Upcoming ASM Meetings

2017 ASM Biothreats: Research, Response, and Policy
February 6–8, 2017 | Washington, DC

Formerly known as the ASM Biodefense and Emerging Infectious Diseases Research Meeting, this premier meeting discusses a wide-range of biological threats and emerging infectious diseases to stimulate knowledge-sharing amongst stakeholders in academia, industry and government; and to help the overlapping communities prepare for, mitigate, and prevent these global threats.

33rd Clinical Virology Symposium
May 7–10, 2017 | Savannah, Georgia

This international symposium delves into the relationship between rapid viral diagnosis, clinical course of viral infections, and preventive and therapeutic modalities for viral infections.

ASM Microbe 2017
June 1–5, 2017 | New Orleans, Louisiana

This unmatched meeting showcases the best microbial sciences in the world, and explores the complete spectrum of microbiology.

Upcoming ASM Conferences

Tentative scheduling of 2017 ASM Conferences is listed below. See the ASM Conferences website (www.asm.org/conferences) for confirmed dates and locations.

6th ASM Conference on Beneficial Microbes
September 9–12, 2016 | Seattle, Washington

ASM Conference on Antibacterial Development
December 11–14, 2016 | Washington, DC

ASM Conference on Innovative Microbial Ecology for Mitigation of Antibiotic Resistance and Bacterial Diseases
March 2017

ASM Conference on Mechanisms of Interbacterial Cooperation and Competition
March 2017

ASM Conference on Tuberculosis: Past, Present and Future
April 2017

ASM Conference on Interplay of Viral and Bacterial Pathogens (ASM-ASV collaboration)
May 2017

2nd ASM Conference on Rapid Applied Microbial Next-Generation Sequencing and Bioinformatic Pipelines
September 2017

6th ASM Conference on Cell-Cell Communication in Bacteria
October 2017

ASM Conference on Vibrio 2017: The Biology of Vibrios
November 2017

4th ASM Conference on Viral Manipulation of Nuclear Processes
December 2017
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33rd Clinical Virology Symposium
May 7–10, 2017
Savannah International Trade and Convention Center, Savannah, Georgia

Presented by ASM, the 33rd Clinical Virology Symposium will be held in its new location next May in Savannah, Georgia! Led by biomedical scientists engaged in research as well as primary care physicians and laboratorians involved with patient care, this international symposium will provide an unmatched forum for the meaningful exchange of ideas dealing with viral infections.

Important Dates

• Call for abstracts opens: Late-October 2016
• Call for abstracts closes: Early-March 2017
• Registration opens to ASM Premium Members: November 17, 2016
• Registration opens to all: December 1, 2016
• Early bird deadline: March 30, 2017
What Seemed Important in 1966?

Review of a major congress five decades ago provides insight into what microbiologists then rated as key issues. How much has changed?

Bernard Dixon

Half a century ago, I was in Moscow, in the then Soviet Union, attending an International Congress of Microbiology. Although the passing of time seems unbelievable, the interval provides an opportunity to reconsider key topics which the organizers chose to focus attention on, since they were then major concerns for the profession. Some of those topics now appear surprising, some have declined in importance, and others have become more so.

Perhaps the most significant issue at the meeting was nonspecific factors in infection, which Andre Lwoff of the Pasteur Institute in Paris highlighted in his keynote address (and indeed which he spent a lifetime studying). Lwoff’s lecture emphasized the paramount importance of factors such as temperature in determining the outcome of virus infection.

“Worship for antibodies has predominated for a long time in immunology and virology” Lwoff said, “since immunity is a specific reaction and antibodies are specific proteins. My purpose is to shake this dogma and to demonstrate that nonspecific factors are also essential determinants of primary virus infection.”

Lwoff pointed out that animals often shook off a virus infection either before antibodies had been formed or when they were present at too low a concentration to be effective. We should pay much more attention, Lwoff said, to nonspecific factors such as interferon production, augmentation of temperature, and the decrease in pH in tissues.

“I have been particularly interested in temperature, the factor which has been the longest known, but least studied,” Lwoff said. Plant pathologists had known for many years that certain virus infections could be successfully treated by warming up the plant, Lwoff said. He then went on to review work which showed that many animal virus infections reacted in a similar fashion.

In one series of experiments, groups of rabbits infected with myxomatosis virus were kept at three different temperatures—from 0 to 27°C. The skin temperature changed no more than a few degrees in proportion to external temperature, but mortality in the three groups was 92, 63, and 30%, respectively. When mice were infected with Coxsackie B virus, a difference in rectal temperature of only 1°C made the difference between 100% mortality and 100% recovery.

Lwoff described his own experiments on the effect of temperature on multiplication of polio virus in tissue culture cells. “The virus grows well at 35°C,” he said, “but increasingly poorly as the temperature approaches 40°C. Between 38.5 and 39°C, the release of viria falls from 95% to 2%. So now we can see why slight differences in body temperature can govern the outcome of a virus infection.”

Other work at the Pasteur Institute provided a further plank in Lwoff’s argument. When the raised temperature of rabbits infected with vaccinia virus was artificially lowered by injection of aminopyrine, mortality increased markedly.

“In one series of experiments on mouse encephalomyocarditis, with a mortality of 90%, animals could be rescued by injection of immune serum, but only if this was done on the first day and with a very high dose. Whereas hyperthermia was effective even if employed on the second or third day.

“In thymectomized mice the course of Coxsackie B virus infection is the same as in normal mice,” he said. “Thus the primary viral infection develops in spite of the possibility or impossibility of synthesizing antibodies. Hence antibodies do not determine the fate of an animal in the course of primary virus infection.”

From here, it was but a short logical step—supported by extensive experimental data—for Lwoff to show that, with polio, mouse encephalo-
myocarditis virus, and others, virulent strains were less sensitive to high temperature than avirulent strains. “Many of the strains of viruses used for animal and human vaccines are thermosensitive strains,” he said.

“In fact, virulent strains are relatively insensitive to each of the three non-specific factors—augmentation of temperature, low pH, and interferon synthesis. These are the three components of inflammatory reaction induced by virus, and we know that an agent such as cortisone, which reduces the intensity of inflammation, increases the severity of virus infection. It is notable, therefore, that a recently published treatise on inflammation did not even discuss the effect on viral infection.”

A topic just as challenging in 2016 as it was in 1966 is the control of influenza. Sobering, though, is the fact that total elimination of the disease seemed relatively close 50 years ago. “Prospects for the eradication of influenza have never been more promising,” said Fred Davenport of the University of Michigan. “Vaccines against each of the strains of influenza A and B which cause epidemic and pandemic recurrences of the disease, and of their subtypes, have been developed and proved to be effective. At present the major limitation on eradication would seem to be inertia concerning the development of expanded programmes in application and research to meet the peculiar problems which influenza presents.

“We now have a great deal of information about the antigenic make-up of influenza viruses,” Davenport pointed out, “but the key to the success of countermeasures against the disease is the prompt acquisition of accurate information. In the world pandemic of 1957, Asian influenza was first isolated in February in China. In May it was identified in Japan and Singapore. By October the pandemic was in full swing. Yet the Chinese strain was not received at the WHO Study Centre in London until long after May. Three critical months were lost. And epidemiological information could be more often read in news media than through official channels.

“The fact that eradication of influenza is not just a fanciful dream is attested by the experience of the United States military forces. Annual vaccination has been routine practice for more than 15 years. During this period the military has not experienced epidemics of influenza A or B, except in two instances when adequate supplies of vaccine were unavailable, yet the civilian population has been repeatedly and heavily affected.

“If influenza can be virtually eradicated from one group, why not from others?” asked Davenport. He went on to suggest that the first aim should be to eliminate the disease, by universal vaccination, from schoolchildren—the group which regularly experiences the highest morbidity, and which was largely responsible for introducing the disease into the home, from whence it spreads further into offices and factories. “This would seem a more rational approach than the helter skelter undirected use of vaccines which now prevails.”

A controversial issue discussed at the 1966 congress was the possible role of RNA in antibody formation. Several groups had recently shown that extracts, containing RNA, of lymphoid tissue from an immunized donor could transfer transplantation immunity to non-immune recipients or cells. The question at issue was: did this represent the transfer of coded information, or were the extracts simply contaminated with antigen which caused a normal immune response?

John Mannick of Boston University School of Medicine presented evidence for the former possibility. “The fact that brief exposure of the RNA to small amounts of ribonuclease destroys its activity, and that the RNA-mediated immunity is short-lived, argue against the possibility that antigen is responsible,” he said. I. N. Kokbrin, of the Gamaleya Institute in Moscow, and Luigi Michelazzi of the University of Genoa, Italy, suggested a similar conclusion, but Herman Friedman of the Albert Einstein Medical Center, Philadelphia, claimed that the amount of specific coding RNA present in the lymphoid extracts was insufficient to transfer immunity. The debate continued—and did so for some years afterwards.
Current Topics

ASM MICROBE 2016
Microbiomes Let Giant Shipworms, Desert Woodrats Conduct Exotic Life Styles

David C. Holzman

*Kuphus polythalamia*, a giant among the bivalve shipworms, or *Teredinidae*, departs from other family members in terms of how it relies on its microbiome to survive in a challenging environment, according to Daniel Distel of Northeastern University in Boston, Mass. Exotic in other ways, woodrats living in Southwestern U.S. deserts rely on their microbiomes to thrive on plants that harbor otherwise harmful toxins, according to Denise Dearing of the University of Utah in Salt Lake City. They and other scientists presented their recent findings at a symposium, “Expanding Host Capabilities through the Microbiome,” during the 2016 ASM Microbe Meeting, held last June in Boston.

