FEATURES

Candida albicans: Love-Hate Relationship with Its Human Host

Tools for Studying Microbial Communities

Fecal Microbiota Transplantation

ASM News
METABOLISM AND BACTERIAL PATHOGENESIS

Editors: Tyrrell Conway, Professor and Head of Department of Microbiology and Molecular Genetics, Oklahoma State University; Paul S. Cohen, Professor of Cell and Molecular Biology, University of Rhode Island

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-- Andreas Bäumler, Professor and Vice Chair of Research, Department of Medical Microbiology and Immunology, UC Davis School of Medicine

August 2015. 352 pages (EST). Illustrations, Index.
Hardcover: 978-1-55581-886-9 | eBook: 978-1-55581-888-3
ASM Member Price: $128 | List Price: $160 | eChapter: $30

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MICROBIAL BIOFILMS
SECOND EDITION

Editors: Mahmoud A. Ghannoum, Professor, Dermatology, and Director, Center for Medical Mycology Case Western Reserve University; Matthew Parsek, Professor, Microbiology, University of Washington; Marvin Whiteley, Director, Center for Infectious Disease, and Professor, Department of Molecular Biosciences, University of Texas at Austin; Pranab Mukherjee, Dermatology, Case Western Reserve University

In the decade since the first edition of Microbial Biofilms was published, the interest in this field has expanded, spurring breakthrough research that has advanced the treatment of biofilm-associated diseases. This second edition takes the reader on an exciting, extensive review of bacterial and fungal biofilms, ranging from basic molecular interactions to innovative therapies, with particular emphasis on the division of labor in biofilms, new approaches to combat the threat of microbial biofilms, and how biofilms evade the host defense. Chapters written by established investigators cover recent findings, and contributions from investigators new to the field provide unique and fresh insights. Microbial Biofilms is a useful reference for researchers and clinicians. It will also provide insight into the dynamic field of microbial biofilms for graduate and postgraduate students.

“Biofilms influence human health and agriculture, and sustain diverse ecosystems. This second edition of Microbial Biofilms provides a masterful overview of critical topics central to fungal and bacterial biofilms by celebrated experts in the field. It is a must read for any professional seeking basic or advanced knowledge of microbial biofilms.”

- David S. Perlin, Professor and Executive Director, Public Health Research Institute, New Jersey Medical School-Rutgers University

September 2015, 440 pages (EST). Illustrations, Index.
Hardcover: 978-1-55581-745-9 | eBook: 978-1-55581-746-6
ASM Member Price: $128 • List Price: $160 • eChapter: $30

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Microbes and Us: Partners in Health

Molly B. Schmid

Throughout the 20th century, the medical relationship with microbes has been framed in terms of warfare—killing the “bad bugs” that were proven disease agents, and winning the “arms race” between the discovery of new antibiotics and resistance development. Though we may talk in our classes about the good bugs that give us yogurt and cheese and beer, most of our health-related microbiology discussions focus on killing the bad bugs that cause disease.

An article in this issue of Microbe may signal an important turning point in our thinking about the medical relationship between microbes and humans—the transplantation of fecal microbiota from healthy donors is resolving cases of recurrent Clostridium difficile infections (CDI) in patients.

Fecal microbiota transplantation (FMT) is not a new technology, but until recently, was seldom used. As a result of the recently increased virulence of C. difficile strains, old FMT methods were resurrected. With the clinical successes in treating CDIs, and few apparent adverse effects, the use of FMT to treat other diseases is under active investigation.

Using a healthy, but complex, microbial ecosystem as a therapeutic agent is a distinct change in our medical relationship with microbes. We are not just taking advantage of microbial capabilities as “master chemists,” but rather recognizing and learning about our probable coevolution with microbes, and our reliance on them for appropriate gut function, immune reactions, and many more aspects of human health that are still to be discovered.

Exploiting the success of this new type of intervention will require different ways of thinking, and input from multiple disciplines. The understanding of microbial ecosystems centers on ecological principles—competition for environmental resources and stability in complex communities. New tools of sequencing, bioinformatics, and data analysis are needed to understand the complexities of human microbial ecosystems in different human body sites and to appreciate the individual differences, while seeing the patterns resulting in homeostasis and health and distinguishing them from patterns that are dysfunctional and causing disease.

Entrepreneurs are recognizing the potential new medical market, and aiming to provide a number of different “off-the-shelf” microbial transplantation materials. There are nonprofits, like OpenBiome and AdvancingBio, and companies like CIPAC Therapeutics that are collecting and processing high-quality donor material, and other companies like Rebiotix, Symbiotic Health, PureFlora, Seres Therapeutics, and 4D Pharma that are deconstructing the fecal microbiome and providing defined microbial solutions that would eliminate the need for fecal microbiota donors.

Fecal microbiota: “ick!,” right? Don’t forget that some of us still faint at the sight of blood, and that blood donation and receipt was not always accepted as it is today. Today, the American Red Cross collects and distributes over 5 million units of blood from over 3 million blood donors. Perhaps in the future, we will have “Brown Cross” donor centers, or perhaps the exploration of the gut microbiome will provide sufficient understanding that fecal donation is unnecessary, because culturing key microbes and making synthetic, defined microbial mixtures is possible.

Where else can we apply this thinking about good bacteria restoring healthy balance? The environment? Other human microbial ecosystems, like oral, vaginal, or skin health? Agriculture? Animals? Over 246 clinical trials using probiotic solutions are currently under way to test effects on various disease states, and in maintaining health. In the 21st century, perhaps we’re turning the corner, where we’ll be courting key microbes and microbial ecosystems as our partners in health.

Molly B. Schmid is a member of the Microbe Editorial Board.
Semmelweis’ Ghost: Student Learning Is in Our Hands

Implementing active learning in undergraduate science education is essential

Gail S. Begley

Two significant and intertwined problems have been identified in undergraduate science education: poor learning outcomes and inadequate retention of students. Biology education reform movements have promoted increased student-centered learning to address these problems. Professional bodies including the National Research Council, the American Association for the Advancement of Science, the National Science Foundation, and the President’s Council of Advisors on Science and Technology have articulated both the need for reform and the necessary steps to achieve it. A move away from traditional lecture to active learning approaches is a centerpiece of these proposals, but the majority of science faculty have not made this shift. Most faculty were educated in the traditional way and have spent a number of years perfecting lecture design and delivery. And students generally respond well to clear, organized lectures. So why change?

A Proven Approach. Countless studies report effectiveness of active learning interventions as compared to traditional lecture format, but these papers are often published in the education literature rather than the discipline-specific literature, limiting their dissemination primarily to educators who already have an interest in the scholarship of teaching and learning and reflective practice. Complicating matters further, there are many variables across studies including class size, academic discipline, type of institution, course level, student audience, etc. A paper about an intervention in a large introductory physics course for nonmajors may not seem to have relevance for an upper-level microbiology course. Faculty who may have previously had concerns about the quality of active-learning data in individual studies will likely find these outcomes compelling, especially when considering the rigor of the analysis and the strict inclusion criteria.

A Historical Analogy. Much has been written about Ignaz Semmelweis, who in the mid-19th century discovered the route of transmission of puerperal sepsis (“childbed fever”) and developed a simple hand hygiene method that dramatically decreased maternal mortality. Perhaps even more has been written about the reluctance of the medical community to accept Semmelweis’ findings and act upon his suggestions. A variety of factors that may have contributed to this resistance, including Semmelweis’ nationality, personality, and politics, as well as delayed and inadequate publication. Physicians may also have been hesitant on some level to accept the fact that they were unwittingly hurting their patients.
Failure to systematically analyze the data and publish them in the widely disseminated scientific literature resulted in lack of awareness of Semmelweis’ groundbreaking work in some quarters, but even those medical educators who were aware did not necessarily accept the new concept of childbed fever transmission and adopt Semmelweis’ infection control practices. Likewise, despite a large body of research, nosocomial infections of various types, including sepsis, still plague modern hospitals and infection control compliance among health care professionals is far from ideal. So while research, education, and policy are critical, the individual has to accept the need for action and then follow through. There are lessons in this narrative for the challenge of widespread adoption of active learning methods in biology education.

A Call to Action (Again). Freeman and colleagues’ rigorous analysis has demonstrated that active learning is a superior educational method for 21st-century classrooms. They also estimated the academic and tuition costs of continuing with traditional lecture format. For the lecture control cohort of the studies that they included, a population of 29,300 students, an estimated 3,516 fewer students would have earned D/F/W grades, for an estimated tuition burden of $3,500,000 that could have been saved had these students been in active learning classrooms. Previous research has shown that active learning has a greater effect on students from disadvantaged backgrounds, providing another compelling argument for change. Broad dissemination of this research can heighten awareness and increase acceptance, but widespread adoption of active learning practices in the science classroom will require action at the level of the individual instructor.

How to Begin. For new and experienced faculty alike, transitioning from a form of instruction that feels comfortable and predictable is daunting. But a major overhaul of a traditional class may not be necessary in order for students to reap the benefits of active learning. Faculty can start by making small changes to supplement lectures rather than trying to radically restructure their courses all at once.

There are good models in the literature, for example in “Learning by Doing,” R. M. Felder and R. Brent present how-to guides for some easy active learning techniques that they have successfully implemented in the classroom (Felder, R. M., and R. Brent, Chem. Eng. Edu. 37:282–283, 2003). Most institutions of higher education have centers of teaching and learning that can provide guidance and resources for faculty. There are also Web resources sponsored by professional societies. For example, the ASM MicrobeLibrary includes active learning exercises for classrooms and laboratories (https://www.microbelibrary.org/) and iBiology, supported by the American Society for Cell Biology, has a dedicated active learning series that includes video demonstrations of active classrooms and examples of exercises (http://www.ibiology.org/scientific-teaching/active-learning.html). A community of faculty focused on improving learning outcomes can provide support and maintain momentum for continued change. This community can take many forms, from in-person meetings of a teaching circle, curriculum committee, or working group within the institution to virtual communities such as the Partnership for Life Sciences Education (PULSE, http://www.pulsecommunity.org/). The Howard Hughes Medical Institute and the National Academies sponsor summer institutes geared towards helping undergraduate faculty transform their classrooms (http://www.acade miessummerinstitute.org/), and ASM sponsors faculty development opportunities including the Biology Scholars Program (BSP, http://www.facultyprograms.org/index.php/biology-scholars-program).

Semmelweis flouted convention and made a historic discovery. Unfortunately, he failed to gain acceptance and stir his colleagues to action. Today, we appreciate his discovery and understand its implications for health care delivery, but patient safety ultimately still rests in the hands of health care providers. Now that the data are clear and convincing that active learning is superior to traditional lecturing, the power to improve student learning is just as clearly in our hands.

ACKNOWLEDGMENTS

I thank the ASM Biology Scholars Program, the Northeastern STEM Education Center, Kostia Bergman, and Erin Cram.

Gail S. Begley is Teaching Professor and Director of the University Pre-Health Program, Department of Biology, Northeastern University, Boston, Mass.
CURRENT TOPICS

NEW FROM ASM

Microbiota Differences in Infancy: Lasting Impacts on Metabolism and Immunity

Shannon Weiman

The impact of gut microbiota on human health begins at birth, and may be influenced by factors such as mode of delivery and early infant diet, according to several researchers who presented recent findings during the 2015 ASM General Meeting held in New Orleans last May. These early influences on microbiome composition can have lasting consequences, particularly on metabolism and immunity, they say. While some researchers document differences in microbial communities, others pinpoint particular species and mechanisms that control host responses, which may prove useful in treating metabolic and immune diseases.

Epidemiologic studies point to an association between Caesarean section delivery and increased fat in later childhood, along with increased rates of autoimmune diseases, including type 1 diabetes, food allergies, and celiac disease, according to Martin Blaser of New York University in New York, N.Y. “Microbiota interactions in infancy may be critical determinants of long-term host metabolic effects,” he says. Further, transient perturbations in the microbiome during infancy, induced by antibiotic treatment of mice, have a long-term impact on fat deposition, he pointed out. “Altering the intestinal microbiota during a critical development window has lasting metabolic consequences... and can result in syndromes of metabolic dysfunction.”

One bacterial species that may protect against such metabolic dysfunction later in life is *Akermansia muciniphila*, says Clara Belzar of Wageningen University in the Netherlands. “*A. muciniphila* treatment reversed high-fat diet-induced metabolic disorders, including fat-mass gain, adipose tissue inflammation, and insulin resistance,” she says, describing studies in mice. Metabolites of this bacterium alter expression of various transcription factors and genes involved in host cellular growth, lipid metabolism, lipolysis and satiety, including fasting-induced adipose factor, G-protein coupled receptor 42, histone deacetylases, and peroxisome proliferator-activated receptor gamma, she says. These bacteria also can increase endocannabinoid levels, which control inflammation, gut barrier function, and gut peptide secretion.

Diet can influence gut microbial populations during infancy, which alters immune development, according to Nicole Narayan of the University of California, Davis. Studying rhesus macaques, she finds that breast-fed infants develop different microbiota and more robust immune systems compared to their formula-fed counterparts. “Early infant diet has significant impact on the gut microbiota... which, in turn is associated with different immune systems in infancy,” she says. “Breast-fed animals manifested greater T cell activation and proliferation and harbored robust pools of T helper 17 cells.” Moreover, these immunologic differences can be sustained for at least 3 to 5 years.

*Lactobacillus reuteri*, also a native bacterium of the human gut microbiota, can modulate host immune re-
sponses, suppressing proinflammatory cytokines while alleviating colitis in mice, says Chunxu Gao of Baylor College of Medicine in Houston, Tex. These bacteria convert the amino acid L-histidine into histamine, which signals via H2 histamine receptors on myeloid cells to suppress the mitogen-activated protein kinase pathway and thus block production of pro-inflammatory tumor necrosis factor (TNF). The presence of L-histidine in the diet is essential for alleviating Lactobacillus reuteri-mediated colitis, he says. “These findings point toward a new strategy for controlling intestinal inflammation via probiotics by dietary interventions or microbiome manipulation.”

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

NEW FROM ASM

Genomics Outpaces “Grind and Find” in Search for Useful Natural Products

Jeffrey L. Fox

Although natural products remain “the best source of antibiotics,” finding ways to accelerate their discovery remains a critical challenge for would-be developers of new drugs, says Ben Shen from the Scripps Research Institute in Jupiter, Fla. The recipient this year of the Promega Biotechnology Research Award, he spoke during the plenary session, “The Third Age of Antimicrobials,” convened at the 2015 ASM General Meeting held in New Orleans last May.

The traditional “grind-and-find” approach of cultivating microorganisms and then extracting natural products from them to search for those with promising antimicrobial or other useful biological activities, is simply too slow, Shen says. For instance, it took about 15 years to comb through more than 80,000 strains and to examine some 250,000 extracts before researchers identified platensimycin, a metabolite of Streptomyces platensis. This natural product has promising antibiotic activity and is part of a new structural class. Another drawback is that this extraction stage typically is a mere prelude to the medicinal chemical manipulations required to convert promising leads into genuine candidate drugs with appropriate pharmacologic properties. Although a solid traditional approach to drug discovery, it can be glacially paced and dreary, he suggests.

To streamline this process, Shen recommends putting microbial genomics to use in setting microbial strain priorities. This newer approach includes a study of the specific genes involved in producing a natural product such as platensimycin, and then using them to probe other strains that can or cannot make particular strategic intermediates of that natural product. An alternate screening strategy is to look more narrowly for genes encoding those enzymes that are called into action very late in the synthesis of a particularly useful natural product, he says. Such information helped him and his collaborators to identify a half-dozen similar but not identical platensimycin-producer strains that had been collected from widely distributed sites around the world, affording an opportunity to tease out strains with higher efficiencies of production or with modified end products.

