the newly published December issue, is available at ASMscience.org, the one-stop shop for ASM books, journals, and reports. Available in PubMed Central, JMBE features peer-reviewed, practical tips for teaching, education research and perspectives, innovations in science, and reviews. The journal is a freely available, open-access publication, and there are no page charges for authors. Manuscript submissions are reviewed on a rolling basis, and editors provide hands-on guidance throughout the review process. To view the journal’s media kit, author guidelines, and sign up for eTOC alerts, visit http://www.asmscience.org/jmbe.

Branches: ASM Activity at the Local Level

Eastern Pennsylvania Branch ASM: Special Meeting To Honor Long-Time Members

The 749th Monthly Meeting of the Eastern Pennsylvania Branch of ASM, held on September 19, 2016, at Thomas Jefferson University, was a special meeting to honor Branch Emeritus members, as well as current Branch members who have belonged to National ASM for 40 years or more. The Branch currently has 23 members in the “40-year plus” category, including two 65-year members, James Smith and Victor Iacocca, both of whom attended the meeting.

The meeting, “Branch Genomics: Mixing the Old and New Branch Generations,” focused on how microbiology and the Branch have evolved over the last 60 years, and included some thoughts on future directions from the current Student Chapter (future Branch leaders!). Presentations included:


“Changes in Microbiology at Temple University—Then & Now” (Toby K. Eisenstein, Lewis Katz School of Medicine, Temple University)

“Clinical Laboratories Microbiology—Then & Now” (Olarae Giger, Main Line Health Laboratories)

“Microbiology Education—Then & Now” (Barbara McHale, Office of the President, Gwynedd Mercy University)

“The Branch Student Chapter—The Future” (Simon Knight, Branch President; Perelman School of Medicine at
the University of Pennsylvania; and Neil Sullivan, Student Chapter President; Drexel University)

Meeting attendees included students, postdoctoral fellows, faculty, and scientists working in laboratories in industry, government and medical schools—a diverse range of old and new members. Photos and a “mix-the-generations” dessert session was held after the formal meeting. Reflecting on her involvement in the Eastern Pennsylvania Branch, Eisenstein commented, “The Branch has served a central role in communicating the depth and breadth of microbiology and connecting microbiologists working in different spheres of the science; the friends and colleagues I have met here over the years have had a major impact on my life and career.”

Established in 1920, the Eastern Pennsylvania Branch of the ASM serves professional microbiologists across Eastern Pennsylvania, Delaware, and South/Central New Jersey through several annual events as well as regular monthly meetings. The Branch also sponsors an active regional Student Chapter. For information on upcoming Branch activities, see https://www.epaasm.org/.

James A. Poupard

Obituaries

Fred Neidhardt

A towering figure in microbiology, our friend Fred Neidhardt died on October 7, 2016 at his retirement home, the Academy Village near Tucson, Ariz., at the age of 85. He made fundamental and abiding contributions to research, teaching, academic administration, and social issues. In each, he left deep-rooted marks that made him greatly respected and highly beloved.

His academic life began at Kenyon College, which he attended on a scholarship he received as a not-particularly advantaged kid from Philadelphia. He had a great love and appreciation for his alma mater, which conferred on him an honorary doctorate (one of three, the other two from Purdue and Umeå, Sweden). He got his Ph.D. from Harvard with Boris Magasanik and did postdoctoral work in Paris with Jacques Monod. He held faculty positions at Harvard, Purdue, and Michigan, where he eventually served as chair of Microbiology and Vice President for Research (when in this post, one of us asked him what his budget was. He replied: “One billion dollars.” “And your “disposable budget”? “Ten thousand dollars!”). Fred served as president of the ASM and the Waksman Foundation for Microbiology, and on numerous government and private advisory and editorial boards. His honors included fellowship in the American Academy of Arts and Sciences, the American Academy of Microbiology, and many others in this country and abroad.