Many other *Teredinidae* members rely on cellulolytic enzymes furnished by symbiotic bacteria to digest wood, according to Distel. In sharp contrast, the microbial symbionts of *Kuphus* oxidize hydrogen sulfide, apparently using energy from this biochemical reaction to fix carbon and produce sugars that feed the host worm, he and his collaborators find. *K. polythalamia* grows in shallow waters near the southern Philippines. The microbial symbionts of both *Kuphus* and the rest of the shipworm species inhabit the gills, which run the length of the shipworm bodies. Although *K. polythalamia* can grow longer than a full-grown human, adults typically are about 100 cm, or 40 inches, in length. Distel and his collaborators cultivated and sequenced the genome of one of its bacterial symbionts, designated 2141T, and also determined the metagenomic sequence of other microbial inhabitants of the gill.

About 20% of that population of symbionts appears to be bacterial, with 17 clusters within that fraction accounting for 99.5% of the bacterial reads, Distel says. “The *Kuphus* gill symbiont community is highly homogenous, dominated by a small number of highly similar genomes, all of which appear to be chemoheterotrophic, and sulfur-oxidizing.” Although they appear closely related to known sulfur oxidizing bacteria, 2141T is 50% larger than the largest known sulfur-oxidizing bacterium.

Notably, genes within the metagenome encode ribulose-1,5-bisphosphate carboxylase/oxygenase, also called RuBisCo, the enzyme that catalyzes the first major step of carbon fixation during photosynthesis, according to Distel. That and other findings make these bacterial symbionts “weird,” he says. For instance, they have unusual membranes and morphologies, with polyhedral bodies. Those polyhedral entities consist of small protein shells similar to virus particles. The carbon fixation enzymes, including RuBisCO, are stored within those shells, along with carbon dioxide. The symbionts also encode genes needed for running the Calvin-Benson cycle—typically found in chloroplasts of green plants, not in animals—that incorporates carbon dioxide into sugar. Instead of relying on light energy, however, these symbiotic bacteria derive their energy by oxidizing sulfur compounds.

Diverse plants make toxins to thwart predators, but some of those predators have ways of overcoming the

Desert woodrat (*Neotoma lepida*) in a century plant (*Agave americana*) in Joshua Tree, Calif. Some desert woodrat populations have gut microbes that allow them to eat and metabolize creosote, a plant exudate containing many compounds that would otherwise be toxic. (Photo by Jules Jardinier.)
feeding antibiotics to woodrats that consume creosote led them to lose their capacity to gobble creosote, she says. In other experiments, juniper-eating woodrats that received fecal transplants from creosote-eating conspecifics improved their ability to metabolize creosote, enabling them to thrive on it, she adds. “Gut microbes are critical to processing a toxic diet.”

David C. Holzman is a science writer in Lexington, Mass.

**ASM MICROBE 2016**

**Candidate Antimicrobials, Enhancers, Potentiators, Combos Plus New Probe**

**Jeffrey L. Fox**

Several new antibacterial candidates shared the stage with promising agents that augment antimicrobial drugs, combination agents that work better than their separate components, and antifungal candidate agents—presented this year during the poster summary session “Early New Antimicrobial Agents,” convened at the 2016 ASM Microbe Meeting, held in Boston, Mass., in June. In addition, participants learned briefly about a new imaging approach for following the course of infections and the drugs or drug candidates that are used and being developed, respectively, to treat them. Although these new antimicrobial agents appear potentially useful, none of them looks startling or could be called a breakthrough.

Among the most intriguing of these new antibacterial candidates is SPR741, which is described as a promising “potentiator” of antibacterial activity—notably broadening the specificity of other antibacterial agents with which it is combined, according to Troy Lister of IHMA in Schaumberg, Ill., and his collaborators at Spero Therapeutics in Cambridge, Mass. This candidate antimicrobial agent is a modified version of polymyxin, a broad-spectrum antibiotic that can be damaging to host kidneys. When reconfigured “to eliminate nephrotoxicity,” however, its antimicrobial activity is sharply reduced. Thus, to be effective, SPR741 needs to be combined with other antibacterial agents, including some that are best known for being active against gram-positive pathogens. Among them, rifampycin seems to “work best” in combination with SPR741, he says. Another plus is that “we could not identify any toxicity” with this combination when tested on nonhuman primates, Lister adds. Whether that combination or others will prove active against pathogens that are resistant to polymyxin antibiotics is not yet known.

Another more conventional antibacterial candidate is Lascufloxacin—a “novel fluoroquinolone with remarkable pulmonary distribution,” says Ryuta Kishi of Kyorin Pharmaceuticals in Tokyo, Japan. It has “potent activity” against many gram-positive bacterial pathogens.
Recent developments involving new means to detect microorganisms and to diagnose infectious diseases include:

- A rapid approach for testing blood for pathogens from patients suspected of being septic proves successful within one hour of sampling in 85% of cases, according to Donald Ingber of Wyss Institute at Harvard Medical School in Boston, Mass., and his collaborators. The approach depends on FcMBL, a genetically engineered pathogen-binding protein that recognizes signature carbohydrates on pathogens, they report. Details appeared June 23, 2016 in *eBioMedicine* (doi:10.1016/j.ebiom.2016.06.014).

- A device that measures changes in electrical conductivity in droplets containing bacteria can determine whether they are alive or dead, according to Muhammad Ashraf Alam of Purdue University in West Lafayette, Ind., and his collaborators. Further development could lead to array-formatted electrical sensors compatible with droplet microfluidics for lab-on-a-chip applications, they say. Details appeared June 28, 2016 in *Proceedings of the National Academy of Sciences* (doi:10.1073/pnas.1606097113).

- A recently developed diagnostic algorithm can be used to detect mycobacteria directly from patient samples, according to Peter Keller of the University of Zurich in Switzerland and his collaborators. Details appeared 13 June 2016 in *eBioMedicine* (doi:http://dx.doi.org/10.1016/j.ebiom.2016.06.016).

- Nanoscale particles—called “nanoflowers” and carrying enzymes to detect specific antigens—make it possible to detect *Escherichia coli* 0157:H7 or other food pathogens using simple pH meters, according to Yuehe Lin of Washington State University, Pullman, and his collaborators. Details appeared 28 April 2016 in *Small* (doi:10.1002/smll.201600273),

and is also “active” against some gram negatives. In preclinical testing, it is active against methicillin-resistant *Staphylococcus aureus* and also macrolide-resistant pneumonia as well as against some anaerobes, he notes. When administered to “healthy human volunteers,” the drug candidate is “remarkably distributed” throughout their lungs without “serious adverse effects.”

Tnp-2092, another antibacterial candidate, is dual-acting, targeting several pathogens that infect the gastrointestinal tract, including *Helicobacter pylori* and *Clostridium difficile*, according to Zhenkun Ma of Tennor Therapeutics in Shanghai, China, and his collaborators. The primary target of this molecule, which consists of a quinolone antibiotic that is linked to rifampycin, is DNA gyrase, while its secondary target is RNA polymerase, he says.

WCK4873, or Nafithromycin, is a novel lactone ketolide with a methylated side chain, according to Mahesh Patel of Wockhardt Research Center in Aurangabad, India. This orally available drug is being developed for treating community-acquired cases of pneumonia, particularly among vulnerable elderly populations who are no longer so well protected by vaccination, he says. This agent “is good at penetrating the lung, better than telithromycin,” and it yields “three logs” of killing when used against pneumonia in mice compared to telithromycin, which is bacteriostatic. The candidate ketolide, soon entering phase 2 clinical testing, appears to be safe for human use, he adds.

Meanwhile, WCK 5222 is a broadly active β-lactam antibiotic “enhancer,” one in a series of such agents that can augment the activity of proven β-lactam antibiotics, including those to which bacterial pathogens are resistant because they produce β-lactamases, according to Patel of Wockhardt Research Center in India. When combined with such antibiotics, particularly cephalosporins, this particular enhancer provides “potent coverage” against a variety of multi- and extensively drug-resistant bacterial pathogens, including clinical isolates of *Acinetobacter baumannii*, *Klebsiella*, and *Pseudomonas aeruginosa*, he says. It is effective when used to treat lung and thigh infections of mice.

ETX2514 is another example of a β-lactamase inhibitor that can enhance the activity of β-lactam antibiotics, including against pathogens such as *A. baumannii*, according to Ruben Tommasi of Entasis Therapeutics in Waltham, Mass. This experimental agent has “excellent activity against A, C, and D” β-lactamases, he says. Based on preclinical testing, ETX2514 appears to work well when combined with sulbactam—itself a β-lactamase inhibitor—against *A. baumannii*, he notes. Thus, ETX2514 exhibits modest intrinsic antibacterial activity, which he says is “likely due” to its ability to inhibit penicillin-binding protein 2. More conventionally, this experimental agent is effective against *P. aeruginosa* when combined with imipenem.

Combining two antifungal agents may improve prospects for treating recalcitrant aspergillosis in patients, according to Vidmantis Petraitis of Weill Cornell Medical College in New York, N.Y., and his collaborators. They are testing the specific combination of Isavuconazole, an azole that interferes with fungal cell membrane development, and Micafungin, an echinocandin that blocks cell wall synthesis in *Aspergillus fumigatus*, a fungal pathogen that can be difficult to treat in humans, he says, “This combination leads to increased survival and decreased
morbiditv in rabbits . . . with significant decreases in the lung burden of A. fumigatus among all groups of animals in all combination groups.”

Multispectral optoacoustic tomography (MSOT) lies at the heart of a new approach for following pathogens when they infect animals as well as drugs used to treat those animals, according to Peter Panizzi of Auburn University in Auburn, Ala. MSOT, whose use he is helping to pioneer for analyzing infectious diseases, depends on infrared lasers to detect differentially dye-marked antimicrobial agents and pathogens, he says.

For example, a pathogen such as S. aureus can be marked with a bioluminescent dye, then injected into mice, and the course of that infection followed using this imaging technology. “You get a three-dimensional movable view of the animal, and see the infectious signal in different organs,” Panizzi says. Similarly, drugs and drug candidates can be marked with different dyes to determine where they move throughout such animals and whether they are effective in effecting and then treating those pathogens. “We do not have a lot of conclusions, but to develop new drugs, we need to understand how a disease progresses,” he says.