Analysis of the genes and intermediates involved in this metabolic pathway helped to uncover a repressor molecule that effectively chokes overall productivity, according to Shen. Blocking that repressor boosts output, enabling the producer strain to over-produce metabolites, in turn, making it easier to

MINITOPIC

Microbiology Policy Bulletin Board

Recent national and international developments involving microbiology and related science policy matters include:

- Following the meeting of the G7 countries in Germany last June, the leaders declared their full support for the WHO Global Action Plan on Antimicrobial Resistance, urging the prudent use of antibiotics and pledging to stimulate basic research as well as development of new antibiotics, alternative therapies, vaccines, and rapid point-of-care diagnostics.
- The U.S. Government Accountability Office (GAO) in July issued a preliminary report on efforts by the Department of Defense (DoD) and the Centers for Disease Control and Prevention (CDC) to address weaknesses in their management of high-containment laboratories. Earlier, GAO recommended mandating a single federal entity to conduct strategic planning for such laboratories and to develop national standards for them to follow. For details, see http://www.gov.gao.gov/products/GAO-15-792T?utm_source=dpi11005 email
- The National Academy of Sciences hosted the first meeting of the Commission on a Global Health Risk Framework for the Future, whose central task is to recommend an effective global “architecture” for recognizing and mitigating the threat of epidemic infectious diseases.
produce greater amounts of potentially useful analogs of platensimycin—or, by generalizing this strategy, other altogether different drug candidates from very different strains.

By avoiding repressor activity, these strains produce about 0.5 g of material per liter, according to Shen. “We can generate all kinds of intermediates and variants, changing linkages to improve activity and stability,” he says. By feeding the producer strains different side chains, it becomes possible to produce a broad spectrum of alternative “final” products, at least a few of which are “as good or better” than the parent antibiotic. This process in culture recapitulates what medicinal chemists do in the lab, while saving time and effort by relying on enzyme-catalyzed metabolic pathways instead of painstaking organic chemistry procedures.

This same genomic analysis-based approach to identifying strains that make natural products with promising biological activities applies as well to the search for anticancer drug candidates as it does to antimicrobial leads, Shen says. “This genomics-based approach holds great promise...and can be applied to discover novel scaffolds and to accelerate drug discovery.”

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

RESEARCH ADVANCES

Versatile Ligand Assay Opens Way to Identifying Signaling Molecules

Carol Potera

A recently developed, high-throughput (HT) method for identifying ligands involved in chemotaxis can also be used for identifying other types of bacterial signaling molecules that bind sensor domains, according to Monica Gerth of the University of Otago in Dunedin, New Zealand, and her collaborators. Details appeared in the May 2015 *Molecular Microbiology* (doi:10.1111/mmi.12964).

In developing this method, Gerth and her collaborators combined fluorescence-based thermal shift (FTS) assays with commercial phenotype microarrays from Biolog, Inc., of Hayward, Calif., whose kits contain dozens of compounds that fuel bacterial growth. To begin with, they focused on 95 such compounds that bacteria use as carbon and nitrogen sources and that can trigger chemotaxis. FTS detects protein unfolding, a marker of ligand binding.

“It was a eureka moment when I realized that I could combine the two technologies,” Gerth says. Each assay, done on microtiter plates, requires only about 10 µl of a purified protein and 2 µl of a screening compound as well as access to PCR equipment for subsequent analyses, and takes less than 2 hours to complete.

To put the new test to a test, Gerth and her collaborators identified 43 chemoreceptors of *Pseudomonas syringae* pv. *actinidiae* strain NZ-V13, a plant pathogen that infects kiwifruit, causing wilting, cankers, plant death, and severe economic losses for kiwi growers, according to Gerth. No one else has yet characterized any of its 43 chemoreceptors, she says. One long-
term goal is to prevent kiwifruit infections by disrupting the ability of P. syringae to sense its host. She’s also using the assay to identify chemotaxis receptors in Phytophthora agathidicida, which is killing kauri, treasured native trees of New Zealand. A close relative of this microorganism caused the Irish potato famine in the 1840s.

After validating the method with a well-characterized amino acid-sensing chemoreceptor from Pseudomonas aeruginosa, known as PctA, the New Zealand researchers tested three chemoreceptors from P. syringae, called PsaA (the counterpart of PctA), PsaB, and PsaC. None of these chemoreceptors shares binding repertoires with their counterparts from P. aeruginosa. For example, PctA strongly binds 18 L-amino acids, whereas PsaA binds only three, namely L-aspartate, L-glutamate, and D-aspartate. Moreover, a single mutation could alter a chemoreceptor’s specificity. “These distinct sensory repertoires may regulate differences in bacterial lifestyles, such as host colonization,” Gerth says.

“Genome sequences reveal vast numbers of genes encoding chemoreceptor proteins,” says John “Sandy” Parkinson, a distinguished professor of biology at the University of Utah in Salt Lake City. “However, discovering the nature of these chemical signals is a tedious process. [Gerth’s] clever assay is now widely accessible to chemoreceptor labs,” and it could “extend to other ligand-binding proteins, such as the vast family of sensor kinases of two-component regulatory systems.”

“Overall, the assay is very flexible,” says Gerth. Other researchers studying chemotaxis have told her about using HT-FTS assays with other ligand libraries, as well as using other Biolog plates to investigate ligand binding in other types of proteins. “Hopefully, this will prove to be a useful technique for a wide variety of research,” she says.

NEW FROM ASM

Noncoding sRNA Deemed Responsible for Onset of Periodontitis

David C. Holzman

Small, noncoding RNA molecules (sRNA) appear to play a key role in regulating the onset of periodontitis, turning on virulence genes and defenses against the host immune system, according to Jorge Frias-Lopez of the Forsyth Institute in Cambridge, Mass., and his collaborators. This research is the first community-wide metatranscriptome analysis of sRNAs in the oral microbiome during the progression of periodontitis, they report. Details appeared 17 July 2015 in Applied and Environmental Microbiology (doi: 10.1128/AEM.01782–15).

“We found that the profiles of expression of sRNAs correlate with activities we identified as important in periodontitis progression,” Frias-Lopez says. He and his collaborators focused attention on sRNAs because they “can be synthesized rapidly under changing conditions, and allow for a faster response than other regulatory mechanisms, such as two-component regulatory systems,” he points out.

The activities that these sRNAs appear to target include cobalamin (vitamin B12) biosynthesis, β-lactam catabolism, and cell adhesion. Other functions the sRNAs modulate, some of which may also be important in disease progression, include proteolysis, ferrous iron transport, potassium ion transport, and protein secretion and import. “Copper-translocating p-type ATPases appear to be critical for bacterial virulence,” he and his collaborators note. Those enzymes act “by overcoming high phagosomal metal levels and are required for the assembly of periplasmic and secreted metalloproteins that are essential for survival in extreme oxidant environments.” Meanwhile, multicopper oxidases apparently boost virulence by sequestering copper.

MINITOPIC

Coarse-Grained Look Reveals Bursts of Diversity in Microbial Phylogenetic Trees

Coarse-graining analytic methods applied to the phylogenetics of microorganisms leads to rearranged trees, revealing “bursts of diversification” that appear “throughout these phylogenetic trees, deep within their history,” says James O’Dwyer of the Carl R. Woese Institute for Genomic Biology at the University of Illinois, Champaign-Urbana. These bursts were found in trees for 22 microbial communities that come from a breadth of habitat types: plant, marine, and human gut and skin, according to O’Dwyer and his collaborators, Steven Kembel from Université du Québec à Montréal in Canada and Thomas Sharpton from Oregon State University. They point to two central findings. First, on finer scales the trees are highly idiosyncratic, while on coarser scales the backbone of these trees is simple and robust, consistent across habitats, and displays bursts of diversification dotted throughout. Second, this approach to building microbial trees is “a clear departure from the predictions of standard neutral theories of biodiversity and that an alternative family of generalized models provides a qualitatively better description,” they note. Details appeared 7 July 2015 in Proceedings of the National Academy of Sciences (doi:10.1073/pnas.1419341112).

Carol Potera is a freelance writer in Great Falls, Mont.
MINITOPIC
Template-Assisted Ligation Model, Collapsed Ribosomes Raise Primordial Questions

Although unrelated, these two recent developments address fundamental questions about how life might take shape. “Even if all you have is template-assisted ligation, you can still bootstrap the system out of primordial soup,” says Sergei Maslov at the University of Illinois, Urbana-Champaign and Brookhaven National Laboratory. In their new model for template-assisted replication, he and his collaborator Alexei Tkachenko argue that the joining of two polymers by using a third, longer one as a template could have enabled polymers to become self-replicating. Template-assisted ligation in this model thus “allows for heritable transmission of the information,” they note. Details appeared 28 July 2015 in the Journal of Chemical Physics (doi:10.1063/1.4922545). In a separate development, ribosomes can be collapsed from two subunits into one, according to Alexander S. Mankin of the University of Illinois, Chicago, and his collaborators. By engineering a hybrid ribosomal RNA (rRNA) composed of both small and large subunit rRNA sequences, they produced a ribosome whose subunits form a single entity that not only functions in vitro, but also supports the growth of *Escherichia coli* cells in the absence of wild-type ribosomes. Details appeared 29 July 2015 in *Nature* (doi:10.1038/nature14862).

organism for defending these microorganisms against host defenses. For instance, copper ions in host cells are bactericidal.

“This is a highly significant paper, with importance far beyond oral infectious disease, in that it reports novel principles likely to apply also to biofilm dynamics in other infectious diseases, as well as in environmental biofilms,” says Ann Progulske-Fox of the University of Florida, Gainesville. Moreover, Frias-Lopez and his collaborators were deft in combining metagenomics, which identifies organisms present in the sample, with metatranscriptome analysis, which identifies genes being expressed by a group of organisms based on the mRNA molecules that are being detected, to study this human disease, she says. Further, by determining the dynamics of sRNAs being expressed over the course of this disease, their findings implicate the biofilm rather than any individual species as driving virulence gene expression, she points out.

“Periodontitis is a polymicrobial disease caused by the coordinated action of a complex microbial community that leads to inflammation of tissues supporting the teeth,” says Frias-Lopez. It is the sixth most disabling health condition, currently affecting 743 million worldwide, or 10% of all humans. Nearly half of American adults have moderate periodontitis, while 10% have the severe form, and this condition is responsible for half of all tooth loss in adults. The disease is considered a contributing risk factor for a series of other chronic health conditions, including diabetes and cardiovascular and respiratory diseases. Even so, efforts to reduce its prevalence have had limited success.

David C. Holzman is the Microbe Journal Highlights Editor.

NEW FROM ASM
Endofungal Bacteria May Determine How These Symbionts Affect Host Plants
Shannon Weiman

Bacteria living within fungi influence host metabolism, reproductive activity, and ecosystem effects, according to several researchers who spoke during the symposium, “Microbes in Microbes (Russian Dolls),” at the 2015 ASM General Meeting, held in New Orleans last May. Thus, for example, some endofungal bacteria and their host fungi form partnerships with plants that range from beneficial to pathogenic. In some cases, these symbioses promote growth among all participants while, in others, the microbial symbionts thrive at the expense of their host plants.

Endophytic fungi and their bacterial symbionts, while previously recognized for their role in plant rhizomes, are also widespread in plant leaves, according to David Baltrus and his collaborators Elizabeth Arnold and Kayla Arendt, all of the University of Arizona, Tucson. “These bacteria occur in living hyphae of phylogenetically diverse endophytes isolated from various plant lineages and in multiple biogeographic provinces,” says Arnold. Earlier, Arnold and her collaborators identified 15 distinct bacterial species, primarily of the *Proteobacter* lineage, within 414 species of leaf endophytic fungi. These bacterial species differ from those found within endophytic fungi in other plant tissues, suggesting they play special roles within leaves.

By treating these systems with antibiotics, Baltrus and his collaborators “cure” the endophytic fungi of their bacterial symbionts, thus dissecting the bacterial influences from the purely fungal impacts of these species on various metabolic properties and ecological functions within the host plants. “Plant-associated fungi harbor bacteria that can alter fungal interactions with host plants in diverse ways,” Arnold says. For example, *Luteibacter* bacteria increase cellulase activity of the host fungus *Pestalotiopsis*, which may help the latter to colonize its plant hosts.

In addition, the fungal-bacterial symbiosis benefits the host plant by producing the phytohormone inde-
Fungal eisosomes are shallow, trough-shaped invaginations of the plasma membrane, of unknown function, that are ubiquitous in fungi. Fungal eisosome assembly requires two conserved proteins carrying “BAR” domains, triple-coiled-coil motifs associated with generation of membrane curvature. Now Ursula Goodenough of Washington University, St. Louis, et al. have identified eisosomes in a subset of red and green microalgae and in cysts of a ciliate. “Microalgal eisosome assembly is correlated with the presence and nature of cell walls,” she says. Though sequenced microalgae lack fungal BAR proteins, she has identified two lineage-specific BAR-encoding gene families that are candidate eisosome organizers. “The presence of eisosomes in algae, fungi, and ciliates indicates that these membrane differentiations were present in ancient eukaryotic common ancestors,” she says. “Experiments probing function in microalgae may yield fundamental insights. Some fungicides are known to bind to ergosterol, which is enriched in fungal eisosomes.” And this, she says, “is the first report of a stable structural patterning of membrane.


NEW FROM ASM
Transgenic Mouse Model with Reporter Gene Enables Monitoring of Progression of Inflammatory Disease

When researchers evaluate the severity of inflammatory disease in experimental mice, they typically must euthanize the mice and then subject tissues to a variety of analytical techniques. For all this, they gain a
snapshot of the phenotype, but with no information on the time course of the disease. Now Takashi Moriguchi and colleagues of Tohoku University, Sendai, Japan have developed a transgenic mouse model that enables investigators to monitor progression simply, by means of a luciferase reporter gene. In their experiments they found that their “WIM-6 system” mice (Whole-body in vivo monitoring with human interleukin-6 luciferase transgenic mouse model) showed robust luciferase luminescence in the central nervous system after experimental auto-immune encephalomyelitis induction. They then crossed their mice with a model deficient for Nrf2, a master transcriptional regulator of antioxidant genes, and demonstrated that the systemic anti-oxidative stress system is crucial for prevention of inflammatory neurodegenerative disease. The new model, Moriguchi says, will help researchers to evaluate the efficacy of candidate drugs, and to find damaged tissue in systemic inflammatory diseases.


NEW FROM ASM
Changes in Chromosome Structure Regulate DNA Replication Initiation

Bacterial chromosomes change organization and structure during the cell cycle, for reasons as yet unclear. Now David Magnan and David Bates of Baylor College of Medicine, Houston, show in Escherichia coli that programmed changes in chromosome structure may regulate initiation of DNA replication. Negative supercoiling, which favors duplex melting, is required to initiate replication. Based on their previous observations, they posited that structural differences before and after initiation of replication changed chromosome supercoiling. They found that artificially tethering the chromosome to the cell membrane decreased negative supercoiling, and blocked replication initiation without affecting other DNA metabolic processes. “This finding may reveal new targets for antibiotics, and may explain why existing antibiotics that affect DNA supercoiling are so effective,” says Bates. “More significantly, this research may lead to better understanding of bacterial cell cycle control, which is a black box, as well as eukaryotic replication initiation, which is also sensitive to changes in chromosome structure.”


NEW FROM ASM
Periodontitis and Heart Disease: Researchers Connect the Molecular Dots

Periodontitis is a risk factor for heart disease. Now doctoral student Boxi Zhang and Torbjörn Bengtsson of the School of Health Sciences, Örebro University, Örebro, Sweden, showed how this happens. Gingipains, virulence factors produced by Porphyromonas gingivalis, boost expression of the pro-inflammatory angiopoetin 2 while dampening expression of the anti-inflammatory angiopoetin 1 in the smooth muscle cells, with the net effect of increasing inflammation. Inflammation is strongly implicated in atherosclerosis. “. . .stimulation with wild-type P. gingivalis dramatically increases the gene expression of angiopoetin 2 in [aortic smooth muscle cells],” the investigators write. Angiopoetin 2 boosts migration of aortic smooth muscle cells, which promotes atherosclerosis, says Zhang. The investigators hope to find biomarkers that can aid in diagnosis and treatment of both diseases.