Fred took the lead in the development of bacterial growth physiology. He explained: “Intrigued by growth as the unique property of living systems, I was captivated upon first observing, early on in graduate school, the speed, efficiency, and adaptability of the growth of bacterial cells such as Escherichia coli. I resolved to learn all I could about how cells grow, and to do so by exploring the physiology of bacteria.” Accordingly, he made centrally important, often innovative, contributions to such phenomena as catabolite repression, the stringent response, and the patterns of response to stress. He pioneered in the development of critical methodologies. He was among the first to use conditional mutants to study essential processes in bacteria. He developed proteomics and is considered the father of this field. He designed a synthetic medium (MOPS) that allowed the study physiological properties of bacteria in a reproducible way.

In an attempt to centralize the knowledge of E. coli as the premier model system in Biology, he initiated and became the editor-in-chief of what became known as the “E. coli bible,” a two-volume book called “Escherichia coli and Salmonella.” An example of his precise and numbers-based approach is his much-cited table of the composition of E. coli found in this tome.

Based in part on his Quaker beliefs, Fred was actively engaged in issues ranging from equality for women (for which he received the first ASM’s Alice Evans award), to the status of minorities in academia and elsewhere, to justice in the penal system, to treatment of immigrants.

The two of us wrote or co-edited five books with him (out of a total of eight to his name), so we knew each other well enough to be able at times to finish each other’s sentences. We knew Fred from our early days in science. He spent a partial sabbatical in one our labs (JI). In the late 1950’s, one of us (MS) was a direct competitor of his on two occasions once he published first, once MS did. Out of this came a deep

and abiding friendship that lasted these many years. We will miss him. His wisdom, his insights, and above, all his kindness and concern for his fellow humans. He was a mensch.

Fred is survived by three children, Rick, Jane, Marc, and three grandchildren, Mia, Caitlin, and Maggie. In lieu of flowers, donations in Fred’s name can be made to the American Friends Service Committee (https://www.afsc.org) or the Leelanau Conservancy (http://leelanauconservancy.org).

Elio Schaechter
John Ingraham

Dwayne Cecil Savage

Dwayne Cecil Savage, 81, of Eagle, Idaho, passed away Tuesday, May 17, 2016 at a Boise hospital from heart and kidney failure, following surgeries for spinal stenosis.

As an eminent intestinal microbiologist, he dedicated his career to physiological and molecular-based systematic studies of the commensal microbiota, and was considered one of the most prominent and instrumental global experts in the field. As a scholar, he was known worldwide and worked with colleagues in many countries furthering their research efforts. Dwayne was the recipient of many awards from British, Japanese, Korean, German, and French microbiological societies.

It is difficult and unfair to reduce a career to soundbites. However in this day and microbiological age, it is often stated with authority that we are outnumbered tenfold by the microbial inhabitants of our respective beings—a statement attributed to Dwayne nearly 40 years ago. He was truly a pioneer and in the company of only a small number of experts giving awareness, rational investigation, and critical scientific study to gastrointestinal tract microbial ecology in an era dominated by microbial pathogens. Such principles that drove his interests and career have undoubtedly provided a landscape and framework for the current scientific renaissance in the microbiome. It is a testament to his approach and contributions to this field in a culture-dependent era that continue to stand the test of time, to be confirmed and further expanded with new culture-independent technological innovations. He embraced new technology but only as a means of furthering investigatory lines of research, instilling in his graduate students a true sense of philosophy rather than mastering of biotechnology per se. Dwayne’s love for academics, particularly research and working with graduate students, never diminished.

Dwayne was born August 8, 1934, in Arco, Idaho, the oldest of three sons and one daughter of Cecil and Pearl Maynard Savage. He attended schools in Aberdeen, Idaho, graduating as Valedictorian from Aberdeen High School in 1952. Although Dwayne was selected to attend the U.S. Naval Academy in Annapolis, Md., he elected to attend the Naval ROTC Program at the University of Idaho. While there, Dwayne served as Director of the Navy Honor Guard and Naval Drill Team. In 1956, Dwayne graduated Magna Cum Laude in Microbiology (Life Science) from the University of Idaho. Following his graduation, in September of 1956, Dwayne continued his naval career on a destroyer stationed in Long Beach, Calif. He served as Damage Control Officer, then as Engineering Officer on the naval warship, Samuel N. Moore DD747 until August 1959. In 1959, after completing his tour with the Navy, Dwayne enrolled in graduate school in Microbiology at the University of California, Berkeley. He graduated with High Honors from Berkeley and worked at the University until he was awarded a position to conduct postdoctoral research at Rockefeller University in 1965 with René Dubos. Dubos was highly respected for his lifelong research, and he directed and inspired Dwayne’s research focus to that of diseases of the digestive system and other gut-related issues.