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

RESEARCH ADVANCES

Crystalized Proteins from Thermophile Reveal Transcription Insights

Carol Potera

The recently determined three-dimensional (3D) structure of a bacterial class II transcription complex helps to reveal how it binds to specific DNA sequences, thus driving transcription of downstream genes. This X-ray-based structural analysis provides the first atomic structure for such an intact class II transcription activation complex, according to Richard H. Ebright at Rutgers University in Piscataway, N.J. He and his colleagues reported their findings on 10 June 2016 in Science (doi:10.1126/science.aaf4417).

About 30 years ago, Ebright began trying to crystallize the catabolite activator complex (CAP) from Escherichia coli—part of its transcription activation complex. Although that specific goal remains elusive, the Rutgers group used electron microscopy in 2009 to obtain a low-resolution structure of this class I transcription activation complex containing CAP from E. coli. However, unsuccessful efforts to crystallize those E. coli components frustrated their attempts to refine those views.

A shift in strategy brought success. Thus, Ebright and his collaborators switched their attention to comparable transcription components from Thermus thermophilus. This thermophile’s TTHB099 activator protein (TAP), which is a homolog of CAP from E. coli, functions at higher temperatures than does CAP or other proteins from E. coli. It is as if “the motion of TAP is essentially frozen at room temperature,” Ebright says. “This often makes [it] more suitable for obtaining ordered crystals.” When members of his group began evaluating CAP ho-

MINITOPIC
New and Improved Microscopes: Some Simple, Others not

Recent efforts to develop and evaluate simpler, cheaper microscopes and microscopes with unusual capabilities include:

- A proposed but not yet realized microscope that “exploits birefringence in an unconventional geometry” could prove useful for examining transparent substrates and reading microarrays of biomarkers; a prototype can detect nanometer-thick surface modulations on glass and in single- and double-protein layers, according to Valerio Pruneri of the Barcelona Institute of Science and Technology in Barcelona, Spain, and his collaborators. Details appeared 10 June 2016 in Science Advances (doi:10.1126/sciadv.1600077).

- The biological use of mirror-enhanced, axial narrowing, super-resolution microscopy begins with growing cells on tiny custom-built mirrors; it improves axial resolution sixfold and lateral resolution twofold, and enables researchers to, for example, visualize the tubular structure of the human respiratory syncytial virus, according to Phil Santangelo at Georgia Tech and Emory University, both in Atlanta Ga., and his collaborators in China and Australia. Details appeared June 17, 2016 in Light: Science & Applications (doi:10.1038/lsa.2016.134).

- High-aspect-ratio titanium dioxide metasurfaces can be used for making lenses that resolve nanoscale features, providing magnifications of 170-fold, according to Federico Capasso of Harvard University in Cambridge, Mass., and his collaborators. Details appeared 3 June 2016 in Science (doi:10.1126/science.aaf6644).

- Portable field microscopes, including a mobile phone-based device, prove effective when used in community-based clinical settings in the Côte d’Ivoire to detect parasites such as intestinal protozoa and the causal agent of schistosomiasis, according to Isaac Bogoch at Toronto General Hospital in Toronto, Ontario, Canada, and his collaborators. Details appeared June 27, 2016 in PLOS Neglected Tropical Diseases (doi:10.1371/journal.pntd.0004768).
mologs from *T. thermophiles*, he recalls, “one of them immediately yielded suitable crystals.”

Its 3D structure shows how TAP can bind to specific DNA sequences upstream of genes being transcribed. Specifically, TAP inserts a pair of α-helices into grooves of the DNA helix while AR4, another exposed segment of TAP, contacts the RNA polymerase α subunit of the C-terminal domain, thus helping the RNA polymerase molecule to latch tightly onto the DNA. Subsequently, two other exposed surfaces of TAP, designated AR2 and AR3, bind the RNA polymerase β subunit and sigma, a transcription initiation factor, helping to unwind the DNA segment that is being transcribed. Simple adhesive, Velcro-like interactions of TAP with AR4, AR2, and AR3 stabilize the connections during RNA polymerase binding and DNA unwinding.

This detailed structural information raises the possibility that small-molecule inhibitors could be designed to disrupt binding at key activator-RNA polymerase or activator-sigma interfaces to interfere with specific gene functions, according to Ebright. Although “you need this type of information to design new inhibitors of gene regulation or virulence,” he says, “there’s no immediate path from this new 3D structure to a therapeutic agent.”

“Decades of biochemical and genetic analyses have indicated that Class II activators like TAP stimulate the transition of the transcription complex from a closed state, in which DNA is double-stranded, to an open state, in which DNA is unwound around the transcription start site,” says Deborah Hinton at the National Institutes of Health in Bethesda, Md. The new structural analysis from Ebright’s laboratory “identifies several molecular interactions between TAP and RNA polymerase that serve to stabilize the open complex,” she adds. “These surfaces reveal targets that may be useful for anti-bacterial strategies.”

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

**RESEARCH ADVANCES**

**Eat Prey, Love? Diverse Soil Cercozoa Tell Tales of Climate Change**

Carol Potera

The enormous species diversity of Cercozoa, important soil protozoans that feed on bacteria there, might provide a means for following climate change trends, according to Flemming Ekelund at the University of Copenhagen in Denmark and his collaborators. Thus, as soil dries with the changes in climate, species composition within the Cercozoa will also likely change, affecting further decomposition within this environmental niche, they say. Meanwhile, high-throughput sequencing of genomic material from soil samples can be used to follow protozoan predators and their prey. Details appeared 8 March 2016 in *The ISME Journal* (doi:10.1038/ismej.2016.31).

Ekelund and his collaborators analyzed four topsoil samples of about a gram each collected from dry-heath grassland. Two of the sampled sites were exposed to artificial drought conditions comparable to those that are predicted to occur in this region by 2075, and the other two plots were left unchanged. The researchers identified more than 1,585 different species of Cercozoa, and four times more unnamed species were discovered than known ones. “It will be very interesting if future microscopic-based studies can reveal new morphological types which correspond to some of the sequences found in our study,” he says.

More than 40% of the sequences were assigned to the Glissomonad genera, which consists of species whose flagella enable them to move by gliding. The most commonly identified genus was the euglyphid *Trinema*. These large-shelled amoebae are sensitive indicators of the water table. *Trinema* were more abundant in untreated soils than in the artificially droughty soils, the researchers report. This difference was not statistically significant, but it suggests that drought-sensitive amoebae within Cercozoa may be indicators of the early stages of climate change.

Further, these broader findings
challenge the traditional species concept, according to Ekelund. “If we can find so many new species, then we must rethink whether the traditional species boxes are an appropriate way to measure protozoan diversity,” he says.

Unlike bacteria, few genomic sequences for protozoan species of Cercozoa are available for Ekelund and his collaborators to compare to the species they were analyzing. “We had to make a thorough analysis of the genome to find the most suited regions, and then construct new functioning primers,” says first author Christoffer Bugge Harder. “We used the hypervariable V4 region of 18S ribosomal DNA, [and] these primers captured all major Cercozoan groups.”

Cercozoa are worthy of study because they are an important component of the food web, and their response to climate change will have consequences for the ecosystem,” says Bryan Griffiths at Scotland’s Rural College in Edinburgh. The sensitivity of Trinema especially stands out, since their tough silica shell should protect them from adverse changes. Although “Trinema could hide in their shell and wait out the bad times,” he says, Ekelund’s team showed that “they are particularly sensitive and, therefore, could be useful indicators for environmental change.”

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

RESEARCH ADVANCES

Monocercomonoides sp. Shed Their Mitochondria Naturally

Barry E. DiGregorio

The unicellular Monocercomonoides sp. lacks traces of mitochondria even though it is considered a standard eukaryotic cell in other respects, according to Anna Karnkowska at Charles University in Prague, Czech Republic, and her collaborators from Dalhousie University in Halifax, the University of Alberta in Edmonton, and the University of British Columbia in Vancouver, all in Canada. Thus, the mitochondrial iron-sulfur cluster assembly pathway, thought to be conserved in all eukaryotic cells is missing, and, in this case, replaced by a cytosolic sulfur mobilization system (SUF) acquired from bacteria—making Monocercomonoides sp. lineage the first known naturally amitochondriate eukaryote. Details appeared May 23, 2016 in Current Biology (doi:10.1016/j.cub.2016.03.053).

Monocercomonoides is a microaerophilic organism, so we anticipated it will have reduced mitochondria,” Karnkowska continues. “We were expecting a much reduced form of mitochondrion, but the absence was a surprise.” Several other types of microorganisms, including parasites such as Giardia, Entamoeba, and Trichomonas, live in anaerobic environments and were suspected of having shed mitochondria, she adds. However, they possess “reduced mitochondria, which are much smaller and often difficult to identify under the microscope.”

“This is first case of a eukaryote which has lost the mitochondrial organelle,” Karnkowska says. “It is important to understand that this is not an ancestral stage, but a loss. Monocercomonoides and its relatives are obligate animal symbionts, and mitochondrial homologs are present in the close free-living relative of Monocercomonoides, which suggests that the absence of mitochondrion in Monocercomonoides sp. is secondary.”

Mitochondria, considered to be of bacterial origin, are energy-producing organelles in eukaryotic cells. Thus, the ongoing search continues for an ancestor of eukaryotes that lacks mitochondria because it did not acquire them through endosymbiosis, she says. “Monocercomonoides is not primitively amitochondriate, but secondarily.” Its loss of organelles presumably arose via “reductive evolution,” a simplifying process through which organisms shed genes and gene-encoded structures. “It is important to note that Monocercomonoides in other respects is a ‘normal’ eukaryotic cell, containing other organelles and systems typical for eukaryotes,” she points out. “That means that loss of mitochondria does not correspond with the loss of other [eukaryotic] traces.”

“It is extremely interesting that the mitochondrial organelle can be lost completely when the system for aerobic respiration is no longer needed,” says Siv Andersson at Uppsala University in Uppsala, Sweden. “This is consistent with our findings that the mitochondrial genome is needed to prevent the hydrophobic proteins of the respiratory chain complexes to be targeted to the ER [endoplasmic reticulum]. When these processes are no longer required, both the mitochondrial genome and the organelle itself can be lost.”