NEW FROM ASM
Long-Distance Travelers Likely Contributing to Antibiotic Resistance’s Spread

Swedish exchange students who studied in India and in central Africa returned from their sojourns with increased diversity of antibiotic resistance genes in their gut microbiomes. Anders Johansson of Umeå University, Sweden, et al. found a 2.6-fold increase in genes encoding resistance to sulfonamide, a 7.7-fold increase in trimethoprim resistance genes, and a 2.6-fold increase in β-lactams, all without any exposure to the antibiotics before or during the 35 students’ travel. Motivating the research was the observation that as head of a hospital infection control department, “it is very evident that resistance is no longer generated primarily in the hospital,” but that patients have become a source of increasing resistance, says Johansson. “Suppressing further spread after travelers return to their home countries is crucial,” he says.

Candida albicans: Love-Hate Relationship with Its Human Host

Among fungi, *C. albicans* is the most common to cause human disease, but it also acts as a commensal, in harmony with its host

Eric F. Kong, Paul Fidel Jr., and Mary Ann Jabra-Rizk

Among fungal species, *Candida albicans* is the one that most commonly causes human diseases, ranging from superficial to life-threatening systemic infections. As part of the commensal microbiota, *C. albicans* asymptptomatically colonizes mucosal surfaces in healthy individuals. However, as an opportunistic microbe, any disruption in the host environment, including immune dysfunction, can lead *C. albicans* to proliferate and invade virtually any site of the human host.

The capacity of this highly adaptable fungal species to shift from commensal to pathogen is due primarily to its ability to switch between yeast and hyphal forms. In addition, during many infections *C. albicans* forms biofilms, where its adhesion to a substrate leads to proliferation and hyphae formation. In particular, biofilm-associated catheter infections are the most serious, resulting in high morbidity and mortality. Meanwhile, the host defense against *C. albicans* involves multiple immune components, which vary by the anatomical site associated with disease. Here we highlight some of the diverse diseases, mucosal and systemic, caused by this microbe as well as pathogenesis and host immune responses.

### Mucosal Infections

The oral cavity is a primary target for opportunistic infections, particularly oral candidiasis, the most common oral opportunistic infection in HIV-infected (HIV+) and other immunocompromised individuals. Oropharyngeal candidiasis (OPC), commonly known as thrush, is characterized by hyphal invasion of mucosal tissue, and is manifested as white lesions formed on the palate, buccal mucosa, and tongue (Fig. 1). In addition to HIV+ individuals, candidiasis occurs in 35% of cancer patients on chemotherapy, Sjogren’s syndrome patients, infants, and the elderly, particularly denture wearers.

In fact, *Candida*-associated denture stomatitis (DS), the most common form of oral candidal infection in healthy individuals, is prevalent in approximately 70% of denture wearers. DS is a chronic disease characterized by localized or generalized inflammation of the denture-bearing mucosa. As a biofilm-associated condition, infection stems from the adherence of *C. albicans* to denture material, followed by hyphal infiltration of the denture-associated palatal tissue. The continuous seeding of biofilm-associated organisms is postulated to induce a chronic immune response resulting in inflammation of oral tissue. Despite therapy, this infection often re-establishes soon after antifungal treatment ceases.

Similar to the oral cavity, *C. albicans* resides among the vaginal microbiota and, opportunistically, is the leading causative agent of vulvovaginal candidiasis (VVC). An estimated 75% of all women of childbearing age develop VVC at least

### SUMMARY

- The capacity of *C. albicans* to shift from commensal to pathogen is due primarily to its ability to switch between yeast and hyphal forms, but also depends on its ability to form biofilms.
- Mucosal infections involving this fungus tend to arise among immunocompromised individuals; however, among those with functioning immune systems, exuberant defense responses may underlie the pathology of the infection.
- The growing use of implanted medical devices on which biofilms form is an important reason why the incidence of *Candida* infections continues to increase.
- While there are considerable gaps in our understanding of *Candida*-bacterial interactions in the host, researchers are beginning to adapt and improve animal models to better understand these interactions.
once. Several properties of *C. albicans* are known to play roles in causing VVC, including the ability to form hyphae. For example, strains of *C. albicans* that cannot form hyphae display significantly reduced vaginitis symptomatology. Further, estrogen production and microbiota disruption are considered primary etiologic contributors to this disease. However, because an exuberant host innate immune response is strongly associated with disease pathology, several investigators are now seeking agents for treating VVC that target this immunopathogenic response.

**Systemic Infections**

*Candida* species are the third most common cause of nosocomial bloodstream infections (BSI) in the United States, with mortality rates of 50%. The growing use of implanted medical devices is an important reason why the incidence of *Candida* infections continues to increase. In particular, biofilms on catheters provide a niche for microorganisms, protecting them from the host immune system and antimicrobial therapies. Successful therapy of these foreign-body infections can be a therapeutic challenge, typically requiring device removal.

Similarly, *Candida* is isolated with increasing frequency during intra-abdominal infections such as peritonitis, a serious complication for patients following surgical procedures and those on peritoneal dialysis. Peritonitis is an inflamma-

tory disease of the lining of the abdominal wall and organs. Polymicrobial peritoneal infections involving *Candida* species specifically are becoming increasingly common in the hospital setting. If untreated, infecting microorganisms can migrate into the bloodstream, causing systemic disease, sepsis, and high rates of mortality.

**Host Immune Responses**

Pattern recognition receptors (PRRs) on innate immune cells are the first to recognize and respond to surface molecules on the *C. albicans* cell wall. Signaling through toll-like receptors triggers release of pro-inflammatory cytokines, attracting macrophages to engulf *C. albicans* and send them into phagosomes, where oxidative enzymes degrade the fungal cells.

Although *C. albicans* triggers a CD4 Th1 phagocyte-dependent, adaptive immune response, it does not trigger antibodies. In the case of oral candidiasis, Th17 cells—not Th1 cells as was long believed—help to confer protective immunity. However, for other *C. albicans* infections, it is still not known whether Th1 or Th17 responses are critical. Other evidence suggests that specific morphological forms of *C. albicans* induce particular Th cell responses.

Innate immune responses appear to promote vaginitis symptoms, with fungal cells attracting polymorphonuclear leukocytes into the vagina, where they stimulate acute inflammatory responses without controlling *C. albicans*. Collectively, these findings point to vaginitis stemming from immunopathological responses and to the importance of understanding mechanisms involved in host-*Candida* interactions.

**Animal Models of Candidiasis**

Studying candidiasis in animals such as rodents is a valuable approach to better understanding pathogenesis and host responses as well as developing better ways to prevent and treat this disease. Although immunocompetent mice generally are not colonized with *C. albicans*, treating them with corticosteroids leads them to develop oral candidiasis, which is medically relevant because patients who use inhaled corticosteroids for asthma are at increased risk for this infection. The mouse version of candidiasis has a similar histopathology to candidiasis in humans, and is widely used for investigating immune mecha-
nisms against OPC, Candida virulence factors, and the efficacy of vaccines and antifungal agents (Fig. 2).

An estrogen-dependent model to study vaginitis in mice is well-established. Although mice do not harbor C. albicans as a commensal, it causes infections that closely parallel those in humans in terms of immunopathological responses and responses to drugs. Moreover, mice maintain a neutral vaginal pH that favors hyphal formation, which is what occurs during human vaginitis despite an acidic pH. Thus, despite these limitations, this mouse model has proved indispensable for dissecting pathogenesis and testing antifungal drugs.

To study Candida-associated denture stomatitis, some investigators are studying acrylic dentures, with both fixed and removable pieces, that can be implanted on the rat palate. The device is well-suited for longitudinal studies, which is important because DS is a chronic condition (Fig. 3). This approach is being used to monitor various stages of the disease and assess pathogenesis in mutant strains. However, one important drawback is that the dentures require relatively high inocula.

During polymicrobial, intra-abdominal infections of mice, C. albicans hyphal formation, known to be important for biofilm formation and virulence, surprisingly does not contribute to pathogenesis. Meanwhile, fungal biofilms can develop on implanted devices such as catheters, making it crucial to test catheter biofilm-associated pathogenesis in vivo. For example, C. albicans biofilms form on catheters implanted in the central venous system of rats, providing a realistic model of central venous catheter (CVC) infection sites. However, implanting CVCs requires considerable expertise, and the site is not easily accessible for monitoring subsequent developments.
A simpler approach involves implanting small catheters under the skin of mice or rats (Fig. 4). Within two days, a biofilm forms within the lumen of these catheters, yielding a means for studying such biofilms that lends itself more readily to screening and validating drugs under in vivo conditions and for studying the biofilm-forming capacity of mutant strains. Although the subcutaneous site is not good for capturing the effects of blood flow dynamics, serum proteins or other blood components, and humoral immunity, it accurately reflects the impact of other host environmental conditions and nutrient supplies on biofilm infections. Another advantage is that several technical repeats can be followed in each animal, which is essential for longitudinal studies.

**Perspective**

*C. albicans* infects many different anatomic sites and evokes equally diverse host responses. Steadily increasing rates of resistance to antifungal therapies provide a strong impetus to understand molecular mechanisms of pathogenesis at those sites as well as drug resistance within *C. albicans* biofilms with the goal of identifying novel therapeutic targets.

While microbial virulence factors were once a central focus of pathogenesis research, we now realize that host immune status and responses may be the major contributor to damage in the case of opportunistic pathogens such as *C. albicans*—a concept framed in 1999 by Arturo Casadevall, now at Johns Hopkins University, and Liise-Anne Pirofski of Albert Einstein College of Medicine. Based on their six categories of a damage response framework, *Candida* species were classified as Class 2 microorganisms, those that cause damage either in hosts with weak immune responses or in the setting of normal immune responses.

However, by itself, this classification does not account for the full complexity of *C. albicans* pathogenesis at various anatomical sites. Indeed, *C. albicans* almost fits in all six categories, depending on the site of infection. Thus, hematogenously disseminated candidiasis makes *C. albicans* a Class 2 microbe. In OPC, *C. albicans* is Class 1, damaging host only in situations of weak immune responses. In denture stomatitis, *C. albi-
is a Class 5 microbe, causing damage across the spectrum of immune responses, but which strong immune responses enhance. In VVC, \textit{C. albicans} qualifies as a Class 6 microbe, causing damage only under conditions of strong host immune responses. In intra-abdominal infections, \textit{C. albicans} is a Class 3 microbe, doing damage at both ends of the continuum of immune responses.

In the host, \textit{C. albicans} typically associates with the broader microbiota in biofilms where extensive interspecies interactions take place. The host is "an entity that houses an associated microbiome/microbiota and interacts with microbes such that the outcome results in damage, benefit, or indifference, thus resulting in the states of symbiosis, colonization, commensalism, latency, and disease,” note Casadevall and Pirofski. Furthermore, the medical community is only beginning to appreciate the fuller significance of polymicrobial etiologies.

While there are considerable gaps in our understanding of \textit{Candida}-bacterial interactions in the host, researchers are beginning to adapt and improve animal models to better understand these interactions. Examples include the oral candidiasis and peritoneal mouse models that are being used to characterize interactions between

\textbf{FIGURE 4}

\textbf{A} and \textbf{B} Up to 5 catheter fragments can be implanted in each mouse. \textbf{C} and \textbf{D} Scanning electron micrographs of explanted catheters with 2-day-old biofilm demonstrating the thick hyphal matrix formed in the lumen of the implanted catheters.
C. albicans and Staphylococcus aureus, a rat model of dental caries being used to study interactions of C. albicans with the cariogenic bacterial species Streptococcus mutans, and the animal catheter models being used to elucidate interactions in polymicrobial biofilms.

Eric F. Kong is a Ph.D. candidate in the Department of Molecular Microbiology and Immunology, School of Medicine, University of Maryland, Baltimore, Paul Fidel Jr. is a Professor at the Louisiana State University Health Sciences Center, New Orleans, and Mary Ann Jabra-Rizk is an Associate Professor in the Department of Oncology and Diagnostic Sciences, Dental School, and the Department of Microbiology and Immunology and Department of Pathology, School of Medicine, University of Maryland, Baltimore.

Suggested Reading


Genomic Sequencing and Other Tools for Studying Microbial Communities

Genomics and "meta'omic" tools are enabling us to explore the microbiome from three complementary perspectives—taxonomic, functional, and ecological.

Emma Schwager, Chengwei Luo, Curtis Huttenhower, and Xochitl C. Morgan

Along with single-cell genomic sequencing, the technologies collectively known as "meta'omics," including metagenomics, metatranscriptomics, metabolomics, and metaproteomics, are powerful new tools for learning how microbes in, on, and around us affect our health and well-being. We can then use this understanding to diagnose, prevent, and treat inflammatory bowel disease, diabetes, and other diseases.

As high-throughput techniques become increasingly more affordable and efficient, they become default tools for examining microbial communities. While applications such as taxonomic profiling are rapidly becoming standardized, others, such as single-cell genomic sequencing and transcriptional profiling, are still developing. Collectively, meta'omic tools enable us to explore the microbiome from three complementary perspectives:

- **taxonomic**, asking which taxa are present,
- **functional**, helping us determine what they are doing, and
- **ecological**, revealing how members of the community interact with each other and affect their hosts.

By combining these three perspectives, we can build models of microbiomes that can be used to predict responses to host changes such as diet, weight gain, or disease.

Meta'omics technologies and single-cell sequencing offer unparalleled new tools for learning about the human microbiome. As our technical capabilities progress, we can shift more of our focus to modeling the effects of the human microbiome on our health. Eventually, these tools can shed light on the dynamics that shape the microbiome from infancy through adulthood, how the microbiome as a community responds to perturbations such as dietary shifts, disease, or antibiotic treatment, and how the microbiome can be measured to predict disease and altered to treat it.

**Taxonomy: the Composition of Microbial Communities**

Until DNA sequencing technology revolutionized microbial community analysis, microbial ecologists were limited to studying microbes that either could be cultivated or identified by staining. Early use of DNA sequencing was limited almost exclusively to the 16S ribosomal RNA (rRNA) gene because much of its sequence is nearly identical across species. However, 10 variable regions with higher mutation rates are useful for distinguishing different taxa, enabling the creation of phylogenetic trees (Fig. 1).

Because this technique amplifies only a single gene, it is both simple and relatively inexpensive to use, and its cost continues to come down. Although powerful, however, 16S gene sequencing does not distinguish between bacterial strains with very similar 16S rRNA gene sequences—for example, between the closely-related *Escherichia*...
Nor does it describe community functions.

However, as sequencing costs decreased substantially, whole metagenome sequencing (WMS), or sequencing of all community DNA, became feasible. Like 16S, WMS can describe which taxonomic categories are represented in different samples, an approach called community
profiling (Fig. 1). Knowing the abundance of each taxon in a sample allows us to compare communities in different environments. For instance, we can compare the species on aerobic, dry skin with those in anaerobic, moist stool; or the gut communities of obese and lean people. The taxonomic profile for each sample is the percentage of sequences that fall into each taxonomic category, but the categories are determined differently for 16S and WMS data. In 16S sequencing, taxonomy is assigned by comparing each group of highly similar sequences to a reference database. In WMS sequencing, taxonomy is assigned by comparing either individual reads or assembled reads to reference genome databases. However, both processes are limited by the quality of the reference database—how many genomes are available and how well they represent the community.