In 1969, Dwayne moved to Austin, Tex., for his first faculty appointment as Assistant Professor of Microbiology at the University of Texas. During the summer of 1972, he spent two months in Denver to participate in research in the gastrointestinal unit at the University of Colorado Medical Center, focusing on gall bladder disease. He then moved to Urbana, Illinois in 1972, as Professor of Microbiology at the University of Illinois. According to Dwayne’s specifications, the University restructured their medical lab facilities to become a prominent germ-free research lab at Burrell Hall, Urbana-Champaign. In 1974, Dwayne received the “Golden Apple” award from medical students for excellent teaching. He transferred from the School of Basic Medical Sciences into the School of Life Sciences, filling the position responsible for pathogenic microbiology. He was elected Fellow of the American Academy of Microbiology. Dwayne and Daniel Bloomfield worked to establish the curriculum and facilities for a new medical school at the university, Morrill Hall. In July of 1988, Dwayne accepted his last appointment at the University of Tennessee in Knoxville, as Professor and Head of the Microbiology Department which included faculty from the Colleges of Arts and Sciences and Veterinary Medicine.

Dwayne married his high school sweetheart, Norma Jean Bradley Savage, in 1957. They had two sons, Marco Dwayne Clark Bradley. As Dwayne progressed through each move of his professional career, Jean was by his side and taught at schools located in each area. In July of 2002, they left their careers in Knoxville, and retired moving permanently to Eagle, Idaho in 2008. His pride and joy were his sons, their families, and especially his grandchildren, Nicholas and Rebecca. Dwayne was an avid stamp collector; he en-
joyed writing and reading poetry, especially poetry by Robert Burns. He enjoyed listening to music, especially Beethoven and that of his children and grandchildren.

Excerpts of this obituary were published in Idaho Statesman on May 22, 2016 and written by the family of D.C. Savage (http://www.legacy.com/obituaries/idahostatesman/obituary.aspx?pid=180054139).

As his last student, I am happy to have worked with and learned from him as surely is the case with many students before me. As a mentor, he instilled confidence in ideas and how to think and write scientifically. His patience and guidance were second to none, as was the experimental independence he permitted in the laboratory. I am convinced, from our candid scientific and personal conversations, that there is an important dynamic associated with one scientific generation to the next.

Christopher A. Elkins
Division of Molecular Biology
CFSAN-FDA

Jeffrey M. Becker
Microbiology Department,
University of Tennessee
Microbe Mentor

A Career Option in Government: Principal Investigator and Regulatory Affairs at the FDA

What are the other options available for grad students besides academia and industry?

Microbe Mentor receives many questions about career options outside of academia. Students are probably most familiar with industry; however, there are many other career options available. For this edition of Microbe Mentor, we chose to highlight a government position at the Food and Drug Administration (FDA), which includes both research and regulatory components.

We interviewed Karen Elkins, Supervisory Research Biologist in the Center for Biologics Evaluation and Research (CBER) at the FDA. She received her B.A. in Chemistry from Wake Forest University and went on to complete a Ph.D. in Microbiology and Immunology from Duke University. After completing two postdocs, she became a researcher at Walter Reed and then moved to her current job at the FDA.

“I knew nothing about the FDA or how scientists worked within [the] FDA,” she remembers. After attending many microbiology seminars on the NIH campus, which all happened to be in Building 29, she learned that Building 29 was actually the home of the Center for Biologics Evaluation and Research (CBER) of the FDA. She met several people who worked as both infectious disease researchers and regulators at CBER. “The combination of job functions sounded appealing [to me]; I enjoyed the subject matter, the lab work, and the possibility of contributing to public health through regulatory review (no matter what happened at the bench),” she comments. Karen then did something courageous; she contacted a director and asked how CBER could use someone with her infectious disease research training. The director connected her with possibilities that led to her current job. “Looking back, that took more nerve than I really knew I had at the time,” she recalls.