How do petite yeast mutants, which lack mitochondria, fit in with the new findings? “When yeast grows anaerobically, they don’t need the system for aerobic respiration, and can survive even without a mitochondrial genome,” Andersson says. “The additional ‘twitch’ is that these [Monocercomonoides] cells don’t even need the organelle.”

“I don’t mind comparison with yeast, but what is important is the context of other anaerobic eukaryotes with reduced mitochondria such as Giardia and Entamoeba,” Karnkowska says. Although what Andersson says is “all true . . . the only problem is that other mitochondria-like organelles—mitosomes, hydrogenosomes—which do not contain genomes, are found in anaerobic eukaryotes.”

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NEW FROM ASM

Candida auris Shows Unique Growth Patterns

The emerging pathogen and multi-drug-resistant fungus Candida auris has at least two different growth forms, concludes a re-
search team from the Mycology Reference Laboratory of Public Health England, located in Bristol, England. First author Andrew Borman and lead scientist Elizabeth Johnson observed that a proportion of C. auris cells from patient isolate strains were unable to release daughter cells after budding, resulting in formation of large aggregates of cells that couldn’t be physically disrupted. Future studies will focus on whether the aggregate-forming behavior affects antifungal susceptibility. “The major challenge facing researchers is to fully understand what makes this particular species behave so differently,” says Johnson. The report is published in mSphere.

Borman AM, Szekely A, Johnson EM. Comparative pathogenicity of United Kingdom isolates of the emerging pathogen Candida auris and other key pathogenic Candida species. mSphere. Published online 18 August 2016; doi:10.1128/mSphere.00189–16.

NEW FROM ASM

Master Regulator of Clostridium difficile Toxin Production

A new mBio study used genetic analysis and mouse experiments to identify the genetic regulator of Clostridium difficile Toxin A and Toxin B production. Charles Darkoh, working with Herbert Dupont at the University of Texas Health Science Center in Houston, Tex., found the accessory gene regulator (Agr) quorum signaling system is responsible for producing these toxins. “Since we know the toxins are the main cause of disease, if we can stop the toxins, we can stop the disease,” says Darkoh. Darkoh plans to investigate compounds that can block the pathways regulated by the agr1 genes, which could act as a nonantibiotic therapy for C. difficile disease.

Darkoh C, Odo C, DuPont HL. Accessory gene regulator-1 locus is essential for virulence and pathogenesis of Clostridium difficile. mBio.

NEW FROM ASM

Bacterial Communities Differ in Gingivitis and Periodontitis

Gingivitis and periodontitis are not the same disease, and can be differentiated by assessing the microbial communities associated with supragingival plaque, reports a scientific collaboration from University of College London in London, United Kingdom, and the University of Malawi in Malawi. First author Liam Shaw and senior author Nigel Klein led a team that tested the bacterial composition of over 90 Malawian women with various stages of oral health using 16S rRNA gene sequencing. They observed differences in bacterial community composition between women with healthy gums and gum disease, and also between women with gingivitis and periodontitis. The findings, published in Applied and Environmental Microbiology, “confirm that periodontitis cannot be considered simply an advanced stage of gingivitis,” says Shaw.


NEW FROM ASM

Vaccine Adjuvant Fails to Protect Obese Mice against Influenza

An mBio study demonstrates that adjuvants can increase a host’s immune response during influenza vaccination, but not enough to protect the obese against infection. “Adjuvants increased the antibody responses to levels considered protective, yet obese mice still succumbed to infection,” says first author Erik Karlsson. “The immune response in our obese animals is reminiscent of the elderly, in that you can increase it but there’s something wrong with it,” says lead scientist Stacey Schultz-Cherry. “We need to focus on understanding why this happens and how to overcome this problem.” The study was a collaboration between scientists at St. Jude Children’s Research Hospital in Memphis, Tenn., and Ben-Gurion University of the Negev in Be’er-Sheva, Israel.


NEW FROM ASM

Ebola Viruses

A team of scientists led by Robert Kozak and Xiangguo Qiu have discovered that ferrets are a superior animal model to mice for studying filoviruses. The scientific team found that Bundibugyo and Zaire Ebola viruses are able to infect ferrets without the need for serial passaging for host adaptation. Ferrets infected with the viruses follow a course of disease that closely mimics that of humans, including disruption of coagulation and decreased immune cell numbers. Viral sequencing showed a majority of the same RNA sequences were present through the course of infection, indicating the ferrets were susceptible to the same isolates that sicken people. This provides a new, robust model with which to study disease progression and investigate future therapeutics.


NEW FROM ASM

New Ferret Model for Ebola Viruses


NEW FROM ASM
Homologous Recombination Transfers Resistance Determinants in Enterococcus faecium

A research team headed by senior scientist Louis Rice of Brown University in Providence, R.I., has identified chromosomal regions where homologous recombination facilitates antimicrobial resistance gene incorporation in the gram-positive bacterium Enterococcus faecium. The research, published in Antimicrobial Agents and Chemotherapy, demonstrates “there is more than one mechanism to mobilize DNA from one strain to another without the need of conventional transposable elements,” says first author Monica Garcia-Solache. E. faecium is a successful pathogen in part due to its ability to resist antibiotics, and the current study demonstrates “there is not a ‘one size fits all’ mechanism this bacterium uses,” says Garcia-Solache.


NEW FROM ASM
Danger Signals from Influenza Infection Increase Risk of Bacterial Pneumonia

A new mouse model designed by scientists at the University of Buffalo, State University of New York in Buffalo, N.Y., is helping scientists understand how the influenza A virus (IAV) causes asymptomatic Staphylococcus aureus infection to transition to invasive disease. Mice with S. aureus-colonized nasal cavities experienced disseminated infection only in response to IAV infection, found first author Ryan Reddinger and senior author Anthony Campagnari. The researchers found a combination of viral-induced changes in host physiology, including body temperature and release of ATP, glucose, and norepinephrine, stimulate dispersal of S. aureus even in the absence of viral infection. The results help explain the prevalence of secondary bacterial pneumonia in influenza patients.


NEW FROM ASM
Toxin Neutralization as Therapy Strategy for Clostridium difficile

A team of scientists led by first author Diane Schmidt and senior author Saul Tzipori has used recombinant antibody technology to generate a potential therapeutic to neutralize Clostridium difficile toxins. The researchers cloned the VHH variable region of two unique immunoglobulin heavy chains to engineer a toxin-neutralizing agent called VNA2-Tcd. VNA2-Tcd administration was able to protect mice, hamsters, and piglet animal models from both purified toxin and C. difficile pathogenesis. Eliminating the bacterial toxins’ effects, which constitute the bulk of C. difficile pathology, may be the first step to neutralize overgrowth during C. difficile infection. The report is published in Clinical and Vaccine Immunology.


NEW FROM ASM
Antimicrobial Stewardship Program Shows Positive Results

Meticulous drug management programs can have a positive effect on drug-resistant infections, finds a new report published in the Journal of Clinical Microbiology. A team of clinical scientists led by Larissa Matukas studied the effect of antibiotic stewardship surrounding the use of ciprofloxacin to treat bacterial infections caused by Escherichia coli or Pseudomonas aeruginosa. Using a stewardship program that involved reporting ciprofloxacin susceptibility only if no other susceptibilities were found when testing isolates against a multidrug panel, the team observed a strong reduction in the use of this particular antibiotic, which correlated with a trend toward increasing susceptibility in E. coli isolates. The study demonstrates that, while small, antibiotic stewardship programs may help prolong the efficacy of antibiotic arsenals.

NEW FROM ASM

**Survey Shows Need for Antimicrobial Stewardship Awareness**

A new study published in *Antimicrobial Agents and Chemotherapy* demonstrates the important role played by the public in antibiotic stewardship. First author Roger Zoorob, with senior author Barbara Trautner, surveyed 400 individuals waiting in primary care clinics about their antibiotic use. Five percent of respondents said they had used non-prescription antibiotics within the past year, and 25% said they would be willing to use antibiotics without talking to a health care professional. The authors found that respondents who said they would use nonprescription antibiotics were more likely in a public health clinic, where patients overall have less education and lower annual income. The results highlight the need for communication and education for a greater public health.

Immune Responses to Viruses and Vaccines Differ Between Men and Women

Sex hormones can trigger differential responses between females and males to infectious agents and vaccines

Shannon Weiman

Human sex differences extend beyond anatomy to encompass important immune system functions, predisposing men and women to respond differently to infectious diseases. For instance, estrogens tend to promote stronger inflammatory, cellular, and humoral immune responses in women than men. While robust immune responses to pathogens can benefit the host, overexuberant inflammatory responses can damage host tissues—predisposing women more than men to develop immunopathologies, comorbidities, autoimmune disorders, and adverse reactions to vaccines, among other deleterious effects.

Several researchers working in this field reviewed examples of sex-specific disease mechanisms, considered their public health implications, and explored possibilities for developing sex-specific strategies for preventing and treating infectious diseases during the plenary session “Sex-Specific Factors and the Pathogenesis of Infectious Diseases,” held as part of the 2016 ASM Microbe Conference in Boston last June.

According to several researchers in this emerging field, many other researchers and clinicians, as well as research funding agencies, have tended to overlook these sex-based differences, doing a disservice to both men and women who might benefit when treated with appropriately gauged, sex-specific therapies and vaccines. Recent policy updates from officials at the National Institutes of Health (NIH) now recognize some of these concerns. Thus, NIH now is requiring investigators to report sex differences that they observe preclinical studies—not only to highlight these issues but also to promote efforts to identify sex-specific factors and treatments to improve clinical care.