At first, researchers sequenced microbial genomes of cultured isolates, but more recently they sometimes reconstruct genomes from WMS data. While read assembly from single-isolate ge-
nomes is much simpler, many microbes cannot be cultured in isolation because their nutritional or environmental requirements are exacting or unknown. Metagenomic assembly circumvents these difficulties, but requires many more sequencing reads to cover low-abundance taxa. Additional computational challenges arise from biological ambiguities such as horizontal gene transfers between unrelated taxa or sequences that are common to many taxa.

Single-cell sequencing sidesteps both these problems and helps to bridge gaps in reference genome databases (Fig. 2). Although single-cell sequencing does not require culture or metagenomic assembly, it presents other technical challenges, such as development of specialized techniques for isolating individual, high-quality cells. Furthermore, because of the amplification necessary to sequence such a small quantity of DNA, it is essential to prevent and identify contamination.

One important benefit of single-cell sequencing is that it expands genomic databases to include more unculturable and rare microbes, in turn bolstering information about these microbes from metagenomic studies. Furthermore, single-cell sequencing provides highly detailed information about populations of cells, allowing us to identify subpopulations and individual strains within a sample (Fig. 1). For example, WMS can uncover antibiotic-resistance genes in *E. coli* in the gut, but single-cell sequencing can show which individual *E. coli* cells have particular combinations of antibiotic resistance genes. Even more recently, synthetic long-read sequencing is offering an alternative means to single-cell sequencing for studying these population dynamics.

**Function: What Microbial Communities Are Doing**

While we can view microbiomes as collections of taxa, and observe how taxonomic profiles relate to patient characteristics such as diet and disease, we can also examine microbiomes from other perspectives. For example, they can be characterized in terms of their metabolic or functional capabilities. Thus, the fundamental unit of the microbiome could be either a taxon or a biochemical function.

Functional profiling tells us about the potential capabilities of the community by identifying genes within WMS sequences, either by searching them for sequences that resemble genes or by mapping them to reference databases of known genes. With such information, we can ask how these potential functions of a community change across different body sites or between disease and healthful states (Fig. 1). For example, stool is abundant in genes for metabolizing complex carbohydrates, while the oral cavity microbiome is rich in genes for metabolizing simple sugars, according to researchers working on the Human Microbiome Project (HMP). They also found that gene functional capabilities are more stable than species compositions across individuals, supporting the idea that overall community function is more important than are individual species within the human microbiome.

Knowing the sequence of a microbial genome tells us its capabilities, not which genes will be expressed in any particular situation. Thus, other metagenomic technologies are needed to understand how the microbiome reacts to its environment by measuring more transient community properties, such as which genes are being expressed or which molecules are being secreted. Specifically, metatranscriptomics provides a snapshot of gene expression by quantifying microbial mRNA, while metabolomics and metaproteomics quantify the metabolites and proteins, respectively.

These pictures of community gene expression and end products are often blurred because all three techniques face unmet technical challenges. For example, samples typically contain more tRNA and rRNA than mRNA, complicating efforts to determine mRNA sequences. Furthermore, in host-associated microbial communities, separating host and microbial RNA can prove difficult because the percentage of microbial RNA varies depending on the anatomic site from which it comes. Finally, in metabolomics and metaproteomics, the data consist of spectroscopy peaks rather than sequences, making it difficult to identify and characterize end products.

Despite these challenges, metagenomic technologies provide us with a wealth of information. We can compare, for example, the DNA and mRNA abundance of a specific gene to determine whether it is over- or under-expressed compared to its abundance in the community (Fig. 1). Some genes, such as those for producing methane in the gut, are present at low levels but are very highly
transcribed, while others, such as those for synthesizing phenylalanine and tryptophan in the gut, are present at relatively high abundance but rarely transcribed in individuals who eat high-protein diets.

We can also compare the metagenomes of healthy and diseased people to their corresponding metatranscriptomic and metaproteomic profiles to link differences in genetic potential with differences in what is being expressed and produced by the community. Knowing how taxonomy and function change between healthy and diseased states leads us to a third question: how do these changes occur?

Ecology: How Microbes Interact with One Another and their Hosts

A third way to characterize microbial communities is to consider them deterministic systems with measurable interactions and effects. Such systems can be characterized by measuring within-microbiome interactions as well as the reciprocal effects that the microbiome and host exert on each other (Fig. 1). Mathematical modeling can then help to predict the effects of interventions on the microbiome, in turn helping to identify treatments that prevent or cure disease. To build such models, we must measure interactions and effects, and iteratively validate these measurements and predictions.

AUTHOR PROFILE

Huttenhower: from Teaching Computers to Read to Teaching Them about Microbes

Curtis Huttenhower blames a series of “goofy” computer games for getting him hooked on problem solving in a data-driven environment. “I was a big fan of the Infocom games; Zork and Ballyhoo were what got me into language processing,” he says. Much later, during graduate school, he extended that interest in computers to harnessing them to analyze the human microbiome. “That was something I stumbled on during the later stages of my Ph.D. that seemed like it would be a good computational challenge.”

Today, Huttenhower, associate professor of computational biology and bioinformatics at Harvard University, works on the Human Microbiome Project and co-leads the Center for Characterizing the Gut Microbial Ecosystem in Inflammatory Bowel Disease. More broadly, members of his research group are developing computational methods for mining large-scale genomic and metagenomics data resources, he says. “My overall goals are...first, diagnostics: can we use the microbiome as a high-dimensional readout of host health to predict disease status, drug response, or other phenotypes [and] second, therapeutics: can we learn how to intervene with antibiotics, probiotics, or pharmaceuticals to shift the microbiome into ‘healthier’ states?”

Huttenhower, 34, was born in Pittsburgh, but at 3, moved with his family to rural Maine, then, at 7, to Weirton, W.Va., and then to Wheeling, at about 11. His parents recently moved to Rhode Island, where his father directs the small business development program at the University of Rhode Island. His younger sister is a materials engineer in Connecticut.

At 15, Huttenhower left high school after his sophomore year to attend Simon’s Rock College of Bard in Great Barrington, Mass. “High school wasn’t an especially challenging academic environment, and I felt ready to start college—and it was a blast,” he says. Two years later he transferred to Rose-Hulman Institute of Technology, where he earned his B.S. in 2000.

From there, he worked as a software design engineer for Microsoft in Redmond, Wash., before returning to school in 2002. Leaving industry to come back to academia was a hard decision, he recalls. However, doing so “makes it easier to advise students or postdocs thinking about industry positions, since there are different benefits and drawbacks.” He received his M.S. in 2003 from Carnegie Mellon University and his Ph.D. in computer sciences in 2008 from Princeton University. He did postdoctoral research at the Lewis-Sigler Institute for Integrative Genomics before joining the Harvard faculty in 2009.

Huttenhower has a few interesting hobbies for his too-infrequent spare time. He is an avid Dance Dance Revolution player, having learned it from the Japanese language team at Microsoft. “It’s great exercise, and it literally takes years to get really good,” he says. He also is a mid-distance, runner, enjoys hiking and camping, and reads a lot of science fiction, fantasy, and magical realism. To get away from technology for a while, he even once spent a vacation learning how to work a dairy farm. “I learned how to milk a cow and discussed antimicrobials and the gut microbiome with the owner,” he says. He lives with his two cats, Boy and Girl, and enjoys Boston’s mix of downtown fun and nearby rural escapes.

Marlene Cimons

Marlene Cimons lives and writes in Bethesda, Md.
We measure interactions and effects differently. To measure interactions, we search for correlations between two taxa, genes, transcripts, or metabolites in any type of meta’omic profile describing the microbiome. To determine which correlations are significant, statistical techniques must account for the complex structure of meta’omic data; this is an active area of research. To measure effects of the microbiome on the host and vice versa, we look for correlations between taxon, gene, transcript, or metabolite abundance with some host characteristic, such as diet or obesity. Because interactions and effects occur within the context of a host environment, measuring and interpreting them requires choosing a model system.

In general, researchers use one of three types of model systems for studying microbiomes: in vitro, animal, and human. In vitro systems are simple, culturing specific sets of taxa under particular conditions. Because the taxonomic profile and environment are so tightly controlled, interactions within them can be measured very accurately. For example, the symbiosis of two taxa can be studied by growing them both separately and in co-culture under the same conditions, and measuring their growth rates, metatranscriptomes, and metabolomes.

Animal models resemble human biology more closely than can in vitro systems. In fact, many of the effects of the microbiome, such as its importance in immune system development, were first noted in animals systems. Animals such as mice are uniform, easy to colonize with specific bacteria, and easy to perturb by administering antibiotics or changing diet. In contrast to mice, the human diet, environment, and genetic makeup vary greatly among individuals. This variability presents challenges when applying what we learn in model systems to diverse human populations, meaning we need much larger numbers of subjects in human studies to detect potential effects of the microbiome on human health. Effects that are real rather than study artifacts should be reproducible across comparable studies.

When measuring microbiomes, differences in methodology can greatly influence measurements. For example, which variable region of the 16S rRNA gene is sequenced affects the resulting abundances of certain taxa. Furthermore, once reads are sequenced, bioinformatic choices affect results as well. Researchers now use at least 20 different tools, reliant on three distinct approaches, to profile taxa. Deciding which tools are appropriate for which tasks would make it easier to compare studies. Further, it is crucial to compare different population groups to understand which microbiome effects are general and which are population specific.

Establishing effects is only part of the goal of characterizing relationships between the microbiome and human health. Another important goal is to predict the response of the microbiome to clinical interventions, a process that depends on developing well-validated models. This validation requires model systems that can be manipulated, and are replicable and inexpensive to use. Although results from studying in vitro model systems may be difficult to extrapolate to how microbiomes affect the human body, these systems are being matched more closely to human physiology, particularly the gut, by incorporating elements such as intestinal epithelial cells and simulated intestinal movement. With such refinements, we may more accurately describe the way multiple microbes interact with one another to form biofilms, the kinetics of diffusion for small molecules and microbes in human-associated habitats such as the mouth or gut.

Although we understand much about the flow of nutrients such as carbon and nitrogen on a macro-ecological scale, we still have much to learn about the physical and ecological dynamics that shape our microbiomes.

Emma Schwager is a Ph.D. Candidate, Curtis Huttenhower is an Associate Professor, and Xochitl C. Morgan is a Research Scientist in the Department of Biostatistics, Harvard T. H. Chan School of Public Health and the Broad Institute of MIT and Harvard, and Chengwei Luo is a Research Associate in the Broad Institute of MIT and Harvard, Cambridge, Mass.

Suggested Reading


Kolmender, C. A., and W. M. de Vos. 2014. Metapro-


Fecal Microbiota Transplantation: Harnessing the Gut Microbiota to Treat Disease

Despite technical and regulatory questions, this procedure appears effective for treating patients with persistent Clostridium difficile infections

Hassan Ziud, Brianna Bakow, and Colleen R. Kelly

Fecal microbiota transplantation (FMT) involves the transfer of consortia of bacteria from healthy individuals to patients with Clostridium difficile infection (CDI) or other conditions to promote recolonization with missing components of intestinal flora. FMT dates as far back as 4th-century China when human fecal suspensions were used to treat food poisoning and severe diarrhea and has been used in veterinary medicine to treat ruminal disorders at least as far back as the 17th century.

Contemporary use of FMT in humans traces to 1958 when Ben Eiseman, an American surgeon, used this procedure to treat four patients with pseudomembranous colitis. Since then, FMT, also known as stool transplant or fecal bacteriotherapy, has been used more and more often to treat patients with CDI. During the past decade, for example, CDI epidemics in the United States and Europe led to a steadily increased use of FMT.

Recurrence of CDI after a course of standard therapy, typically with metronidazole or vancomycin, is a common clinical problem. Though previously considered a “last resort” for patients with CDI, interest in FMT among physicians and researchers is surging, leading to increased numbers of publications and registered clinical trials. Its high efficacy in treating CDI symptoms is prompting some investigators to test whether FMT will prove useful for treating several other disorders associated with microbial dysbiosis, including inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), the metabolic syndrome, neurodevelopmental disorders, autoimmune diseases, and allergies.

In 2013, the FDA announced it was classifying fecal matter for FMT as both an investigational new drug (IND) and a biologic, requiring formal regulatory review of INDs before beginning clinical procedures (Microbe July 2013, p. 274). The agency later agreed to exercise enforcement discretion by waiving this IND requirement when FMT is used to treat CDI patients who fail to respond to standard therapies provided that their physician obtains adequate informed consent, including a signed statement that the use of FMT products to treat C. difficile is investigational and to hold discussions with patients about FMT risks. Well-designed and well-executed randomized trials are now needed to further define the role of FMT in these microbiota-related conditions.

FMT for Treating C. difficile Infections

Of 536 patients treated with FMT for C. difficile infection, 87% experienced clinical resolution with no serious adverse events, according to Antonio Gasbarrini of A. Gemelli University Hospital in Rome, Italy, and his collaborators in their review from 2014. Cumulative experience is based on data from case reports.

SUMMARY

➤ Fecal microbiota transplantation (FMT) involves transfers of bacterial mixtures from healthy individuals to patients infected with Clostridium difficile or facing other medical conditions.
➤ Despite evidence that FMT is safe and effective, randomized controlled trials are necessary to evaluate FMT more fully, to determine the optimal route for administering microbiota to patients, and to investigate other variables.
➤ Criteria for choosing or excluding donors for FMT procedures are based mainly on medical histories and laboratory tests for infectious agents.
➤ Diverse efforts seek to standardize the collection, storage, and formulation of donor FMT samples, including to develop alternative “defined microbiota ecosystems” to use instead of fecal materials.
Separately, Els van Nood of the University of Amsterdam, Josbert Keller of the Academic Medical Center, both in Amsterdam, and their collaborators completed a randomized controlled trial in 2013. They infused donor feces into the duodenum of CDI patients, effectively resolving disease in 81% of those patients, compared to only 31% efficacy in another set of patients who instead received a standard course of vancomycin administered orally. Not only did FMT appear safe, with no serious adverse events, but the safety monitoring board halted the study early because it was deemed unethical to continue treating patients with the inferior antibiotic therapy.

Long-term follow-up of FMT patients is limited, according to Lawrence Brandt of Montefiore Medical Center in Bronx, New York, and his collaborators. In their follow-up study, 77 patients who were treated with FMT were followed for 10 years or less. Of these, four developed autoimmune diseases, rheumatoid arthritis, Sjögren’s syndrome, idiopathic thrombocytopenic purpura, or peripheral neuropathy, albeit without a clear relationship between the new disease and FMT.

Further randomized controlled trials are necessary to evaluate the efficacy of FMT, to determine the optimal route for administering microbiota to patients, and to investigate other factors that can or do affect intestinal microbiota composition.

**TABLE 1. Donor Exclusion Criteria**

<table>
<thead>
<tr>
<th>Absolute Exclusion</th>
<th>Possible exclusion</th>
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<tbody>
<tr>
<td>Risk of infectious agent</td>
<td>History of gastroenteritis co-morbidities</td>
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<tr>
<td>Known HIV, Hepatitis B or C infections</td>
<td>History of inflammatory bowel disease</td>
</tr>
<tr>
<td>Known exposure to HIV or viral hepatitis</td>
<td>History of irritable bowel syndrome, idiopathic chronic constipation, or chronic diarrhea</td>
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<tr>
<td>High-risk sexual behaviors</td>
<td>History of GI malignancy or known polyposis</td>
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<tr>
<td>Use of illicit drug</td>
<td>Systemic anti-neoplastic agents</td>
</tr>
<tr>
<td>History of major GI surgery</td>
<td>Metabolic syndrome</td>
</tr>
<tr>
<td>History of major GI surgery</td>
<td>Systemic autoimmunity</td>
</tr>
<tr>
<td>History of major GI surgery</td>
<td>Atopic diseases (asthma, eczema, eosinophilic GI disorders)</td>
</tr>
</tbody>
</table>

variables, including safety data. Publication of a double-blind, randomized controlled trial is comparing FMT delivered via colonoscopy with a sham procedure in which a recipient’s own stool is delivered via colonoscopy is expected by the end of 2015.