Currently, her job includes two main functions that are split approximately equally. First, she is the principal investigator of a research group that studies the nature of protective immunity to intracellular bacteria. A major focus of her work is identifying correlates, such as immune mediators that can be measured in blood, that predict successful vaccination against bacteria like *Mycobacterium tuberculosis* and *Francisella tularensis*. Second, she serves as a product reviewer for investigational bacterial vaccines that are regulated by the FDA as they proceed through clinical trials. She is responsible for evaluating the plans for manufacturing, quality control testing, and clinical immunogenicity testing.

Because of her extensive background in research, she easily transitioned into the role of principal investigator, which includes tasks like working with her group members to design projects and experiments, reading the literature, writing papers, reviewing manuscripts and grants, and executing experiments. The regulatory side of her job was accompanied by an initial learning curve; however, she quickly became skilled at the regulatory review process. In this process, products are evaluated for their characterizations, data that manufacturers submit are scrutinized, the information about the product and its claims are reviewed, and any FDA issues that were identified are communicated to the manufacturers. The entire process is done with a team of clinical and statistical reviewers to ensure that the clinical trials were done to maximize protection of patients and yield useful data.

For those that are interested in working at the FDA, Karen says, “the prospects for knowledgeable, thoughtful scientists working in government in non-bench positions (such as FDA regulation) are rather good, and they seem likely to stay stable.” While Karen has a research component to her job, there are many Ph.D. and master’s level scientists who work at the FDA in full-time regulatory positions.
Looking back, Karen says, “I never would have predicted that I’d end up in FDA—or like it well enough to stay for over 20 years now”. She encourages people to be open to unexpected possibilities and to become comfortable with networking. “Odds are that’s where most of your best job possibilities will come from,” she comments. Also, she recommends mastering a scientific topic that fascinates you regardless of its marketability and to demonstrate that mastery through published papers and techniques. “Dive deep to learn as much theoretical knowledge and technical information about it as you can, and then build your knowledge outwards from there.” Lastly, she advises that students build their nontechnical skills, such as writing effectively, producing engaging presentations, and managing projects from the strategic planning steps to budgets.

**ASM’s New Career Website: Cultivate Your Career**

Visit asm.org/careers for

- Professional development, volunteer, and funding opportunities
- ASM’s job board—Career Connections
- Profiles of microbiology career paths
- Articles on writing resumes, elevator pitches, networking, and more!
Reviews and Resources

BOOKS

Microbe, 2nd Edition
Michele Swanson, Moselio Schaechter, Gemma Reguera, Frederick Neidhardt, and Rachel Horak ASM Press, 2016, Washington, DC, 833 p., $100

Twenty years ago, I took the transformative “Microbial Diversity” course at the Marine Biological Laboratories in Woods Hole, Mass., taught by the late Edward Leadbetter and the late Abigail Salyers. Awe by the depth and breadth of what I soon called “matters microbial,” and perplexed by textbook options for use in the classroom, Ed laughed and told me I needed three texts: one for the students, and two for me. Microbiology is changing constantly, and expanding its scope to so many other disciplines as it changes. There was simply, as he put it, not enough paper for the subject matter in one book.

Over the years, I have used several textbooks to teach microbiology; they appear to be growing in size, depth, and sheer weight. Since I adore microbiology, this is not a problem. However, I only teach one microbiology course at my institution. In the classroom, having students drink from a metaphorical firehose of microbial information is not pedagogically optimal.

In 2005, the first edition of Microbe squarely hit the microbial “sweet spot” for my pedagogical needs: accessible in size and scope, conceptually driven, filled with fascinating images and relevant information, and clearly written with boundless enthusiasm. It was a pleasure to teach with such a text, and students responded well.

I was thus delighted when 11 years later, the second edition of Microbe appeared. It does not disappoint. The authors of the first edition bring their near-encyclopedic knowledge and overview of matters microbial to bear to this essential update, and are joined by Swanson and Reguera. The latter two authors bring medical and environmental microbiology to the forefront, respectively, as well as great clarity, fine prose style, and enthusiasm to the subject matter. Finally, Schaechter (and now Reguera) write for the wonderfully accessible microbiology blog “Small Things Considered” (http://schaechter.asmblog.org/). It is thus no surprise to see the microbial enthusiasm, clarity, topicality, and accessibility evident on each page.