Inflammatory Responses to Influenza Can Lead to Immunopathologies in Women

“Epidemiological evidence from influenza outbreaks and pandemics reveals that morbidity and mortality are often higher for women,” says Sabra Klein of Johns Hopkins University in Baltimore, Md. This pattern proves consistent based on public health reports compiled over many years for seasonal flu outbreaks as well as for the 1957 H2N2 pandemic, 2009 H1N1 pandemic, and smaller outbreaks in humans infected with avian H5N1. This cumulative evidence prompted officials of the World Health Organization in 2010 to urge researchers and epidemiologists to consider sex differences in evaluating exposures to the influenza viruses and outcomes.

Klein investigates and confirms that male mice tolerate much higher doses of influenza virus than do females. For example, the lethal dose of the H1N1 flu virus is 11-fold higher for males than comparable female mice. However, both sexes control viral replication in the lungs equivalently. “Host-mediated immunopathology, rather than virus replication, underlies sex differences in influenza pathogenesis,” she says. Fe-

SUMMARY

➤ Sex differences extend beyond anatomy to encompass important immune system functions, predisposing men and women to respond differently to infectious diseases.
➤ These differential responses suggest that both men and women could benefit when treated with appropriately gauged, sex-specific therapies and vaccines.
➤ Estrogens appear to play a leading role in predisposing females to immunopathology as they respond to specific infectious agents.
➤ Differential responses can include the innate, humoral, and cellular immune systems.
male mice mount an excessive proinflammatory response called a “cytokine storm,” releasing higher levels of tumor necrosis factor-α (TNFα), interferon-γ (IFN-γ), and interleukin-6 (IL6) in lungs. They, in turn, do more damage to host tissues in females than males, leading to greater weight loss, hypothermia, and earlier deaths.

Sex hormones play a leading role in predisposing females to immunopathology, according to Klein. “Sex steroids alter the functioning of immune cells by binding to specific receptors expressed in various lymphoid tissue cells, circulating lymphocytes, macrophages, and dendritic cells (DCs),” she says. Testosterone inhibits CD8 T-cell mediated inflammatory responses to influenza in males, decreasing immunopathology and promoting survival. In females, estrogen receptor-α on DCs, macrophage, and T-cells inhibits nuclear factor-κb (NFκb) signaling to block inflammatory responses when estradiol levels are high. However, during an influenza infection, estradiol levels drop, boosting inflammatory responses.

Restoring estradiol alleviates this exaggerated female susceptibility to influenza in mice, reducing levels of chemokine (C-C motif) ligand 2 (CCL2) and TNFα by more than 10-fold and blocking inflammatory cell recruitment, Klein says. “Administration of E2 exogenously . . . significantly protected females by suppressing inflammatory cytokines and chemokines, reducing morbidity and mortality following H1N1 infection.” Progesterone can also protect female mice from immunopathology by promoting epithelial cell proliferation in the lungs to heal inflammatory damage. Whether such hormonal treatments quell influenza symptoms in women is not known.

For Women with HIV, Heightened TLR-7 Responses Accelerate Disease and Comorbidities

Men and women respond differently when infected with HIV, according to Marcus Altfeld of the Heinrich-Pette Institute in Hamburg, Germany. Initially, due to heightened Toll-like receptor-7 (TLR7) responses, women tend to control HIV better than men. “Plasmid dendritic cells (pDCs) from women and men respond differently to TLR-7 stimulation, including stimulation with HIV-1-derived TLR-7 ligands, thus contributing to sex-specific differences in HIV-1 pathogenesis,” he says. TLR-7 detects viral single-stranded RNA, prompting pDCs to produce the proinflammatory cytokine IFN-α, which initiates antiviral immune responses. Estrogen enhances TLR-7 signaling by upregulating transcriptional regulators in the pathway, doubling IFN-α production from female pDCs. These strong antiviral responses in women keep the virus at bay early following HIV infection, keeping their viral loads about 40% lower than in men.

Although HIV replication at first is controlled better in women than men, chronic HIV disease later progresses faster and can lead more quickly to comorbidities when elevated host inflammation and other host immune responses lead to collateral damage. In women, higher and persistent IFNα responses, which suppress viral replication, also help to activate CD4 and CD8 T-cells, according to Altfeld. These CD8 T-cells target HIV-1-infected CD4 T-cells, depleting their numbers and leading more quickly to the hallmark immunodeficiencies of AIDS.

In addition, chronically heightened inflammatory responses can damage other tissues, leading to non-AIDS related comorbidities, cardiovascular disease, and premature aging, according to Altfeld. “HIV-1 infection results in a significant increase in levels of innate immune activation, which in turn may contribute to the elevated risk of inflammation-related diseases in HIV-1 positive women,” he says. “Women experienced two-fold more combined HIV- and AIDS-related illness than men for the same amount of viral infection.”

These sex-related effects also appear to influence how men and women respond to antiviral treatments. “Side effects of antiretroviral therapy (ART) can differ dramatically between women and men,” says Altfeld. “With first- and second-generation antivirals, women experience more frequent occurrences of skin rashes, mitochondrial toxicity, lactic acidosis, gastrointestinal intolerance, and lipodystrophy, which led to increased rates of treatment nonadherence among women.”

Heightened TLR-7 Responses Sometimes Benefit Females, Other Times Do Not

Hyperactive immune responses in females can be detrimental against some viral infections but beneficial against others, according to Linde Meyaard of University Medical Center Utrecht.
in Utrecht, the Netherlands. Although heighten-
ened TLR-7 responses in females contribute to
influenza-triggered immunopathology, such re-
sponses can protect women against coronavi-
ruses by helping to clear the viruses more quickly.

TLR-7 detects viral RNA and triggers critical
antiviral defenses such as production of type-I
IFN. “Sex has a profound effect on type I IFN
production and viral clearance. Infection resulted
in detectable IFN-α production only in female
mice,” Meyaard says. Female mice control coro-
navirus infections better than do their male coun-
terparts. Similarly among humans, men appear
to have higher fatality rates than do women fol-
lowing infections with coronaviruses such as
SARS-CoV.

However, CD200, a modulator of TLR-7 activ-
ity, can dampen these responses, keeping them
from running rampant and damaging the host
but also limiting how quickly an infected mouse
clears the coronavirus. When this brake on TLR-7
production lets up, female immune responses
skyrocket, accelerating coronavirus elimination.

“The combination of female sex and CD200
deficiency results in increased type I IFN pro-
duction and decreased viral load and pathology
upon mouse hepatitis virus infection,” says
Meyaard. This modulator may be a target for
developing new ways to treat respiratory coronavi-
ruses such as SARS-CoV or MERS, she
suggests.

In contrast, enhanced CD200 and TLR-7 re-
ponses are detrimental to females during influ-
enza infection. TLR-7-mediated inflammation
causes immunopathology resulting in worse
outcomes in females, particularly when the
CD200 brake is removed in mice. “Lack of
CD200 response signaling has a more profound
effect on beneficial but also on pathological im-
mune responses to viruses in female mice as com-
pared to male mice, which can be attributed to the
capacity of CD200 response to inhibit TLR-7 re-
sponses,” says Meyaard.

This immune braking mechanism also con-
tributes to noninfectious diseases, including au-
toimmunity and cancers, according to Meyaard.
A malfunctioning CD200 regulator may predis-
pose women to developing the autoimmune dis-

Women and men differ in their responses to a variety of vaccines, including the flu vaccine. This often boosts
vaccine efficacy in women, but can also mean more frequent and more severe side effects.
order lupus. “The immune suppressive CD200 response fails to suppress TLR-7 signaling in lupus patients,” she hypothesizes. “Since TLR-7 responses are intrinsically increased in women, this may explain the sex-bias in lupus.” Women with lupus outnumber men 9 to 1.

In humans with cancer, CD200 signaling is upregulated, damping immune functions that could otherwise identify and eradicate tumors. In particular, multiple myeloma and acute myeloid leukemia patients tend to overexpress the inhibitory CD200 signal, which is associated with a poor prognosis for such patients. “A clinical trial with a blocking anti-CD200 antibody aims to enhance antitumor responses toward CD200-expressing malignancies,” Meydaard says. However, she adds, CD200 blockers could exert pathological effects on women, elevating their risk of developing autoimmune disorders and increasing the severity of influenza infections.

Some Vaccines Generate Stronger Responses, including Side Effects, in Women than Men

Sex differences in immune responses to viral antigens also underlie variability in vaccine efficacy between men and women, according to Klein from Johns Hopkins. “Sex differences are observed in response to diverse vaccines, including the Bacillus Calmette-Guerin (BCG), yellow fever, influenza, hepatitis, smallpox, and dengue vaccines,” she says.

Humoral immune responses are particularly strong in women, potentially due to estradiol’s stimulating B-cells to proliferate and produce antibodies. “Antibody responses to bacterial and viral vaccines are consistently at least twice as high in women,” Klein says. Indeed, women generate nearly twice the hemagglutinin inhibition (HAI) antibody titers after being vaccinated against the influenza virus than men do. Further, women achieve equivalent antibody titers to men when administered merely half the influenza vaccination dose. Females also mount stronger cellular and innate immune responses. “Females exhibit higher cytotoxic T-cell activity along with up-regulated expression of antiviral and proinflammatory genes, many of which have estrogen response elements in their promoters,” says Klein.

Vaccinating individuals to protect them from the yellow fever virus up-regulates innate immune pathways, including TLR and IFN-associated genes, to a far greater extent in women than in men, according to Katie Flanagan of the University of Tasmania and Monash University in Australia. “These transcriptional signatures predict subsequent protective (adaptive) responses,” she says.

This heightened immune reactivity in females benefits them in several ways—better protecting them when vaccinated against a specific viral strain, but also providing cross-protection from similar viral strains, according to Klein. In both mice and humans given seasonal influenza vaccines, females generate more cross-reactive antibodies that protect against emerging pandemic strains like H1N1 than do men. “Following vaccination, female (mice) are better protected against lethal challenge with heterosubtypic (novel) strains of influenza viruses than males,” she says.