Despite these uncertainties, many physicians now recommend using FMT to treat recurrent or relapsing CDI when there are at least three recurrences and standard therapy has failed; refractory CDI, meaning cases of moderate CDI that do not respond to standard therapy with vancomycin after at least a week; and severe CDI which does not respond to standard therapy after 48 hours, according to Brandt and his collaborators. In all cases, primary consideration must be given to the severity and pace of a patient’s CDI when deciding whether early use of FMT is appropriate.

Choosing and Preparing Donors for FMT Procedures

Criteria for choosing or excluding donors for FMT procedures are based on their medical histories and specific laboratory test procedures (Table 1). Although identifying whether a donor is “optimal” is not yet possible, several factors are worth considering. For example, intimate contacts such as spouses likely share other, non-CDI infectious risks with their respective recipients, theoretically minimizing the risk of transmitting additional infectious agents.

However, fecal material from unrelated healthy donors is being used successfully at clinical centers and appears effective in treating CDI. Thus, there may be advantages in using fecal material from unrelated, healthy, but rigorously screened donors for FMT clinical procedures. For example, the greater availability of this broadly defined, volunteer donor pool could facilitate FMT procedures. Further, insisting that donors be related to recipients may lead some family members to feel coerced, while in other cases, potential donors might be excluded because of diseases or other risk factors, leaving their sick family members without recourse.

Donors should be free of any disease or condition that might, even theoretically, be associated with or transmitted by gut microbiota. The physicians performing FMT assume responsibility for evaluating potential donors. The primary purpose of questioning the donor is to ensure that he or she is in good health, and that any risk factors for diseases transmissible by stool can be identified. The donor interview is especially important to identify such risks, particularly those for which there are no or no appropriately sensitive laboratory tests.

Those meeting eligibility criteria then undergo serologic and stool testing for pathogens (Table 2). Pathogen tests supported by current professional society guidelines include HIV, hepatitis viruses, and *Treponema pallidum* for syphilis, cultures for pathogens commonly identified in stool specimens, such toxin-producing *C. difficile*, and ova and parasite tests. More rigorous testing may be advisable when donors have a history of residing in or traveling to tropical countries where such diseases are prevalent or in cases where the recipients are immunocompromised.

### Protocol for Donors, Recipients and FMT Clinical Teams

Physicians who are using experimental FMT protocols to treat CDI patients agree on follow-

<table>
<thead>
<tr>
<th>TABLE 2. Donor screening assays</th>
<th>Serologic</th>
<th>Stool</th>
<th>Other potential tests</th>
<th>Possible tests</th>
</tr>
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<tbody>
<tr>
<td>HIV 1 &amp; 2</td>
<td>Routine bacterial culture</td>
<td>Giardia</td>
<td>CMV</td>
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<tr>
<td>Hepatitis A, B, C</td>
<td>Ova &amp; Parasites</td>
<td>Cryptosporidium</td>
<td>Human T cell lymphoma virus</td>
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<tr>
<td>Syphilis (RPR)</td>
<td><em>C. difficile</em></td>
<td>Isospora &amp; <em>Cryptosporidium</em></td>
<td>EBV</td>
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<td><em>E. coli</em>0157</td>
<td><em>Dientamoeba fragilis</em></td>
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<td>Rotavirus</td>
<td><em>Blastocystis hominis</em></td>
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<td></td>
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<td>Listeria</td>
<td><em>Strongyloides stercoralis</em></td>
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<td>Vibrio</td>
<td><em>Entamoeba histolytica</em></td>
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<td><em>Helicobacter pylori</em></td>
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<td><em>Schistosoma</em></td>
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<td></td>
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<td><em>JC virus</em></td>
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...
ing several additional criteria as prudent. For instance, donors should avoid eating foods to which recipients are allergic for about 5 days prior to a procedure. Donors also are asked to notify the practitioner if they develop any one of several symptoms of an acute infection, including fevers, diarrhea, and vomiting between screening and donation. A gentle osmotic laxative may be used the night before the procedure and before the donor collects a stool sample of 50 to 100 g the morning of the procedure.

Antibiotic treatment of CDI patients with vancomycin typically continues until 1 to 3 days prior to the procedure. Recipients are typically asked to undergo a bowel cleansing preparation regardless of how the FMT will be administered and, optionally, to be treated with an antidiarrheal product such as loperamide prior to the procedure, which may aid in retaining the transplanted material. If FMT is to be delivered by nasogastric or nasointestinal tube, a proton-pump inhibitor may be administered to the recipient to prevent gastric acid from damaging or inactivating the donor microbiota.

To preserve microbiota for near-term use, samples should be kept in airtight containers on ice or room temperature but not frozen, and then samples should be used for FMT within 6 hours of being collected, if possible. Whole stool is then diluted and homogenized to make it easier to administer. Although the choice of diluents differs among practitioners, either preservative-free normal saline or sterile water is most commonly used. Household blenders, hand mixers, or simply shaking of the stool with diluents is effective. Diluted samples may be filtered to remove particulate matter using gauze pads or a strainer. Because stool is considered a level 2 biohazard, one may consider conducting these mixing procedures within a laboratory hood. Those who handle and mix fecal transfusion material should wear fluid-resistant gowns, gloves, and masks with goggles or another type of eye shield.

Frozen, encapsulated FMT samples also are being evaluated for safety and efficacy, according to Elizabeth L. Hohmann of Massachusetts General Hospital (MGH) in Boston and her collaborators. Of 20 recurrent CDI patients treated with frozen FMT capsules, 90% of them responded and there were no serious adverse events, they report.

Although the ideal volume for sample instillation into recipients is not established, 25–50-ml samples are typical for the upper gastrointestinal (GI) tract and larger volumes of 250–500 ml, for the lower GI. Whether these routes or others will prove best for administering FMT is not known and may vary with the needs and status of individual patients. Means used to administer FMT include fecal suspensions given via nasogastric and nasointestinal tubes, through a colonoscope, or as retention enemas. Delivery to lower rather than the higher GI tract leads to better CDI eradication rates, note Gasbarrini, and his collaborators. However, the nasogastric route appeared to be as effective as colonoscopic administration in a more recent, open-label pilot study, according to Hohmann and her collaborators at MGH in Boston.

Challenges before FMT Is Used More Widely

Despite good efficacy data, ease of administration, and lack of effective alternatives for many patients, FMT procedures still are not widely available. Challenges include questions regarding safety, about donor materials, and regulatory issues.

Although FMT appears safe for recipients, prospective and long-term data are lacking. Moreover, although the procedure is well tolerated, there are case reports of fevers, bacteremia, and flare-ups of inflammatory bowel disease after FMT. For example, among 80 immunocompromised patients with recurrent, refractory, or severe CDI, 12 patients (15%) treated with FMT had a serious adverse event within 12 weeks, with most of these events being unrelated to FMT, according to our multicenter retrospective analysis. Of the two deaths, one was the result of aspiration during sedation for FMT administered via colonoscopy. Importantly, however, there were no infections related to FMT, although other adverse reactions included self-limited diarrhea and ulcerative colitis flare ups. Concerns over transferring microbiota are not limited to potential infections among recipients, but include transmission of microorganisms which may increase risk for other conditions such as obesity and IBD.

Meanwhile, some patients face difficulties identifying suitable healthy donors, and, even if one is found, screening protocols may be
cumbersome leading to further delays from laboratory testing before treatment. Relying on fresh fecal material presents obvious logistical difficulties. Lastly, the FMT regulatory landscape is rapidly changing, and how long the recent FDA policy of enforcement discretion will remain in effect is not known.

Evolving Concepts in FMT

In the near future, individual physicians may no longer need to identify FMT donors or rely on fresh stool. Stool banks, such as the nonprofit OpenBiome in Medford, Mass., are centralizing donor screening and stool processing procedures, supplying physicians researchers who are either using FMT to treat individual patients or are conducting FMT clinical trials. Meanwhile, several for-profit companies also are supplying physicians and researchers with minimally modified stool preparations for testing in clinical trials. Alternative, defined microbiota ecosystems, in which the several species that are responsible for FMT therapeutic effects are being isolated, and several of these mixtures have proved effective in animal and human clinical trials. Ultimately, encapsulated formulations would be the most convenient method of delivery to patient recipients.

Evidence supporting the use of FMT for the treatment of recurrent C. difficile infection continues to build. Innovative approaches to collecting and preparing samples, including stool banks and commercial preparations of mixed bacterial cultures, provide hope for streamlining these practices in the future. Although challenges remain and regulation is necessary, agencies must recognize the unusual nature of FMT and adapt their policies as microbial-based therapeutics emerge.

Suggested Reading


Hassan Ziud is a hospitalist with the University Medicine Foundation in the Department of Internal Medicine, Alpert Medical School of Brown University. Brianna Bakow is a medical student at the Alpert Medical School of Brown University, and Colleen R. Kelly is a Gastroenterologist and an Assistant Professor of Medicine in the Department of Internal Medicine, Alpert Medical School of Brown University, and Lifespan Women’s Medicine Collaborative, The Miriam Hospital, Providence, Rhode Island.
The 2016 ASM Biodefense and Emerging Diseases Research Meeting will unite the individuals carrying out the research to defend against the growing threat of bioterrorism with the decision makers shaping the future biodefense research agenda, recognizing that emerging infectious diseases serve as a paradigm for handling the public threat of bioterrorism.

Join nearly 1,000 attendees at this event and stay up-to-date with the latest challenges and developments in the field.

Abstract submission opens: September 8, 2015
Abstract submission closes: October 29, 2015

www.asm.org/biodefense2016

Join ASM Speakers’ Bureau!

Interested in sharing your microbiology or immunology career experience with ASM Student Chapters?

ASM is looking for members employed in the clinical lab or industry, such as —

- Bioremediation
- Biosafety
- Biotechnology
- Dairy
- Food Safety
- Indoor Air Quality
- Medical Device
- Pharmaceuticals
- Policy
- Public Health
- Tech Sales
- Water Quality

The Speakers’ Bureau is designed to attract students to microbiology career opportunities. Speakers share with ASM Student Chapters information about their careers, how they got started and tips for success. Speakers can give a live, recorded or video call presentation!

ASM Members can visit http://bit.ly/ASMspeakers to learn more and sign up!
2016 Membership Dues Increase Approved

A Membership Task Force charged with analyzing our three-tier membership structure deliberated over the past year, and some excellent recommendations emerged from that group. ASM Members will be kept aware of those as the Membership Board moves to implement some of those suggestions.

One area evaluated by the Task Force was the dues rates for our three tiers, with particular emphasis on dues of other scientific societies. Emerging from that evaluation was a recommendation that dues be increased by 10% for the upcoming year, and the Membership Board proposed this to the Finance Committee, which approved the increase. As the leading Society in the microbial sciences, ASM has strived to keep membership dues affordable, while providing resources and opportunities for members to advance their science, careers and network.

The rationale for an increase includes three main items: (1) ASM has not had an increase in dues rates since the three-tier membership model was instituted three years ago; (2) ASM membership dues rates are well below those of scientific societies of similar scope and size; and (3) The cost to ASM of providing member benefits increases each year.

The renewal process will begin in September, so be on the lookout for your renewal notice then. We thank our members worldwide for their continued support.

<table>
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<tr>
<th>Tier</th>
<th>2015</th>
<th>2016</th>
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<tr>
<td>Premium</td>
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<tr>
<td>Contributing</td>
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<td>Postdoc</td>
<td>$20</td>
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Futures and Membership Strategic Planning

As you know, a broad cohort of ASM members, led by the Officers, are analyzing the future direction of ASM, including how we govern ourselves as a Society, how we should use our resources to be most effective, and assessing new capacities that we need to develop. Some of this process has been captured in the Futures Project, which you may have heard about if you were at the General Meeting in New Orleans, or through other contacts with the Society. An exciting part of this Futures strategic planning is in the beginning stages for the Membership Board.

Initial efforts have begun with two focus groups hosted in August at ASM Headquarters. ASM Officers and other leaders including Membership Board Chair Victor DiRita met with Branch and Division leaders. The discussions were wide ranging but focused on ways that ASM HQ and these two groups could work together to advance the Society and microbial sciences. The groups also discussed proposed new governance structure for the society. Valuable feedback was obtained that will shape future discussions about improving the nimbleness and efficiency of ASM’s decision-making, as well as ensuring that the Society remains the leader in advancing the microbial sciences.

Over the next six months, we will look at membership in a broad, global perspective, explore why ASM Membership matters to members, and people we would like to be members. Once this review has been completed, we will have a roadmap for the future ASM membership. We look forward to involving and informing our members about this process and the results.

Just Published by ASM Press: Principles of Virology

Available now through ASM Science, Principles of Virology is the leading virology textbook because it does more than collect and present facts
about individual viruses. Instead, it facilitates an understanding of basic virology by examining common processes and principles. Using a set of representative viruses to illustrate viral complexity and, this rational approach enables students to understand viral reproduction, and provides the tools for future encounters with new or understudied viruses.

This new edition is fully updated to represent the rapidly changing field of virology. A major new feature of this edition is the inclusion of 26 video interviews with leading scientists who have made significant contributions to the field of virology. These in-depth interviews, conducted by Vincent Racaniello, provide the background and thinking that went into the discoveries or observations connected to the concepts being taught in this text. Students will discover the personal stories and twists of fate that led the scientists to work with viruses and make their seminal discoveries.

*Principles of Virology* is ideal for teaching the strategies by which all viruses reproduce, spread within a host, and are maintained within populations. It is appropriate for undergraduate courses in virology and microbiology as well as graduate courses in virology and infectious diseases. Volume I: Molecular Biology covers the molecular biology of viral reproduction. Volume II: Pathogenesis & Control addresses the interplay between viruses and their host organisms. The two volumes can be used for separate courses or together in a single course. Each includes a unique appendix, glossary, and links to Internet resources such as websites, podcasts, and blogs.
ASM Public Affairs

ASM Comments on NIH RFI on the Framework for the NIH-wide Strategic Plan

In August, ASM submitted comments to the National Institutes of Health (NIH) RFI on the Framework for the NIH-wide Strategic Plan. The comments will help NIH develop a five-year strategic plan to outline a vision for biomedical research that will pursue fundamental knowledge about the nature and behavior of living systems and apply that knowledge to extend healthy life and reduce illness and disability. A description of the NIH’s strategic plan project is available at http://www.nih.gov/about/strategic-plan/. The ASM comments are posted on the Web at https://www.asm.org/index.php/publicpolicy-2/statements-testimony/statementstestimony/93633-nih-sp-8-17-15.

ASM Comments on Department of State and Commerce Control Regulations for Certain Pathogens

ASM submitted comments to the U.S. Department of State and Department of Commerce regarding the Category XIV materials (Toxico logical Agents, Including Chemical Agents, Biological Agents, and Associated Equipment) included on the United States Muni tions List and the Commerce Control List. The ASM also addressed the proposed definition of fundamental research in the regulations, which is problematic and fails to adequately encompass the full scope of activities and outcomes of such research. The ASM pointed out that the too-narrow definition has significant impacts on both the research community and the export of U.S. technology. To read the comments, go to https://www.asm.org/index.php/publicpolicy-2/statements-testimony/137-policy/documents/statements-and-testimony/93632-bis-8–17-15.

ASM Meeting at DARPA

In July, Ronald Atlas, Chair of the Public and Scientific Affairs Board, Kenneth I. Berns, Chair, Committee on Biodefense and Janet Shoemaker, Director, ASM, Office of Public Affairs, met with program officials from the Defense Advanced Research Projects Agency (DARPA) to discuss microbiology research. The mission of DARPA is to make pivotal investments in breakthrough technologies for national security. They met with COL Matthew Hepburn, M.D., Program Manager, Biological Technologies Office. This office addresses the dynamic threats of emerging infectious diseases.