Microbe is less weighty than many microbiology texts, but has enhanced value in many respects. The conceptual divides in sections and chapters make sense, and relate well to one another. As expected from a 2016 copyright, there is much up to date information as well as well-loved familiar topics. In particular, I appreciated the pathogen-driven sections on medical microbiology, as well as overarching microbiological themes throughout. A chapter on “Succeeding in the Environment” was particularly pleasing to me. The glossary and index are well organized and clear (particularly important for students).

In addition, Horak brings the ASM Curricular Guidelines into the mix. This respect for pedagogy is reflected in a “key concepts” section (relating to the curricular guidelines) in each chapter. Learning outcomes are present in most chapter subsections. Special topics and case studies appear plentifully; there is great respect to both written and visual resources. I particularly appreciated the supplemental activities and “Dig Deeper” sections at the conclusion of each chapter.

I have used many microbiology textbooks over the years. For a one-semester course in microbiology, I can think of very few choices to match this new edition of “Microbe” in terms of thematic/conceptual coverage, current knowledge, accessibility to students, and clear enthusiastic prose.

Ed Leadbetter would be happy with the choice of this textbook for my own students, I think. There is no higher praise in my opinion.

Note: My condolences to friends, family, and students of the late Frederick Neidhardt (http://schaechter.asmblog.org/schaechter/2016/10/frederick-c-neidhardt-19312016an-obituary.html).

Mark O. Martin
University of Puget Sound
Tacoma, Wash.

Infections of Leisure,
4th edition

What a happy title! This book could have been called “The Wages of Sin” or something equally judgmental. It deals with the microbial penalties that may accompany such pleasurable activities as ocean cruising, immersing in hot tubs, camping, or having pets. Even taking your kids to the petting zoo may come at a cost. And never mind such items as body piercing and tattoos, or, as one chapter says: “Sexually Transmitted Diseases: From Boudoir to Border.”

Written by experts (and there are some for every kind of people-microbe interactions), this is perhaps the most
entertaining book on microbiology in my memory. Here are discussions of the multitude of infections that can afflict us, practically from the time we get out of bed in the morning. But to show you whose side the book is on, each chapter contains a section on “Practical Tips.” Among them are such nuggets as: “Use a silk scarf to breathe through at high altitude to help humidify the cold air,” “Sporotrichosis should be considered in people who regularly consume alcohol and work in a garden,” (“Dog”) feces should not be used as fertilizer.”

But don’t be fooled by this folksiness, this book is replete with good science. Hats off to the editor and writers!

Moselio Schaechter
San Diego, Calif.

Zoonoses: Infectious Diseases Transmissible from Animals to Humans (4th ed.)

Issues surrounding transmissions of infectious agents from animals (wild and domestic) to humans have become an increasingly important topic of discussions not only among clinicians and scientists but also in the general public. A search in the PubMed data base (www.ncbi.nlm.nih.gov) using the key word “zoonoses” reveals a significant increase in publications over the years. For example, as of June 1, 2016, an astounding 1,338 papers have been published on zoonoses in 2015 alone, compared to 836, 537, and 362 papers in 2010, 2005, and 2000, respectively. It is therefore not surprising that existing books about zoonoses need to be frequently updated in order to provide readers with information about the most recent research findings and developments in this field.

The book Zoonoses: Infectious Diseases Transmissible from Animals to Humans is now in its fourth edition and is a much-anticipated publication. The authors divided the book into four chapters (viral-, bacterial-, fungal-, and parasitic-zoonoses) and added four appendices that deal with additional issues, such as infections caused by animal bites and animal-origin foodborne illnesses/intoxications.