In addition, vaccination sometimes protects recipients, particularly females, against unrelated infectious agents by inducing stronger T-cell and inflammatory responses, according to Flanagan. For example, the BCG vaccine developed to protect against tuberculosis reduces “all-cause” infant mortality rates, apparently protecting children not only against Mycobacterium tuberculosis but also against non-mycobacterial diseases and even cancers. “BCG vaccination showed enhanced proinflammatory innate immune reactivity to TLR stimulation in vitro, more in females than males, suggesting BCG enhances innate immune development early in life,” she says.

However, their strong reactivity to vaccines can prove a double-edged sword, sometimes predisposing women to more frequent and severe adverse side effects than men who receive the same vaccine. “Males and females respond differently to influenza vaccines, with women initiating higher humoral immune responses but experiencing more adverse reactions to seasonal influenza vaccines than men,” says Klein. Side effects such as localized inflammation, headache, fever, nausea, rash, and fatigue are more common in women than men for both viral and bacterial vaccines. Earlier, these differences were attributed to reporting biases. Now researchers say overactive immune responses and inappropriate dosing in women are likely to blame.

This heightened immune reactivity to vaccines in females may go beyond mere discomfort,
according to Flanagan. Overzealous responses to vaccines can trigger allergies and autoimmune responses in females. For example, the diphtheria-tetanus-acellular pertussis vaccine (DTaP) is more likely to cause allergic hypersensitivity in girls than in boys, she says. In other cases, exuberant immune responses are more serious, even deadly. In the 1990s, a high-titer measles vaccine was withdrawn because it doubled mortality rates in infant girls. Additionally, she says, “The malaria vaccine RS,S/ASO1 has also recently been shown to have sex-differential effects on all-cause mortality in phase 3 trials in African infants and children, with increased all-cause mortality observed in females but not males.”

These findings warrant a serious review of how vaccines are formulated and administered, according to Klein and Flanagan. “It is apparent that the design of vaccines and vaccine strategies should be sex-specific, to reduce adverse reactions in females and increase immunogenicity in males,” says Klein. Moreover, she adds, adjuvant vaccines that target TLRs could trigger especially divergent outcomes and side effects between the sexes. Meanwhile, Flanagan recommends looking into different dosing regimens or schedules to address these differences, particularly as they differentially affect girls and boys during infancy. “One key move in this direction would be to define the critical sex-specific factors that determine both specific and heterologous effects,” she says.

Anticipating Sex-Specific Treatments of Infectious Diseases

More broadly, sex-specific responses should be taken into account when developing both prophylactic and treatment strategies for infectious diseases and for those noninfectious diseases such as autoimmune diseases, inflammatory conditions, and cancers, for which immune system responses play important roles. “Our hormonal environment may affect the kinetics, magnitude, and skewing of these differential responses when faced with immunological challenges,” Klein says. “Sex may be a fundamental factor to consider when designing and administering treatments for diseases.”

Thus, men and women might benefit from receiving different dosages of vaccines, antiviral drugs, or anticancer agents—and, furthermore, might experience different side effects. Additionally, treatment strategies might call for manipulating sex hormone levels differently in male and female patients to optimize host defenses against specific diseases. The advent of systems vaccinology will help to reveal more of these sex-specific mechanisms and candidate biomarkers to target, according to Flanagan. “Systems vaccinology identified a testosterone sensitive gene cluster . . . that correlates with poor antibody responses to influenza vaccine, providing insight into mechanisms controlling sex differences in vaccine immunogenicity,” she says. This and other insights could lead to vaccine and drug designs that exploit beneficial immunogenic effects while minimizing deleterious effects.

However, researchers, clinicians, and regulatory officials are far from fully aware of these findings, a major factor in delaying progress so far, according to Klein. “The status quo is to assume that the sexes do not differ, which has hindered our understanding of the pathogenesis of immune-related diseases and the underlying mechanisms,” she says. And, says Altfeld about HIV and other diseases, “failure to perform analysis with stratification by sex can lead to underestimation of vaccine protection, skewing of immunogenicity data, and an incomplete side-effect profile.”

In the case of clinical trials to evaluate a vaccine to prevent herpes simplex virus infections, lumping men and women together has delayed—and, ultimately, may block approval of an otherwise useful product, according to Klein. “When data were analyzed by sex, the efficacy of the vaccine was 73% in women and only 11% in men,” she says. However, when aggregated the results mask how well the vaccine protects women. Failure to move this vaccine forward is particularly tragic, she says, because its use in women could not only protect them against this sexually transmitted disease but might also protect men indirectly as well.

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Microbes as Intein Havens

These microbial, intron-like polypeptides are self-splicing elements that remove themselves posttranslationally from their host proteins

Cathleen Green and Marlene Belfort

Inteins are polypeptide escape artists, with an extraordinary ability to excise themselves from fully folded proteins without leaving a trace. Inteins are best described as protein introns, self-splicing elements that remove themselves posttranslationally from their host proteins. They occur in all three domains of life—archaea, bacteria, and single-celled eukaryotes (Fig. 1A). Even so, inteins are rarely discussed among microbiologists, but this relative silence is about to be broken.

Since the discovery of an intein in the vacuolar ATPase of yeast 25 years ago, researchers have documented more than 1,000 inteins. Up to this point, however, inteins’ greatest claim to fame has been their utility in protein engineering. Inteins are highly efficient at breaking and making peptide bonds, rendering them extremely useful for purifying and modifying proteins, segmental isotope labeling, and developing sensors. Their biotechnological value aside, recent research shows that protein splicing can respond to different environmental conditions, suggesting that inteins play important roles as adaptive regulatory elements.

Despite their wide distribution in the genomes of many important microorganisms, the field of intein biology is in its infancy and much remains to be learned about how these elements are regulated. Here, their role in human pathogens is of particular relevance, not only to probe a potential influence in the infectious process, but also to develop novel antimicrobials.

Inteins Are Widely Distributed

The mobility of inteins at the DNA level helps to explain their widespread distribution across microbes. Most inteins have two components: a splicing domain and an endonuclease domain (Fig. 2A), the latter of which enables an intein to cleave DNA and transfer its gene into the inteinless target (Fig. 2B). The double-strand break of the inteinless allele is repaired using the intein-containing allele as a template, helping the recipient acquire a new intein. Thus, inteins get around, and are found widely distributed, including in some human pathogens, often lurking in provocative places such as within essential proteins. This distribution pattern raises not only the question of why they occur at such sites, but also whether they might be exploited as antibiotic targets.

Curiously, despite this freedom of movement, inteins distribute sporadically and irregularly. Thus, even among very closely related species, inteins might be present or absent. A recent bioinformatics survey analyzed about 10,000 sequenced genomes from bacteria, archaea, and eukaryotes, looking for inteins. Beyond revealing many new inteins, this mining exercise indicated that about one-quarter of bacterial genomes and one-half of archaeal genomes carry at least one and sometimes more inteins (Fig. 1A). Further, only about 1% of eukaryotes contain inteins, and these are found only within unicellular organisms, each with only one intein per genome.

Horizontal gene transfer appears responsible for the spread of inteins among species and between the different domains of life. Lateral transfer was underscored by a study in which inteins in archaeal halobacteria proved to be strikingly similar to those in bacteria. This gene flow is likely facilitated by the homing endonuclease.

Another question about inteins is where they are found within genomes. Intriguingly, they tend to localize within genes encoding specific functional categories of proteins, namely heli-
cases, recombinases, and polymerases (Fig. 1B, RRR). Moreover, several nonorthologous but functionally equivalent proteins of the replisome across bacteria and archaea also carry inteins. An interesting example is the bacterial DnaB and archaeal MCM replicative helicases, which are structurally distinct and unwind DNA in opposite directions. Yet, many inteins are found in DnaB and MCM helicases, suggesting that this biased presence of inteins in different domains of life is based on function.

Other functionally important categories of proteins within which inteins are found include nucleotide transport and metabolism proteins, followed closely by proteins involved in transcription and translation (Fig. 1B, NT/M, T, and T/R). Astonishingly, 70% of inteins localize to proteins with ATPase and ATP-binding domains. Moreover, inteins cluster overwhelmingly within the active centers of these proteins, such as catalytic sites, binding regions, and interfaces of protein complexes.

Although inteins are not common in eukaryotic genomes, they are found in nuclear genes encoding a handful of different proteins. Once again, these inteins interrupt important genes at critical sites. The first intein discovered in the vacuolar membrane ATPase was found across saccharomyces yeasts only. The second described nuclear intein was found in the pathogenic yeasts Cryptococcus neoformans and C. gattii in the PRP8 protein, important for intron RNA splicing. Inteins occur widely across fungi in RNA polymerases, chitin synthase, glutamate synthase, and threonyl-tRNA synthetase. To appreciate how such critical proteins are expressed and to begin to comprehend the peculiarities of intein distribution, it is important to understand the basics of protein splicing.

**Inteins and Protein Splicing**

After being translated from a messenger RNA, a nonfunctional precursor protein undergoes splicing to release its intein and to join the flanking peptide segments, known as exteins (Fig. 2A). This self-splicing reaction depends upon a few characteristic sequence motifs, or blocks, and conserved extein junction residues (Fig. 2C). The first amino acid of the intein, designated the 1 residue, is usually a cysteine or serine. The last two residues of the intein are customarily the dipeptide motif histidine-asparagine. At the C-terminal splice site, the first amino acid of the C-extein is invariably a cysteine, serine, or threonine. Since this residue belongs to the extein sequence, it is designated the +1 amino acid. The chemical properties of these conserved residues are vital to the protein splicing pathway.

The canonical splicing pathway occurs in four steps (Fig. 2C, shown using two cysteines, C1 and
C1). First, the C1 cysteine residue acts as a nucleophile, attacking the preceding amide bond at the N-extein-intein junction, creating a thioester bond. Second, the +1 cysteine residue initiates a nucleophilic attack on the thioester, leading to a branched intermediate species. Third, the...
branch
ed intermediate is resolved by cyclizing the asparagine at the end of the intein, freeing the intein from the precursor and ligating the flanking exteins by forming an ester bond. In the final step, the ester linkage rearranges to form a regular peptide bond, giving rise to the functional protein.