ASM Supports Increased Funding for Biodefense

In August, the ASM signed onto a letter from the Informal Coalition on Biodefense and Public Health Preparedness expressing concern over the funding levels for programs critical to the nation’s preparedness against threats both naturally occurring, like Ebola and pandemic influenza, and deliberate, such as chemical, biological, radiological or nuclear (CBRN) events. The letter pointed out that the $255 million funding levels included in the Senate and House FY 2016 Appropriations bills are not sufficient to build and maintain key capabilities to prepare for public health emergencies. To read the entire letter, go to http://www.asm.org/images/PSAB/Biodefense-House-8–15.pdf.

NIH Salary Limit Reductions Coalition Letter

In August, ASM signed onto a letter requesting that the House Appropriations Committee reject a proposal to reduce the salary limit imposed on extramural researchers funded by the Department of Health and Human Services (HHS) to Level III of the Executive pay scale. Section 203 of the FY 2016 Labor-HHS appropriations would reduce the salary limit on HHS extramural grants from Executive Level II to Executive Level III ($168,700 in 2015), a cut of $14,600 (8%). This cut follows a $20,000 (10%) cut from Executive Level I to Executive Level II in the FY 2012 funding bill. Lowering the extramural salary limit particularly disadvantages the most productive investigators who have a sustained track record in breakthrough discoveries, and will have a chilling effect on research institutions’ ability to recruit and retain the most gifted new investigators. The letter urged congressional appropriators to retain the extramural salary limit at Executive Level II, which will help institutions continue to attract and retain the most talented investigators. To read the entire letter, go to http://www.asm.org/images/PSAB/FY-2016-Salary-cap.pdf.

ASM Sends Request for Personal Stories About S&T Meetings

ASM is a member of a coalition of societies working with the American Association for the Advancement of Science (AAAS) to encourage governmental support for scientific meetings. Funding for scientific meetings and for federal scientists to attend these meetings has been cut drastically. The AAAS asked scientists to provide stories highlighting the important role that meetings play in advancing science. Through personal anecdotes the key role of scientific meetings can be demonstrated for those making federal policy regarding travel and meetings. The AAAS plans to compile stories from various disciplines and communicate them to Congress and federal agencies to show the value of science and technology meetings. If you would like to participate in the campaign, go to http://www.aaas.org/yourstory. An overview of the campaign is available at http://www.aaas.org/call-for-conference-stories.

ASM Presents at June CCCLW Meeting

ASM Public and Scientific Affairs Board Professional Affairs Committee
member Janice Matthews-Greer attended the Coordinating Council on the Clinical Laboratory Workforce (CCCLW) meeting on 29 June in Chicago, Ill. Matthews-Greer highlighted ASM’s educational efforts on behalf of clinical laboratory professions and participated in discussions on patient outcome data. The CCCLW is a coalition of laboratory organizations working together to ensure a high-quality workforce by increasing the number of qualified clinical laboratory professionals, increasing public awareness of clinical scientists’ value in achieving positive patient outcomes, and enhancing the image of clinical laboratory professionals. More about the organization can be found at http://www.ccclw.org/.

**ASM Participates in S-FAR Summer Series**

The U.S. Stakeholder Forum on Antimicrobial Resistance (S-FAR) presented a series of webinars between July and August 2015 on various areas of concern in antimicrobial resistance. ASM staff participated in “S-FAR Summer Series #1: Antimicrobial Stewardship and Data Collection Components of the National Action Plan—Human Medicine” on 15 July; “S-FAR Summer Series #2: Stewardship, Data Collection, and Research Components of the National Action Plan—Veterinary Medicine” on 30 July; and “S-FAR Summer Series #3: Research & Development (R&D) and Incentive Components of the CARB National Action Plan” on 20 August. S-FAR is a national partnership convened by the Infectious Diseases Society of America (IDSA) consisting of over 70 national health organizations. You can learn more about the S-FAR partnership by going to http://www.s-far.org/.

**ASM Presents at Annual CMS Clinical Lab Fee Schedule Meeting**

On 16 July, ASM presented comments at the annual Public Meeting Regarding the Clinical Laboratory Fee Schedule for CY 2016 at the Centers for Medicare & Medicaid Services (CMS) in Baltimore, Md. This meeting allows stakeholder input on the basis of payment and the amount of payment by CMS for clinical laboratory tests introduced each calendar year. To read ASM comments and see the meeting agenda, please go to http://www.asm.org/index.php/public-policy-2/137-policy/documents/statements-and-testimony/93598-clfs-7–15.

**FedEx Discontinues Transport of Select Agents**

On 17 July, FedEx notified federal agencies that they would no longer accept Select Agents for transport on FedEx Express. Because FedEx is a large multinational shipping company, many laboratories that identify and ship biological select agents and toxins may be affected by this decision. Recently, a national medical courier organization assembled a list of couriers who offer transport of medical specimens, many of them willing to carry Select Agents. To see this list, click the link and join https://integritydelivers.webconnex.com/MedCourierCnxMemberList.

**ASM Attends DURC Stakeholder Workshop**

On 22 July, ASM staff attended the USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (DURC) Stakeholder Engagement Workshop, a public meeting co-hosted by The White House Office of Science and Technology Policy and the National Institutes of Health. The purpose of the meeting was for interested stakeholders to discuss their experiences and challenges in the implementation of the U.S. Government Policy for Institutional Oversight of Life Sciences DURC (the Policy). There were interactive case studies that illustrated the factors that investigators and institutions consider when determining whether research is subject to the Policy as well as a series of panels comprised of institutional representatives to share their respective approaches to the Policy. To see the resources from this Workshop, please go to http://www.phe.gov/about/OPP/DURCworkshop/Pages/overview.aspx.

**ASM Meetings and Conferences**

**ASM Microbe 2016: Abstract Submission Opens Soon**

Call for abstracts opens in November 2015 for the all-new ASM Microbe 2016 (16–20 June 2016, Boston, Mass.). Showcasing the best microbial sciences in the world, this inaugural meeting integrates ASM’s General Meeting and ICAAC and explores the full scope of the microbial sciences. Submit your abstract to share your latest researching findings with peers from around the world. Come to this one-of-a-kind event to benefit from targeted trans-disciplinary sessions, topic-based networking events, an expanded Poster Hall, and more. For more information, visit www.asm.org/microbe2016.

**2016 ASM Biodefense and Emerging Diseases Research Meeting: Submit Your Abstract Today**

Abstract submission for the ASM Biodefense and Emerging Diseases Research Meeting (8–10 February, 2016, Arlington, Va) closes on 29 October 2015. Submit your abstract today for a chance to present your research in front of nearly 1,000 scientists, public health researchers, and policy makers.

Recognizing that emerging infectious diseases serve as a paradigm for handling the public threat of bioterrorism, this meeting unites the individuals carrying out the research to defend against the growing threat of bioterrorism with the decision makers shaping the future biodefense research agenda.
Save the Date: 32nd Clinical Virology Symposium

Join your peers from 19 to 22 May in 2016 at Daytona Beach, Fla., for the 32nd Clinical Virology Symposium. Stay up-to-date with the latest research on viral infections through focused plenary sessions as well as poster and case presentations. New for 2016: the Symposium will take place from Thursday through Sunday, and will include increased networking opportunities for you to expand connections with fellow laboratorians, physicians, and biomedical researchers involved in patient care and public health. Learn more at www.clinicalvirologysymposium.org.

Upcoming ASM Conferences

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

- 7th ASM Conference on Biofilms (24–29 October 2015, Chicago, Ill.)
- 4th ASM-ESCMID Conference on Meticillin-resistant Staphylococci in Animals: Veterinary and Public Health Implications (2–5 November 2015, Chicago, Ill.)
- @ASM Conference on The Individual Microbe: Single-cell Analysis and Agent-Based Modeling (18–20 March 2016, Washington, D.C.)
- 13th ASM Conference on Candida and Candidiasis (13–17 April 2016, Seattle, Wash)
- ASM Conference on Streptococcal Genetics (31 July–3 August 2016, Washington, D.C.)
- 5th ASM Conference on Salmonella (29 August–1 September 2016, Potsdam, Germany)
- 6th ASM Conference on Beneficial Microbes (9–12 September 2016, Seattle, Wash.)

Education Board

ASM Education Planning Calendar

The 2015–2016 ASM Education Planning Calendar is now available! With descriptions, deadlines, and other details about the Society’s education programs, the calendar highlights ASM activities and resources designed to help members deepen their knowledge and enhance their skillsets. It’s a must-read for educators, students, and postdoctoral scientists seeking success in the microbial sciences. Download the calendar today at http://www.asm.org/educationcalendar.

Biology Scholars Program Update: New Cohort, Future Planning

This year, 38 biology educators who seek to improve both their teaching and student learning were selected as scholars of the 2015–2016 ASM-NSF Biology Scholars Program. The new cohort gathered in Washington, D.C., for the annual program institutes, which took place this summer at ASM headquarters.

Sponsored by the Education Board with support from the National Science Foundation since 2005 (grant no. 1022542), the Biology Scholars Program is a comprehensive professional development initiative that helps biologists (i) make evidence-based enhancements to their teaching at the undergraduate level and (ii) work with professional societies to lead science education reform.

The program achieves its goals through its Assessment, Research, and Transitions Residencies— independent, yet intertwined training experiences that meld online learning with in-person and intensive multiday institutes.

“Our 2015–2016 scholars are outstanding biologists committed to improving undergraduate biology education,” says ASM Education Director Amy Chang. “Through this program, they’ll receive professional development, close mentoring from facilitators, support from a national network of peers and advisers, opportunities to participate in special activities at the annual ASM Conference for Undergraduate Educators (ASMCUE), and preparation for leadership and mentoring roles within the education research community.”

Twenty biologists entered the fifth annual Assessment Residency. Led by Carol Hurney (James Madison University), Sarah Ades (Penn State University), Gail Begley (Northeastern University), Bryan Dewsbury (University of Rhode Island), and Jordan Moberg Parker (University of California, Los Angeles), the Assessment Residency helps Scholars design course goals and assessments aligned with evidence on how people learn. Participants also create and implement evaluations that provide formative and summative feedback. At the residency’s Measuring Student Learning Institute in June, the new scholars learned to develop measurable and effective course goals, identify methods and instruments to measure student learning, and establish collaborations with colleagues to improve student learning.

Fifteen biologists entered the Research Residency, which helps scholars deepen their understanding of evidence-based research in biology education learning. Participants also design and implement experiments to assess student learning. Led by Loretta Brancaccio-Taras (Kingsborough Community College), Stephanie Gardner (Purdue University), Nitya Jacob (Oxford
College/Emory University), Cynthia Miller (University of Louisville), and Miriam Segura-Totten (University of North Georgia), the residency is now in its 11th year. At the Scholarship of Teaching and Learning Institute in July, incoming Research Residency Scholars refined their research questions, identified existing resources, and developed their understanding of data collection and interpretation methods for assessing student learning in biology.

Three biologists entered the Transitions Residency, now in its seventh year. In this residency, participants “transition” from conducting scholarly work in student learning to preparing for publication in peer-reviewed biology and science education venues. In July, the residency’s From Science Education Research to Publication Institute offered a forum for leaders Marcy Peteroy-Kelly (Pace University), Johanna Krontiris-Litowitz (Youngstown State University), and Elisa Stone (University of California, Berkeley) to help participants organize data, identify relevant literature, and develop plans and timelines for writing and submitting manuscripts.

After their yearlong residencies, the cohort will join the Biology Scholars Alumni, a group committed to creating and disseminating examples of scholarship in teaching biology. Alumni are encouraged to remain involved with the Biology Scholars Program in a number of ways, including participating in the program’s online community, scholar-established writing club, and select program meetings at ASM/CUE.

The Biology Scholars Program has grown from 16 scholars in its first iteration to more than 270 scholars and alumni in five countries. NSF funding of the program expired in September 2015. However, the Biology Scholars Program’s positive impact on participants and stakeholders has resulted in Societal efforts to sustain the initiative. These efforts include modifying the overall program to focus more on online activities and shifting the face-to-face mentoring component to an annual scholar gathering concurrent with ASM/CUE.

To learn more about the Biology Scholars Program, visit www.biologyscholars.org.

2015 Education Board Programs Awardees
An important goal of ASM’s Education Board (EB) has been to provide educational opportunities and professional development experiences for individuals who choose a career in microbiology. EB sponsors a wide array of programs for undergraduate, graduate, and postdoctoral fellows. The undergraduate and graduate fellowships are funded by ASM, and the postdoctoral fellowship is funded by the Centers for Disease Control and Prevention (CDC).

The fellowships programs that EB supports include the ASM/CDC Postdoctoral Research Fellowship Program, ASM Robert D. Watkins Graduate Research Fellowship, ASM Undergraduate Research Fellowship, and ASM Undergraduate Capstone Program.

The Board continues to promote the “Fellowship Cost Sharing Program” in an effort leverage funds with participating institutions and maximize the number of awards offered. The program allows institutions to partner with ASM and provide partial or full student stipend. The success of the cost sharing program resulted in a total of 65 awards made for the four programs in 2015.

ASM/CDC Postdoctoral Research Fellowship Program. The ASM/CDC Postdoctoral Research Fellowship Program is a two-year training program that supports postdoctoral fellows to conduct full-time research with the overall objective of developing practical applications of microbiology, immunology, and epidemiology for the diagnosis and prevention of infectious diseases. The fellowship supports comprehensive, interdisciplinary training on global public health issues.

Eight fellows were offered the 2015–2017 awards, and six accepted. Award packages provide up to $48,600 for stipend and up to $5,500 for professional development and health insurance benefits. Fellows will perform research at the Centers for Disease Control and Prevention (CDC) in Atlanta, Ga.

This fellowship is managed by ASM. Funds are provided by the Centers for Disease Control and Prevention.

ASM Robert D. Watkins Graduate Research Fellowship Program. One of the important focuses of ASM’s strategic plan is to foster higher levels of educational preparation in the sciences, particularly the microbiological sciences for underrepresented groups. The goal of the ASM Robert D. Watkins Fellowship is to help increase the number of students from underrepresented groups who complete doctoral degrees in the microbiological sciences. The fellowship supports senior-level graduate students completing their doctoral degree in the microbiological sciences and provides professional development training to facilitate student success. The award includes a stipend of up to $21,000 a year for up to three years, travel funds for fellows to present at ASM Microbe annually if their abstract is accepted, and funds to participate in a student professional development program one time during their three-year tenure of the fellowship.

Through the success of the Cost Sharing Program, 6 students were awarded the 2015–2018 fellowship and 15 students received Honorable Mentions. Honorable Mentions recognize the achievements and accomplishments of the many outstanding applications received but that could not be funded due to limited funding. Students who receive Honorable Mention do not receive a monetary award, however they are listed in Microbe with funded fellows and also invited to par-
participate in ASM Education Board activities. Funding for the Robert D. Watkins Graduate Research Fellowship is provided by the Society.

ASM Undergraduate Research Fellowship Program (URF). The goal of this fellowship is to encourage students to pursue careers or advanced degrees in the microbiological sciences. The fellowship provides an opportunity for students to participate in a research project at their home institution and gain experience presenting the results of their research at the ASM General Meeting.

Forty-three awards were given to undergraduate students to conduct a research project with an ASM faculty mentor beginning in the summer of 2015. Of the 43 students awarded, 30 students are from research and doctoral degree-granting universities and 13 students are from primarily undergraduate and masters’ degree-granting institutions. Each student receives a stipend award of up to $4,000, travel award to attend the Research Capstone Institute held prior to the 2016 ASM Microbe, and two year student membership to ASM. Funds for the program are provided by the Society.