Bauerfeind et al. have produced an excellent book about a large number of infectious diseases that are transmissible from animals to humans. The strengths of this book lies in its structure and in the clarity of the writing. The supplementation of the text with high-quality maps (e.g., the distribution of Dengue virus infection), flow charts (e.g., the infection chain of rabies), and tables (e.g., Borrelia spp. of medical and veterinarian significance in North America, Europe, and Asia) will help readers understand the importance of zoonoses. The photographic presentation of the clinical manifestations of zoonotic diseases, the microscopic images of the infectious agents, and the developmental cycles and transmission chains of zoonotic pathogens are outstanding. If there is any shortcoming in this book, I would name the lack of a glossary—perhaps the authors could consider developing a glossary for a next edition. Nevertheless, the book does contain a list of abbreviations and a 28-pages long, functional index for keyword searches.

I believe that Zoonoses: Infectious Diseases Transmissible from Animals to Humans will not only be of great value to physicians, veterinarians, microbiologists, and epidemiologists, but also to environmental scientists and public health specialists, including health policy makers, international health managers, and health communicators. It is a book that can serve both as an instructional text in academia and as a zoonoses reference source for researchers and practitioners in infectious diseases. I highly recommend the 4th edition of Zoonoses: Infectious Diseases Transmissible from Animals to Humans to the reader.

Christian T. K.-H. Stadtlander
St. Paul, Minn.
Employment

POSITIONS AVAILABLE

Postdoctoral Positions in Enzymology and Microbiology

Postdoctoral positions are available for enzymologists and microbiologists in enzyme and pathway discovery as part of a new multidisciplinary Program Project (P01GM118303, Novel Strategies for the Discovery of Microbial Metabolic Pathways). We are especially interested in applicants with demonstrated expertise in microbial genetics or mechanistic enzymology. The Program Project has the goal of developing sequence/structure-based strategies for facilitating assignment of in vitro enzymatic and in vivo metabolic roles of widely conserved enzymes of unknown function discovered in genome projects, a crucial limitation in microbial genomic biology. The project integrates bioinformatics, genetics, and metabolomics, structural biology, and computation with enzymology. The components of the Program Project are located at the University of Illinois (enzymology and microbiology; J. E. Cronan and J. A. Gerlt), Albert Einstein College of Medicine (structural biology and ligand screening; S. C. Almo), and University of California, San Francisco (modeling, docking, pathway prediction; M. P. Jacobson, A. Sali, and B. K. Shoichet). Due to the collaborative and multidisciplinary environment, the Program Project provides an opportunity to receive training in several areas. To apply or request details, please send an e-mail to enzymes@igb.illinois.edu.

Physician-Scientists/Basic Scientists

The Division of Infectious Diseases and International Medicine and Program in HIV Medicine of the Department of Medicine at the University of Minnesota invites applications for tenure-track positions at the Assistant Professor or tenured Associate Professor ranks. We seek candidates with an M.D., Ph.D., or M.D./Ph.D. degree who have a track record of exceptional accomplishment and promise in infectious diseases research. The Program in HIV Medicine’s current areas of interest include virus evolution; virus persistence and tissue reservoirs; lymphoid tissue pathology and CD4 T cell depletion and reconstitution; HIV co-morbidities, and HIV-related coinfections, particularly TB; and innate and adaptive immunological responses to infection or co-infections that might eventuate in therapeutic or preventive vaccines. The successful candidate will join a collegial community with outstanding scholarly and scientific resources and opportunities to collaborate with faculty in the Department of Microbiology and Immunology, Center for Immunology, Center for Clinical and Translational Science Institute, Center for Drug Design, and the Institute for Molecular Virology at the University of Minnesota. Individuals licensed to practice medicine in the State of Minnesota will also have the opportunity to provide outpatient care for HIV-infected patients or general ID patients at the University of Minnesota HIV/ID clinic and to provide inpatient ID consultation. Salary will be commensurate with qualifications and expertise and competitive startup packages are available. Qualified applicants are invited to apply on-line at www1.umn.edu/ohr. In addition to the online application, applicants should send a 3-page letter describing research interests and expertise, along with a current curriculum vitae and names of three references by e-mail to Scott Povolny (pov0006@umn.edu), addressed to: Timothy Schacker, MD, Director of the Program in HIV Medicine. The University of Minnesota School of Medicine is an Equal Opportunity, Equal Access, Affirmative Action Employer.