Two other classes of noncanonical inteins perform similar splicing chemistry, but the initiating nucleophile is not at the same 1 position. Another curiosity is the trans-splicing inteins, which are found mainly in cyanobacteria. Their conserved splicing blocks are divided between two open reading frames, typically located remotely from one another in the genome. Because the N- and C-extein halves are separately transcribed and translated, the two polypeptides must first find each other before they can be spliced.

**Inteins as Sensors**

Why do inteins localize to key proteins, often at critical functional sites, such as ATPase domains? At least three possibilities come to mind, and they are not mutually exclusive. The first is that such positioning provides a tolerant spot for inteins to fold, allowing them to excise and splice efficiently from the host protein. Second, inteins might become trapped in active sites from which imprecise intein loss would be catastrophic. A third possibility is that inteins are not mere silent passengers but, instead, have a regulatory function that cells cannot afford to lose.

Recent advances hint that specific inteins respond to environmental cues, which inhibit or facilitate splicing. Thus, some inteins sense potentially stressful conditions and manipulate...
splicing rate, thereby regulating their respective host protein functions. These signals are transduced through cysteine chemistry or intramolecular protein-protein interactions (Fig. 3). Inteins thus have the potential to serve as novel, posttranslational regulatory sensors.

A bioinformatics search inspired by thioredoxin, a protein whose CXXC motif forms disulfide bonds to reduce cellular proteins, was conducted to see if a CXXC motif might occur in association with inteins. This search revealed several intein-containing, redox-related proteins, including MoaA, an oxygen-labile molybdate-biosynthesis cofactor of the deep-sea archaeon *Pyrococcus abyssi*. This intein contains a cysteine at the 1 position and a cysteine two residues upstream in the N-extein, allowing redox-based regulation (Fig. 3, top). Not only does this redox-controlled intein allow splicing under reducing conditions when MoaA function is necessary, but it also inhibits splicing in an oxidizing environment, thereby sparing MoaA from oxygen toxicity.

Other inteins also seem to be regulated through cysteine chemistry. For example, the splice-site cysteines of the mycobacterial intein in the SufB protein are responsive to oxidative and nitrosative stresses. These stresses, which prevail in macrophages during infection, lead to cysteine modification, inhibiting splicing (Fig. 3, middle). Again, the intein may be sensing stress signals to shut down protein activity during adverse conditions to prevent the functional protein from being damaged.

Inteins also sense temperature stress. The RadA recombinase from the hyperthermophilic archaeon *Pyrococcus horikoshii* exhibits a striking intein-extein interaction that blocks intein function and is regulated by temperature (Fig. 3, bottom). The intein is active only at 65°C or higher, corresponding to the organism’s ambient temperature. Splicing activation corresponds to the thermal sensitivity of the native intein-extein interactions. This novel form of posttranslational control would allow maximal expression of RadA at the optimum growth temperature of the host, while shutting off splicing at cooler temperatures. The RadA intein is in the ATPase domain, and splicing inhibition may prevent expensive ATP degradation.

Protein splicing as a potential antibiotic target. Inteins provide novel, underexplored targets for antibiotics. Inhibitors could include compounds that target cysteines. Targeting C1 and/or C+1 could inhibit splicing and result in precursor accumulation, C- or N-terminal cleavage. Targeting other residues is also possible.
hydrolysis when the organism requires energy to mount a cold-shock response.

More generally, the ability to spare ATP under conditions of stress may in part account for the preponderance of inteins in ATPase domains. Regardless, these examples of sensing their surroundings and of conditional protein splicing suggest that some inteins have regulatory roles under specific environmental conditions, thereby providing selective advantages to their microbial hosts.

**Inteins as Targets for Antimicrobial Drugs**

Inteins reside in some human pathogens, including *Mycobacterium tuberculosis*, the cause of tuberculosis (TB), which harbors three inteins. Additionally, *Coxiella burnetti*, which causes Q fever, hosts a single intein, as do several fungal pathogens, including *C. neoformans*, *C. gattii*, *Blastomyces dermatitidis*, and *Histoplasma capsulatum*. Because essential proteins containing inteins are nonfunctional if their splicing is inhibited, such proteins provide a novel, attractive, and understudied drug target. The search is now on for inhibitors that can bind either the precursor or its intein to prevent a functional protein from forming by blocking activity at the intein C- or N-terminus, or both (Fig. 4). The absence of inteins from animals adds to the appeal of drugs that could target microbial inteins.

One well-known and widely used chemotherapeutic anticancer agent, cisplatin, specifically inhibits intein splicing in *M. tuberculosis* and immediately arrests growth of this microorganism. While this drug damages DNA to stop growth in eukaryotic cells, how it inhibits inteins needs to be further explored. Because many metals bind inteins, one possibility is that this platinum-based compound forms complexes with the catalytic cysteines of inteins to halt the splicing pathway. Mechanistic and structural insights into its activity could inform the design of alternative intein inhibitors with less-toxic side effects.

The idea of novel drugs against TB is alluring in a world with incidence rates of this disease on the rise along with emergence of multidrug-resistant strains. Success with intein inhibitors against *M. tuberculosis* would bolster the idea of inteins as antibiotic targets, and could lead to the development of novel drugs that are active against other intein-containing pathogens, especially hardy fungal pathogens for which the drug development pipeline is nearly dry.

Marlene Belfort is a distinguished professor in the Department of Biological Sciences and RNA Institute, University at Albany, SUNY, Albany, N.Y. (mbelfort@albany.edu), and Cathleen Green is a graduate student in the Department of Biological Sciences at the University at Albany.

**Suggested Readings**


ASM Meetings

Save the Date: ASM Microbe 2017. Mark your calendar for ASM Microbe 2017 (June 1–5, New Orleans, La.)—the premier event in the field that features cutting-edge science, world-class speakers, abundant networking opportunities, and much more. Don’t miss the rare opportunity to explore the full scope of microbiology by choosing from more than 200 engaging sessions and workshops and over 3,000 posters at this unique event. For more information, visit www.asm.org/meetings.

2017 ASM Biothreats: Research, Response and Policy

Formerly known as the ASM Biodefense and Emerging Infectious Diseases Research Meeting, the 2017 ASM Biothreats meeting discusses a wide-range of biological threats and emerging infectious diseases to stimulate knowledge-sharing amongst stakeholders in academia, industry and government; and to help the overlapping communities prepare for, mitigate, and prevent these global threats. Learn more at www.asm.org/biothreats.

Mark Your Calendar: 2017 Clinical Virology Symposium

Join more than 1,000 peers from across the globe at the 33rd annual Clinical Virology Symposium (May 7–10, Savannah, Ga.). This international symposium delves into the relationship between rapid viral diagnosis, clinical course of viral infections, and preventive and therapeutic modalities for viral infections. For more information, visit www.asm.org/meetings.

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.

6th ASM Conference on Beneficial Microbes (September 9–12, 2016, Seattle, WA)

ASM Conference on Infection and Cancer (October 24–27, 2016, Washington, DC)

ASM Conference on Antibacterial Development (December 11–14, 2016, Washington, DC)

Tentative scheduling of 2017 ASM Conferences is listed below. For confirmed dates and locations, visit www.asm.org/conferences.

ASM Conference on Innovative Microbial Ecology for Mitigation of Antibiotic Resistance and Bacterial Diseases (March 2017)

ASM Conference on Mechanisms of Interbacterial Cooperation and Competition (March 2017)

ASM Conference on Tuberculosis: Past, Present and Future (April 2017)

ASM Conference on Interplay of Viral and Bacterial Pathogens (ASMASV collaboration) (May 2017)

2nd ASM Conference on Rapid Applied Microbial Next-Generation Sequencing and Bioinformatic Pipelines (September 2017)

6th ASM Conference on Cell-Cell Communication in Bacteria (October 2017)


4th ASM Conference on Viral Manipulation of Nuclear Processes (December 2017)
ASM Public Affairs

ASM Advisory on Gain of Function Research Report

In July, ASM sent an advisory to members regarding the National Science Advisory Board for Biosecurity (NSABB) approved recommendations for the evaluation and oversight of proposed Gain of Function Research of Concern (GOFROC), following a process involving a risk/benefit and ethical analysis and several public meetings. The recommendations focus on a small subset of Gain of Function (GOF) research proposals, or research generating a pathogen with pandemic potential that entails risks that warrant additional oversight beyond the current oversight. Decisions about whether to fund GOFROC would be based on a set of principles, including merit, a risk/benefit analysis, consideration of alternative methods, history of the investigator and the institution, ability to respond to lab accidents, and whether an organism contains a virulence gene from another organism with which it could not recombine in nature. Following approval by the NIH director, HHS Secretary, and other department heads, the Office of Science and Technology Policy (OSTP) will develop new guidance for funding and oversight of GOF research. OSTP hopes to complete an overarching structure for GOF research and then to lift the year-and-a-half funding pause on certain projects involving influenza, SARS, and MERS. The NSABB recommendations are available online at http://osp.od.nih.gov/sites/default/files/NSABB_Final_Report_Recommendations_Evaluation_Oversight_Proposed_Gain_of_Function_Research.pdf. The ASM advisory is available at https://www.asm.org/index.php/public-policy/93-policy/94293-nsabb-7-5.

ASM Meets with OSTP’s Fast Track Action Committee on Biosafety

In late June, Ronald Atlas, Chair of the ASM Public and Scientific Affairs Board and Janet Shoemaker, Director, ASM Office of Public Affairs, met with the Office of Science and Technology Policy’s Fast Track Action Committee on Biosafety (FTAC). The FTAC was tasked with gathering information on two issues: whether to bring all bioscience institutions, or at least all those operating at or above Biosafety Level 3, or high containment, under federal biosafety regulation and the feasibility of adopting a “risk-based” approach to managing the safety and security oversight of biological agents and toxins. ASM’s presentation is online at http://www.asm.org/images/PSAB/ASM-Presentation-6-29-16.pdf. This meeting was a follow-up to an ASM presentation to the Federal Experts Security Advisory Panel on Issues Related to Biosafety and Biosecurity in 2014.