ASM Capstone Research Experience. The ASM Capstone Research Experience seeks to enhance the professional development of students after their research experiences. Sixteen Capstone awardees were supported to attend the 2015 ASM Research Capstone Institute held prior to the asm2015 and also to attend the

### 2015 Education Board Fellowship Awardees

(*Institution participated in Education Board Fellowship Cost Sharing Program)

(**Pending CDC funding approval.)

**ASM Undergraduate Research Capstone Program (Awardees)**

- **Ivan Albino Flores**, Food and Drug Administration (Mentor, Manuel Osorio), Inactivated *Shigella* as Effective Vaccines and Vaccine Vectors
- **Nicole Colon**, University of Puerto Rico, Cayey (Mentor, Chad Lizarda), Analysis of Endophyte Fungi in Rice Grains
- **Jennifer Gil Acevedo**, University of Puerto Rico, Rio Piedras Campus (Mentor, Javier Avalos), Electroporation and Its Effects in Population Growth Curves and Bacterial Inhibition in the GQD with Silver
- **Arielle Gomes-Williams**, Smith College (Mentor, Christine White-Ziegler), The Thermoregulation of Uropathogenic *E. coli* Gene Regulation during a Fever
- **Floriciel Gonzalez**, Washington State University (Mentor, Birgit Scharf), Both Rotating Flagella and Lipopolysaccharides are required for Infection of *Agrobacterium* sp. H13–3 by Flagellotrophic Bacteriophage 7–7–1
- **Manhin Lam**, New York City College of Technology (Mentor, Davida Smyth), Microbiology of the Built Environment: the Changing Microbiome of New York City College of Technology
- **Lucy LeBlanc**, University of Nevada, Las Vegas (Mentor, Penny Amy), Isolation and Characterization of a Novel Phage Lysin Active against *Paenibacillus larvae*, a Honeybee Pathogen
- **Lacey Lopez**, University of Missouri-Columbia (Mentor, Deborah Anderson), The Type VI Secretion System of *Yersinia pestis* Influences Intracellular Survival
- **Livia Lown**, University of New Mexico (Mentor, Samuel Lee), An Optimized Solution Containing Micafungin, Ethanol and Doxycycline Inhibits *Candida albicans* Biofilms
- **Megan Miller**, New Mexico State University (Mentor, Kathyn Hanley), Role of Interleukin-1 in Expression of Pro-Inflammatory Cytokines during *Streptococcus pneumoniae* Colonization
- **Quang Nguyen**, Duke University (Mentor, Sallie Permar), Robust ADCC and Virus Capture Activity of Env-specific Monoclonal Antibodies Isolated from Blood and Breast Milk of Chronically Infected African Green Monkeys
- **Samuel Pannoni**, University of Montana (Mentor, William Holben), Developing Microbial Biomarkers for Elk (*C. canadensis*) Health Monitoring
- **Madhusudan Rajendran**, University of Wisconsin – Madison (Mentor, Douglas Weibel), Characterization of the Mechanism of Action of Gyramide C2, an Inhibitor of Bacterial DNA Gyrase
- **Jason Thomas**, California State University, Fresno (Mentor, Mamta Rawat), Oxidative stress in *Staphylococcus aureus* and *S. epidermidis* iNfection in Macrophages and Lung Epithelial Cells
- **Dorothy Tovar**, University of Massachusetts Amherst (Mentor, Wilmore Webley), Delta-Tocotrienol Reduces Susceptibility to Chlamydial Infection in Macrophages and Lung Epithelial Cells
- **Theresa White**, Towson University (Mentor, Michelle Snyder), Structural Characteristics of *Dictyostelium discoideum* Tir Domain

**ASM Undergraduate Research Fellowship Program (Awardees)**

- **Michael Bamimore**, Rutgers University (Mentor, Eric Klein), Role of MreB in Stalk Synthesis in *Caulobacter crescentus*
Megan Barefoot,* Georgetown University (Mentor, Heidi Elmendorf), The Role of Flagella Frequency in the Attachment Mechanism for *Giardia lamblia*

Jesse Black,* University of Illinois at Champaign-Urbana (Mentor, Rachel Whitaker), Host-Virus Interactions between Purified Viruses from Yellowstone and Kamchatka Hot Springs and Panel of *Sulfobus islandicus*

Cassie Bonavita,* Radford University (Mentor, Justin Anderson), Examination of Bacteria of Mosquitoes in the Amazon Rain Forest in Relation to Various Arboviruses, Specifically Dengue Fever

Joshua Bram, Pennsylvania State University (Mentor, Andrew Read), The Effect of Combination Therapies on the Emergence of Drug Resistance

Lucas Dailey, Rochester Institute of Technology (Mentor, Michael Savka), Overexpression of novI in *Burkholderia pseudomallei* to Identify the Complement of Acyl-Homoserine Lactone Communication Signals

Roslyn Dermody,* Colorado State University (Mentor, Torsten Eckstein), Identification of the Lipid Profile of the Bp82 Strain of *Burkholderia pseudomallei*

Daniel Desaults,* University of Wisconsin-Madison (Mentor, Cameron Currie), Characterization of Symbiotic Microbes Associated with the Monarch Butterfly (* Danaus plexippus *)

Jasmine Donkoh,* Colorado State University (Mentor, Brian Foy), Mosquito-palatial Properties of Targeting Dieldrin Resistant Channel in Malaria Transmitting Vectors

Jonah Einson,* University of Massachusetts, Amherst (Mentor, David Sela), Microbial Community Analysis of Industrial Food Production Facilities

Adam Fishburn,* University of California, Merced (Mentor, Clarissa Noble), Interspecies Interactions between *Streptococcus* and *Candida* in Biofilms

Katherine Fullerton,* Rutgers University (Mentor, Lily Y. Young), Determination of the Presence of the Anaerobic Benzoyl-CoA Degradation Pathway in Animal Samples

Aakash Gandhi,* Washington University in St. Louis (Mentor, Audrey Odom), Characterization of the Unique Phosphofructokinase of Malaria

Matthew Hapstack,* Clemson University (Mentor, Lesly Ternes-vari), The Effect of Stress on Protein Translation in *Entamoeba histolytica*

Desiree Huerta, University of Nevada, Las Vegas (Mentor, Duane Moser), Comparison of Microbial Communities of an Endangered Desert Fish Habitat (Devils Hole) and Its Mannmade Replica

James Iordanou,* Oakland University (Mentor, Sara Blumer-Schueette), Contact Mechanisms Associated with Metal Oxidation in Acidic Environments

Natasia Jacko,* Rutgers University (Mentor, Siobain Duffy), What and Where Are the Native American Begomoviruses?

Joseph Johnson,* St. Joseph’s University (Mentor, Catalina Arango), Identification of the Regulatory Sequences of the apg-melA Operon in *Sinorhizobium meliloti*

Adam Kiro Singh,* University of Nevada Reno (Mentor, David Au-Coin), In Vivo Fate of *Burkholderia pseudomallei* Capsular Polysaccharide

Duncan Kountz,* The Ohio State University (Mentor, Joseph Krzycki), Investigation of the Enzyme Activities of MtTB Superfamily Members in the Intestinal Acetogen *Eubacterium limosum*

Nicholas Lea,* Boston College (Mentor, Michelle Meyer), Fitness Impacts of Mutations to the Glycine Riboswitch in *Bacillus subtilis*

Alysha Lee,* University of Minnesota, Twin Cities campus (Mentor, Ryan Hunter), Identifying Genetic Determinants for Antibiotic Resistance in the Cystic Fibrosis Pathogen *Achromobacter xylosoxidans*

Joshua Leitao,* Roger Williams University (Mentor, Avelina Espinosa), Biochemical and Structural Characterization of ADHE Enzymes in *Entamoeba Strains*

Siyung Lin,* Catholic University of America (Mentor, Venigalla Rao), Mechanism of Control of the Speed of the Bacteriophage T4 DNA Packaging Motor

Stephen Olney, Indiana University (Mentor, Julia van Kessel), Identification of the Regulators of the Type VI Secretion System in *Vibrio harveyi*

Serry Park,* Wellesley College (Mentor, Vanja Klepac-Ceraj), Microbial Communities in an Extreme Euxinia and Their Role in Sulfur Cycling

Christine Peters,* University of California San Diego (Mentor, Joe Pogliano), Role of Wall Teichoic Acids in Cell Shape in *Bacillus subtilis*

Amanda Reese, Pennsylvania State University (Mentor, Scott Lindner), The Recycling of a Drug Selectable Marker to Delete Multiple Genes in *Plasmodium*

Zachary Resko,* Duquesne University (Mentor, Joseph McCormick), Using Bacterial Spores For Vaccine Delivery

Bradley Reynolds,* University of Wisconsin-Madison (Mentor, Douglas Weibel), Evolution of *Escherichia coli* and *Pseudomonas aeruginosa* In Cocultured Biofilm Communities

Lauren Rice,* Colorado State University (Mentor, Torsten Eckstein), Isolation and Characterization of BP82 Exopolysaccharides Based on Cellular Environment

Alexi Schnur,* University of Michigan, Ann Arbor (Mentor, Melissa Duhaime), Microcystis Viruses: Hunting the Killers of Lake Erie’s Algal Blooms

Megan Smith,* University of Nebraska-Lincoln (Mentor, Nicole Buan), Physiological Purpose of Chondroitin Adhesion Proteins in the Human Archaeon, *Methanobrevibacter smithii*

Jessica Spring,* Arizona State University (Mentor, Hinsby Cadillo-Quiroz), Evaluating Phage Control on Heterotrophic Decomposition in Amazon Peatlands

Morgan Stark,* Otterbein University (Mentor, Jennifer Bennett), Determination of Cyclic di-GMP-Controlled Gene Expression in a Pharmacologically Important Bacterium Using RNA Sequencing and Real Time PCR

Anne Sung,* University of Connecticut (Mentor, Marcy Balunas), Antibacterial Activity and Chemical Profiling of Symbiotic Bacteria from the Accessory Nidamental Gland of *Euprymna scolopes*
Stephen Tahan,* Westminster College (Mentor, Betsy Kleba), Quantifying Microbial Life in the Bonneville Salt Flats Salt Crust Has Implications for Search for Extraterrestrial Life

Niketa Ulrich,* Juniata College (Mentor, Regina Lamendella), An Assessment of Microbial Response to Hydraulic Fracturing Fluids Through Comparative Genomic Analysis

Cody Vientos,* University of North Carolina at Chapel Hill (Mentor, Edward Miao), Detection of the SPI-2 Type III Secretion System Needle Protein by Mouse NAIP1

Madeline Vroom, Ohio Wesleyan University (Mentor, Laura Tuhela), Characterization of the Motility and Chemotaxis of Bacillus spp. Isolated from Songbird Plumage

Chengyu Weng,* University of North Carolina, Chapel Hill (Mentor, Joseph Duncan), Role of Neisseria gonorrhoeae Lytic Transglycosylases and Host Lysozyme in Mediating Resistance to Host Inflammatory Responses

Evan Yang,* University of Pennsylvania (Mentor, Mechthild Pohltschroder), Identification and Characterization of Archaeal Motility Mutants

Alaina Zappas,* Pennsylvania State University (Mentor, Sarah Ades), The Role of Suppressors and the Sigma E Pathway

ASM Robert D. Watkins Graduate Research Fellowship Program (Awardees)

Christine Endicott,* University of Connecticut (Mentor, Ranjan Srivastava), Directed Evolution of Highly Effective Antisense

Osafame Ewaleifoh,* Northwestern University (Mentor, Gregory Smith), A Molecular and Cellular Dissection of the Pathogenesis of Herpes Simplex Encephalitis with iPSC Derived CNS and PNS Neurons

Ejirof Ezekwe,* University of North Carolina, Chapel Hill (Mentor, Joseph Duncan), Cellular Mechanisms of Alpha-Hemolysin-Mediated Pathogenesis

Dacia Leon,* University of Texas at Austin (Mentor, Jeffrey Barrick), Engineering Evolutionary Stability in Biological Systems

Maximillion Mize,* University of North Texas, Health Science Center (Mentor, Jerry Simecka), Interleukin-17A Acts to Exacerbate Pulmonary Inflammation in Susceptible Mice Infected with Mycoplasma pulmonis

Monica Sanchez,* University of Arizona (Mentor, Maitreya Dunham), Directed Functional Characterization of a New Model Yeast Species

ASM Robert D. Watkins Graduate Research Fellowship Program (Honorable Mention)

Ashley Anderson, Wayne State University (Mentor, Melody Neely), Functionally Characterize the Domains of Streptococcus agalactiae CpsA and Identify Binding Partners

Francine Arroyo, Cornell University (Mentor, Esther Angert), Investigating the Symbiotic Relationship between the Intestinal Endosymbiont Epulopiscium Type B and Its Surgeonfish Host Naso tongoanus

Jessica Franco, University of California, Davis (Mentor, Gitta Coaker), Investigating Dynamic Changes in Citrus Proteins during HLB Progression

Elizabeth Gray, Boston College (Mentor, Marc-Jan Gubbels), Determining the Role of Mitochondrial Calcium Signaling Proteins STEP1 and Enkurin in the Lytic Cycle of Toxoplasma gondii

Leah Guthrie, Albert Einstein College of Medicine (Mentor, Libusha Kelly), The Influence of the Human Gut Microbiome on Xenobiotic Metabolism

George Kasun, Portland State University (Mentor, Kenneth Stedman), RNA-DNA Hybrid Viruses: Replication In Vitro and In Vivo

Travis Kochan, University of Michigan (Mentor, Hanna Philip), Investigating Early Events in Germination of Clostridium difficile Spores

David Martinez, Duke University (Mentor, Sallie Permar), Mapping and Characterizing Neutralizing Antibody Responses in HIV-1 Infected Pregnant Mothers That Predict Reduced Mother to Child Transmission Risk

Amilcar Perez, Indiana University (Mentor, Malcolm Winkler), Mechanisms Regulating EzrA and FtsZ-Ring Dynamics in Streptococcus pneumoniae

Sherlynette Perez Castro, San Diego State University (Mentor, David Lipson), Impacts of Exotic Annual Grasses and Altered Rainfall on Soil Microbial Communities and Ecosystem Functioning in Coastal Sage Scrub Ecosystems

Sandra Sanchez, Indiana University Bloomington (Mentor, Daniel Kearns), Role of Hydrolases in Flagellar Stability and Construction in Bacillus subtilis

Sarita Santos, University of Puerto Rico-Medical Sciences Campus (Mentor, Otero Miguel), Elucidation of Immune Responses Induced by Vaccinia Virus E6R in DNA-Based Immunization against Smallpox

ASM/CDC Postdoctoral Research Fellowship Program (Awardees)

Andrew Beck,** Preceptor(s), Paul Rota and Bettina Bankamp, CDC Location, Atlanta, Ga., Division of Viral Diseases

Nsa Dada,** Preceptor, Audrey Lenhart, CDC Location, Atlanta, Ga., Division of Parasitic Diseases and Malaria

Animesh Dhara,** Preceptor, Dr. Venkatachalam Udhayakumar CDC Location, Atlanta, Ga., Division of Parasitic Diseases and Malaria

Anne Lopez-Ona,** Preceptor(s), Christina F. Spiropoulou and Michael Lo, CDC Location, Atlanta, Ga., Division of High Consequence Pathogens and Pathology

Ivana Parker,** Preceptor(s), Kelly Curtis and Sherry Michele Owen, CDC Location, Atlanta, Ga., Division of HIV/AIDS Prevention

Susan Realegeno,** Preceptor(s), Panayampalli, Subbian Satheshkumar and Darin Carroll, CDC Location, Atlanta, Ga., Division of High Consequence Pathogens and Pathology
Microbe Mentor

How does a young woman best survive and thrive in the sciences? In a field that some still see as a man’s territory, what advice would you give to a female scientist?