Full-time, 100% (12-month basis) Clinical or Tenure-Track Assistant or Associate Professor in Veterinary Virology

The University of Illinois College of Veterinary Medicine’s Veterinary Diagnostic Laboratory is seeking a clinically trained Diagnostic Virologist to enhance services for clinicians and referring veterinarians, and to assist with test development, oversight, and reporting. Minimal requirements include a D.V.M. degree or equivalent and an M.S. in Microbiology, with a Ph.D. in Microbiology preferred. Diagnostic laboratory experience is also preferred. Salary is commensurate with experience. Please apply by December 16, 2016. To view the position and submit an application, visit: http://go.illinois.edu/Vet_Virology. The University of Illinois conducts criminal background checks on all job candidates upon acceptance of a contingent offer. Additional information about the position may be obtained from Dr. Carol Maddox, Search Chair, at maddox@illinois.edu. The U of I is an EEO Employer/Vet/Disabled.

Professors, Associate Professor, or Assistant Professor without Tenure

The Department of Laboratory Medicine, University of Washington School of Medicine, 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 respon-
sibility 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.
Small Things Considered

Need Protection?
Hire a Virus!
http://schaechter.asmblog.org/schaechter/2016/02/need-protection-hire-a-virus.html
by Jamie Henzy

Is there any denying that pregnancy is a form of parasitism? After all, the developing organism carries foreign DNA from an outside source, and reroutes nutrients at the host’s expense. In cases where “parasite” hatchlings require maternal care, a balance has been struck that minimizes damage to the mother-host. However, creatures that do not require this attention can take a more cynical approach. Observe the parasitoid wasps, who outsource the incubation and feeding of their progeny by injecting their eggs into the larvae or eggs of other insects: the host is expendable, so evolution doesn’t bother to forge a truce between the two parties. Instead, the newly hatched wasplings simply eat the inside of their unfortunate host.

But what about the problem of self versus nonself? Whether incubation occurs in a mother-host or an alien-host, the developing organism, perceived as nonself, needs to be protected from the host immune system. Who in nature has tons of experience at fighting immune systems? Viruses! These immune-fighting machines are skilled at entering host cells and shutting down immune systems—an excellent strategy as the capsids, being injected during infection. These VLPs contain viral virulence proteins, not DNA, but otherwise follow the same strategy as the capsids, being injected along with the eggs into the larva-host.

The viral capsid genes and genes for packaging DNA produce chimeric particles that contain dsDNA circles carrying wasp virulence genes. These particles are then injected along with eggs into the larva-host, where they eventually enter the nucleus of host cells. There, the wasp DNA is transcribed to produce factors that suppress the host immune system.

The third salvage event involves the wasp species Venturia canescens (V. canescens), another ichneumonid wasp. Instead of producing ichnovirus-like capsids like its relatives, V. canescens contains genes from the nudivirus lineage and produces “virus-like particles” (VLPs): lipid vesicles carrying viral envelope proteins, which bud from the host cell during infection. These VLPs contain wasp virulence proteins, not DNA, but otherwise follow the same strategy as the capsids, being injected along with the eggs into the larva-host.

The VLPs originated from the genus alphanudivirus, whereas the bracovirus that produces capsules in the braconid wasps originated from a betanudivirus. The alphanudivirus has only been found in V. canescens so far, and may have been acquired much more recently than the 100 million-year-old ichnovirus of the same wasp lineage. The implication? Two related nudiruses became endogenized in different wasp lineages at different times. Though closely related, they left different salvageable parts—some envelope genes here, some capsid genes there. Notably, each virus was coopted by the host to perform the same function—to protect its eggs!

This story is mirrored in placental mammals, who have coopted envelope genes from ancient viruses for their ability to fuse cells. Called “syncytins,” these proteins form placental tissue that protects the fetus from the mother-host and may even suppress the mother’s immune system. These parallels implicate virus cooption in the evolution of sexual reproduction. Viruses can enter host cells and thwart host immune factors—skills also needed in sexual reproduction. So, like companies who coopt hackers to build firewalls to protect their data, perhaps early eukaryotes exploited viral sequences to protect their nonself progeny in sexual reproduction. And from there you have the birds and the bees, as well as the wasps and the placental mammals.

In addition to being an Associate Blogger for STC, Jamie is a postdoctoral researcher and part-time teaching faculty at Boston College.