As a woman, mid-career environmental microbiologist with a Ph.D. working in the chemical industry, I am fortunate to work with a group of excellent women engineers, geologists, chemists, and biologists. As women in STEM careers we are in the minority (for now). However, being of the minority gender for much of my career does not mean that it’s been a grim, lonely slog over the last 25 years. The vast majority of men I’ve worked with have been positive forces in my daily life as valued friends and mentors.

Having written that, I began to wonder, is my experience the norm? Is it specific to the field I’m in? Or am I clueless to when I’ve been dissed because of my gender? I suspect the answer to all three questions at different times might be “yes.” To gain more perspective I canvassed my women friends and colleagues about how they would answer this question. The following points are a distillation of these conversations; admittedly with my own bias. And for young male scientists who are reading this, these tips will benefit your career development as well!

Be Confident: Women’s lack of self-confidence has been cited as a key reason for why we still have a pronounced gender gap in jobs and earning. Not surprisingly, the subject of self-confidence came up a lot in my discussions. When I think of the role of confidence in my own career I think of “owning my expertise,” meaning I know my input and experience are needed so I am responsible for making a contribution. One of my colleagues thinks of this as, “It’s not fake it until you make it, it’s fake it until you become it.” She doesn’t mean fake your credentials or knowledge, but rather, fake your sense of confidence and belonging until you do get comfortable. Another colleague’s advice in this arena is “never accept the first offer.” You can think about this in terms of the content of job offers, or in terms of applying to a job or pursuing an opportunity. Do not self-limit just because you might not look like the exact job description. Don’t let fear of the new or different control your options. If pursuing an opportunity takes us out of our comfort zone we need to remember that discomfort isn’t necessarily a sign that we’re doing something wrong. Most often it’s simply a sign that we’re doing something new.

Be Persistent: Several colleagues noted that in the beginning they did need to work a little harder to gain credibility and build trust in the work environment. One saw this as a challenge to demonstrate her fitness to do the job, and did not see it as a reflection of what she knows to be her abilities. Another pointed out that people often say “no” but if you know you can do the job, then you need to keep pushing forward and applying and putting yourself out there. You can’t allow one rejection to determine the course of your career. To be successful, you need to be your own advocate and not wait to be recognized.

Seek Out Mentors: The mentor role can be filled by either women or men, but support from a successful woman is extremely valuable when you’re starting out. Your mentors and the issues you will need advice on will change as time goes on but it is important to expose yourself to a diversity of experiences and opinions. Honest feedback isn’t always comfortable, but it sure is valuable.

Build and Maintain Your Networks: Career trajectories have changed dramatically in the last decade. These days you can’t expect to spend an entire career at the same corporation or institution. To keep your options open you will need to maintain and cultivate your networks at all levels of your professional sphere.

Find Your Balance and Know Yourself: The one constant in life is change. We need to find the balance between security and risk, personal and professional lives, passions and what pays the bills. The “right” balance in these areas will change over time so we need to know our core values, priorities, interests, and goals so we can recognize and pursue opportunities as they arise or have the confidence to take a pass if they are not the right fit.
Apply the Golden Rule: If we want to be respected and given the opportunity to do well, then we need to extend the same to others. Let’s be supportive and encouraging of other women and their choices. There’s plenty of opportunity out there in the STEM careers and the success of one woman is a success for all of us. While we’re at it, let’s assume until proven otherwise that our male colleagues want us to be here and want us to succeed. We are talking about humans and because of this, mistakes will be made. We have all experienced discouraging moments where the prejudices embedded in our culture manifest themselves. Where we can, we need to address these issues respectfully (and maybe even with humor) and help root them out. But, this is very different from someone treating you in a demeaning or malicious way whether because of your gender or for any other reason. Discrimination is never acceptable and if you are being discriminated against you will need to address the issue, but that is a topic for a different column.

These rewarding discussions have been fascinating, thought provoking, and far more nuanced than I was able to cover here. I am so grateful to my colleagues for their candidness and time and look forward to a continuing dialog about women’s experiences in STEM careers.

Elizabeth Erin Mack

Elizabeth Mack joined DuPont Corporate Remediation Group (CRG) in 2002. In this role she serves as a technical expert in the areas of mercury fate and transport, biodegradation, and environmental microbiology. She currently serves as a technical resource and manages external research programs in these areas for DuPont. Dr. Mack has applied results from these external programs to address remediation of mercury, chlorinated solvents, and nitroaromatic compounds in the field. Prior to this, she was a post doc in DuPont Central Research and Development.

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

ASM Science Teaching Fellowship Program
Graduate students, postdoctoral fellows, and early-career scientists are encouraged to apply for the 2015–2016 ASM Science Teaching Fellowship Program, a five-month online training experience that guides doctoral-trained participants in understanding the essentials of science teaching positions at non-doctoral institutions (community colleges, minority-serving institutions, regional or state colleges, and primary undergraduate institutions). Program activities combine structured mentoring with in-depth webinars, pre- and post-webinar assignments, and a highly interactive community of practice, all focused on four areas: teaching science to undergraduates, curriculum and course design and assessment, student-centered learning, and students as research collaborators.
WWW: http://www.facultyprograms.org/stf
Deadline: 2 November 2015.

ASM Scientific Writing and Publishing Institute The ASM Committee on Graduate and Postdoctoral Education welcomes applications to the 2016 ASM Scientific Writing and Publishing Institute (SWPI) Program, an effort that supports beginning researchers in understanding the writing, publishing, and review processes for scientific journals. Led by ASM members who have published widely, reviewed manuscripts, and served on the editorial boards of major journals, the program is a two-part training initiative. The first part, known as SWPI Online, consists of several introductory webinars, and the second part, known as SWPI Face-to-Face, is a multi-day in-person workshop. Participation in both programs is beneficial for attendees, but not required.
ASM offers the SWPI with partial support from the Burroughs Wellcome Fund.
SWPI Online. SWPI Online is a three-month overview of scientific writing and publishing concepts. Open to graduate students, postdoctoral fellows, and early-career scientists, the experience includes six webinars, pre- and post-webinar assignments, structured mentoring, and a community of practice. The topics covered will include condensed discussions of titles and abstracts; introduction, results, discussions, and methods sections; figures and legends; and the manuscript review process. The 2016 program takes place in January through March, and the application deadline is 1 December 2015.
SWPI Face-to-Face. At the SWPI face-to-face workshop, emphasis is placed on substantial time for participants to benefit from one-on-one feedback from facilitators, writing practice, and stimulating discussions and interactions. The institute is open to senior-level graduate students, postdoctoral fellows, and early-career scientists who are ready for an immersive and intensive writing experience. Before the institute, participants submit in-progress manuscripts for pre-SWPI assessment, and afterward, leave with detailed plans for improving their manuscripts, tools and resources for developing future publications, and a network of peers and mentors for critiques and advice. The next SWPI workshop will take place in the summer of 2016 in Washington, D.C., and the application deadline is 10 April 2016.

About Application Deadlines
The Application Deadlines section provides ASM members with information about certification programs, awards, and fellowships sponsored by ASM. More resources are available to members on the website at http://www.asm.org/index.php/awards-grants-whats-new-in-asm-awards-grants-fellowships-and-professorships.html. The website provides direct links to program Web pages for complete details, including eligibility requirements and application information.

ASM-IUSSTF INDO-US Professor in Microbiology Sponsored by the Indo-US Science & Technology Forum and managed by ASM, this program offers two professorships with the intent to foster collaboration and scientific exchange between the United States and India. "Teaching Professorships" provide microbiologists in India and the United States with an opportunity to visit institutions in the other country to teach an interactive short course on a topic in any of the microbiological disciplines. "Research Professorships" provide support to microbiologist in India and the United States to conduct a novel research project in partnership with a colleague at a research facility in the other country. Applications should be submitted jointly by the prospective visiting professor and host.
Deadline: 15 December 2015.

National Registry of Certified Microbiologist (NRCM) Certification The NRCM certifies microbiologist at the prebaccalaureate/baccalaureate, master’s and doctoral levels. Certification is offered in biological safety and quality; and pharmaceutical and medical device. NRCM certification is achieved by passing an online multiple-choice exam that is offered daily in the month of April at testing centers worldwide.
WWW: www.asm.org/nrcm
Deadline: 1 February 2016.
ASM Meetings Calendar

24–29 October 2015.
7th ASM Conference on Biofilms.
Chicago, Ill.
WWW, http://conferences.asm.org/

2–5 November 2015.
Chicago, Ill.
WWW, http://conferences.asm.org/

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

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

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

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

ASM Microbe 2016.
Boston, Mass.

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

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

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

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

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

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

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

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

POSITIONS AVAILABLE

Tenure-Track Faculty Position in Prokaryotic Biology

The Microbiology Program in the Indiana University Department of Biology (http://www.bio.indiana.edu) invites applications for a tenure-track faculty position in Prokaryotic Biology at the level of assistant professor. We are particularly interested in scientists exploring the systems biology, physiology, development, cell biology, environmental biology, and/or pathogenesis of prokaryotes, although all areas will be considered. This position is part of a significant, continuing expansion in the life sciences at IU Bloomington and represents an exceptional opportunity to join a strong Microbiology Program and new interdisciplinary initiatives. The successful candidate will be provided with a competitive startup package and salary, and will have access to outstanding research resources including state-of-the-art facilities for genomics and bioinformatics, light and electron microscopy, flow cytometry, protein analysis, analytical chemistry, biophysical instrumentation, and crystallography. Applicants must hold a Ph.D. and have relevant postdoctoral experience with a strong record of research accomplishments. Successful candidates will be expected to develop a vigorous externally funded research program, and to participate in teaching at the undergraduate and graduate levels. Applications received by October 15, 2015 will be assured of full consideration. Applicants should submit a cover letter, a CV, a research statement (5 pages emphasizing current and planned research), a statement of teaching interests (1 page), a list of three (or more) references, and up to three pdfs of published and/or submitted manuscripts using the submissions link at http://indiana.peopleadmin.com/postings/1707. For questions about the application procedure please contact Jennifer Tarter (jentjones@indiana.edu) or by mail at 1001 E. Third Street, Bloomington, IN 47405-3700 and for all other questions please contact Yves Brun (ybrun@indiana.edu). Indiana University is an equal employment and affirmative action employer and a provider of ADA services. All qualified applicants will receive consideration for employment without regard to age, ethnicity, color, race, religion, sex, sexual orientation or identity, national origin, disability status or protected veteran status.

Employment Advertising

Microbe is published monthly and available to nearly 40,000 ASM members and institutional subscribers. Lead time for employment ads is about 3 weeks. Microbe is mailed around the 8th of the month of issue, but the delivery date is not guaranteed. Please consider delivery dates when setting application deadlines. ASM does not accept classified advertisements that indicate a limitation, specification, or discrimination on the basis of race, religion, national origin, sex, mental or physical disability, age, or any other matters which may not be lawfully considered in making employment decisions. Employment notices that discriminate against microbiologists on the basis of a particular board certification or doctoral degree will not be accepted. Such advertisements will be rejected unless it can be established that the position by state or federal law or regulation requires a specific board certification or doctoral degree.

Classified

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

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

Deadlines: Your ad must be received by the 1st of the month before the publication month to ensure timely publication (e.g., to appear in the November 2015 issue, your ad must be received by 1 October 2015).

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

Rates:

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

Display

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

**Wood Digestion with Nary a Microbe in View**


by Elio

Eating wood is a way of life for creatures such as termites, bark beetles, and certain mollusks, including the infamous shipworms. A few invertebrates make at least some of the enzymes needed to digest cellulose and other complex plant polysaccharides, but most of them, like all vertebrates, require bacteria for this job. Consider termites, in whose gut bacteria, archaea, and protists furiously metabolize wood particles while interacting and communicating with one another. It had been thought that this microbial xylrophy takes place only in the animal's digestive tract. While the practice of localizing the microbes to the gut works well for most wood eaters, it is not the way shipworms do it.

Shipworms are worm-shaped mollusks—naked clams, really—that nibble at submerged wood to the detriment of, for instance, wooden ships. These voracious eaters are often several centimeters in length, but some are over a meter long. To wreak their havoc they grind away the wood into small pieces using tiny teeth located on the front end of their shells. The triturated fragments are ingested and eventually passed to their shells. The triturated fragments are the only ones secreted by the bacteria. Their transport from the gills to the cecum might be via the duct going from the gill microbiome to the gut. The cecum is almost free of bacteria. As reported by Distel, Haygood, and colleagues, the bacteria that make the enzymes that decompose the wood reside not in the intestine, but in the animal's gills! This distant location of the enzyme-producing bacteria seems to be unique in biology.

In the gills, the bacteria reside intracellularly in bacteriocytes, just like insect symbionts do. The gill microbiome is made up almost entirely of four cultivable strains of a clade that includes relatives of a gammaproteobacterium, *Teredinibacter turnerae*. These bacteria are aerobic as well as cellulolytic, and one is a nitrogen fixer. Collectively they encode a couple of hundred enzymes that contribute to digestion of cellulose-type components of wood (not lignin, which is apparently excreted undigested). These enzymes, a delight to biopolymer enzymologists, include glycoside hydrolases, carbohydrate esterases, and some with carbohydrate-binding modules.

Proteomic analysis of the gills came up with the expected panoply of proteins involved in all aspects of bacterial metabolism, only 11% of which were in a group known to degrade plant cell wall polysaccharides (PCWPs). But 41 out of 42 detectable proteins in the cecum’s lumen were enzymes active on PCWPs, including cellulose and hemicelluloses. That only these few proteins are present could be explained if these are the only ones secreted by the bacteria. Their transport from the gills to the cecum might be via the duct going from the gills to the esophagus.

How come the cecum houses only a few bacteria (the technical term is “depauerate”)? Is it because there are antimicrobial compounds present that deter colonization? Could be. At least one such compound is known to be made by the endosymbionts in the gills, although its in vivo function remains to be determined. There is also a siderophore involved in the story, so perhaps keeping iron in short supply helps to limit the bacterial load.

Why is it advantageous to carry these bacteria in the gills instead of the intestine? The authors wrote: “…..by virtue of their aerobic metabolism, the shipworm gill bacteria may consume less carbohydrate per unit of digestive enzymes produced than would typical gut anaerobes. Furthermore, the placement of these bacteria away from the gut content may allow the host greater control over the products of wood digestion, as well as their downstream transformations and fluxes.” When I wrote to one of the lead authors, Margo Haygood, for further comment, she replied: “I think it is all about maximizing the benefit from the symbionts while minimizing the cost. The host can keep the symbionts well under its thumb as intracellular symbionts in the gill.”

It’s not often that a strategy adopted by the vast majority of animals gets turned upside down. Of course such surprises are not unheard of in biology, as evolution has explored almost every possible way to transact its business.

*Elio is an adjunct professor at San Diego State University and University of California at San Diego.*

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Georgia Tech students enjoying a trip to the Children’s Healthcare of Atlanta laboratory

The Speakers’ Bureau currently features experts in areas such as biosafety, clinical microbiology and immunology, dairy, food safety, medical device, pharmaceuticals, and public health, and they want to talk to ASM students about their dynamic careers in microbiology.

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If you are interested in hosting a live, recorded or video call presentation, visit http://bit.ly/ASMspeakers.
Showcasing the best microbial sciences in the world, ASM Microbe 2016 brings ASM’s two premier events—General Meeting and ICAAC—under one roof, and provides a one-of-a-kind forum to explore the full scope of microbiology from basic science to translation and application.

Join more than 10,000 of your peers from across the globe at this unprecedented event. Choose from over 200 thought-provoking sessions and more than 5,000 posters across seven program tracks, gain valuable insights from the field’s foremost leaders, interact with multi-disciplinary microbiologists, and meet leading product and service providers.

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**Important date:**
Call for abstracts opens November 2015.

www.asm.org/microbe2016