ASM Comments on Laboratory Fees at CMS Meeting

On July 18, ASM Public and Scientific Affairs Board Professional Affairs Committee Chair Robert Jerris addressed the Medicare Public Meeting Regarding New and Reconsidered Clinical Diagnostic Laboratory Test Codes for the Clinical Laboratory Fee Schedule (CLFS) for Calendar Year 2017 on new clinical microbiology codes. Every year, the public CLFS meeting is held at the Centers for Medicare & Medicaid Services (CMS) in Baltimore, Md., and influences what the payment level will be for clinical laboratory tests. Concomitant with the morning session of the public fee-setting meeting was a meeting of the Advisory Panel on Clinical Diagnostic Laboratory Tests Meeting, as prescribed by the Protect Access to Medicare Act (PAMA) of 2014. To learn more about the meeting and to see the comments, go to http://www.asm.org/index.php/issues-we-follow/98-policy/issues/94307-clfs-7-16.

Fiscal Year 2017 Spending Bills

On July 14, the House Appropriations Committee approved its FY 2017 Labor, Health and Human Services (LHHS) spending bill. The legislation includes funding for the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC). The bill provides a total of $33.3 billion for the NIH, $1.25 billion above the fiscal year 2016 enacted level and $2.25 billion above the President’s discretionary budget request. The Senate Appropriations Committee bill reported on June 9 includes $34 billion for NIH, a $2 billion increase over 2016. The legislation includes a total of $7.8 billion for CDC, $605 million above the fiscal year 2016 enacted level and $800 million above the President’s budget request. Within the total, the bill provides $390 million to fight the Infectious Diseases Rapid Response Reserve Fund, which will give the CDC Director immediate access to funds to respond to any future infectious disease emergency such as Ebola or Zika.

In April, Senate appropriators approved an FY 2017 Commerce, Justice, Science (CJS) Appropriations bill to fund the National Science Foundation (NSF) and other agencies. The House approved their FY 2017 CJS bill in May and would fund the NSF with $7.4 billion, $158 million below the President’s request and $57 million below FY 2016. NSF Research and Related Activities (R&RA) would receive just over $6 billion, or $46 million above the FY 2016 level and the same as the President’s request.

In May, House and Senate appropriators approved an FY 2017 Energy-Water Appropriations bill to fund the Department of Energy (DOE) and other agencies through September 30, 2017. The House bill would fund the DOE Office of Science at $5.4 billion and ARPA-E with $306 million. Basic Energy...
Sciences (BES) would receive $1.9 billion, $77 million below the President’s request and $11 million above FY 2016. Biological and Environmental Research (BER) would receive $595 million, $14 million below FY 2016 and $67 below the President’s request.


**Education Board**

**ABRCMS 2016: Register by 12 October to Receive $100 Discount**

The 16th Annual Biomedical Research Conference for Minority Students (ABRCMS) will take place 9–12 November 2016 in Tampa, Fla. Register early (by 12 October) to receive a $100 discount off the onsite registration fee. ABRCMS 2016 attendees will benefit from a distinguished roster of speakers, along with numerous workshops, scientific presentations, professional development opportunities, networking events, and more. For more information, visit http://www.abrcms.org. ABRCMS is managed by ASM and supported by the National Institute of General Medical Sciences of the National Institutes of Health under award number T36GM073777.

**Scientific Writing and Publishing Online Course (SWP Online)**

SWP Online is a four-month overview of scientific writing and publishing concepts. Geared to ASM members who are graduate students, postdoctoral fellows, and early-career scientists, the course includes seven 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 2017 program takes place from January through April, and registration for the course will be accepted until 1 December 2016. For more information, visit bit.ly/swpo17n.

**Interested in Teaching? Apply to Be a 2017 ASM Science Teaching Fellow!**

The ASM Science Teaching Fellows Online Course is a five-month professional development opportunity that prepares doctoral-trained students for science teaching positions at a variety of nondoctoral institutions. The course will develop introductory teaching skills on course design, student-centered learning strategies, and career preparation. Participants will be part of an online community of fellows, mentors, and facilitators with exclusive access to interactive webinars, readings, and skill-building activities presented by experts in the field. The application deadline is 2 November 2016. For more information, please visit: http://bit.ly/stf17.

**Webinar Series Helps Faculty Integrate Quantitative Concepts into Courses**

This fall, ASM, in partnership with the Quantitative Undergraduate Biology Education and Synthesis (QUBES) project, has organized a new, four-part webinar series focused on increasing quantitative biology in undergraduate education. This faculty development offering is based on the concept of “massive open online courses” and will be coupled with an online faculty mentoring network where participants can share and develop curriculum. The 60-minute webinars will address common issues around teaching quantitative skills and reasoning, ranging from dilutions to graphing to data analysis. The program will run from September to December, 2016. The registration deadline is 14 September. To learn more and register for this professional development opportunity, please visit www.facultyprograms.org.

**Branches: ASM Activity at the Local Level**

**Indiana Branch 2016 Annual Meeting and Plans for 2017**

The Annual Meeting of the Indiana Branch of ASM (IBASM) took place on April 1–2, 2016, on the campus of Indiana University-Purdue University, Fort Wayne (IPFW). There were over 60 in attendance with 27 abstracts in microbiology and immunology presented by 15 undergraduate, four M.S. graduate, and eight Ph.D. graduate students.

The meeting began on Friday evening with a talk from ASM CEO Stefano Bertuzzi highlighting ASM programs and resources, followed by a presentation by ASM Past-President Timothy Donohue (University of Wisconsin-Madison), who spoke on how microbial sciences help to produce fuels and chemicals from plant biomass. Saturday morning opened with a student poster session and was followed by a public health talk from the Allen County Health Commissioner Deborah McMahan. ASM Distinguished Lecturer Nancy Hanson (Creighton University) closed out the meeting with her presentation on the regulation of β-lactamase production.

Student oral presentations were well received and covered a variety of research topics. Chance Smith from Indiana University Southeast discussed the characterization of bacteriophages from water samples using Caulobacter crescentus as the host organism, while M. F. Mohamed from Purdue University shared his research on “Targeting Intracellular Pathogenic Bacteria with a Kanamycin Antibiotic Peptide Conjugate.” Additional student presenters included Melissa Beaty from IPFW, who spoke about “Mycobacterial Acyltransferase Involved in Dormancy Associated Lipid Biosynthesis,” and Sylvie Kristoff from Indiana University-Purdue University Indianapolis (IUPUI), who shared her findings on...
the effects of nicotine in the binding of Streptococcus mutans to collagen, fibrinogen, and laminin.

Awards were presented to the first- and second-place student poster presentations at the undergraduate, M.S. graduate, and Ph.D. graduate levels. At the undergraduate level, first place went to Janine Bennett of IPFW for her work on the regulation of sunscreen biosynthesis in cyanobacteria, while second place was awarded to Xyryl Pablo, also of IPFW, for her poster entitled “Mycobacterial Protein mEtTα and its Role in Resuscitation from Stationary Phase.” M.S. student award winners included first place to James Price of IPFW, who looked at the microbiome of the green sea turtle, and second place to Jamison Law of IPFW for his work studying the biochemistry of a mycobacterial glycerol-3-phosphate acyltransferase. All of the award winners in the Ph.D. division were from Purdue University, with first place awarded to Shankar Thangamani, who presented research on “Re-purposing Auranofin, an FDA Approved Antirheumatic Drug for the Treatment of Staphylococcal Infections.” There was a tie for second place for two excellent poster presentations, one by Waleed Younis, who discussed the use of carbonic anhydrase inhibitors against enterococcal infections, and the other by M. F. Mohamed, whose research was also delivered in the oral presentation noted above.

The IBASM meeting was organized by the executive committee and student officers Jamison Law of IPFW and Grace Gomez of IUPUI. Our sponsors include the ASM Branches program for support and funding, Pearson Publishing, and the College of Arts and Sciences and Department of Biology at IPFW.

To view short video vignettes from the meeting, check out the Web page containing highlights of ASM CEO Stefano Bertuzzi’s Branch Listening Tour at http://www.asm.org/index.php/listening-tour.

Mark Your Calendar for 2017 IBASM Meeting. Please join us for next year’s meeting at Turkey Run State Park in Marshall, Indiana on March 31-April 1, 2017! For more information on the Indiana Branch please visit http://ibasm.iweb.bsu.edu/; for more information on the ASM Branch program see http://www.asm.org/branches.

Tanya Soule
President-Elect, Indiana Branch ASM

Eastern PA Branch of ASM “Whiskey Meeting”

The Eastern Pennsylvania Branch of ASM (EPA-ASM) held its inaugural “Patrick’s Day Meeting” on March 28th. The meeting has been named to honor past EPA-ASM president and Professor of Microbiology, Temple School of Medicine, Patrick Piggot, Ph.D. (deceased).

Patrick, originally from Ireland, was born on St. Patrick’s Day, and every year on his birthday he would bring a bottle of fine Irish whiskey to work, pour everyone a small dram and offer a toast, reminding people that the whiskey was to be “sipped, not shot.” During the Branch meeting, in honor of Patrick, and to ensure the whiskey was sipped, Bettina Buttaro led a three-part toast to Patrick, as a scientist, as a mentor, and as a friend.

Sunny Shin (Perelman School of Medicine University of Pennsylvania) was the scheduled speaker, but unfortunately lost her voice with a laryngitis infection and was unable to participate. However, her husband Igor Brodsky (University of Pennsylvania, School of Veterinary Medicine), also a microbiologist, nobly stepped in at the eleventh hour and gave a presentation in her stead in which he described some of his latest research addressing pathogen-host interactions of Yersinia and Salmonella.

The Branch meeting was well attended (52 people) and it may be possible that the encouragement to drink was part of the reason. Indeed, a couple of postdocs were overheard earlier in the day—one asking the other if they were going to the “whiskey meeting.” The reply was affirmative!
For more information on the Eastern PA Branch, see https://www.epaasm.org/; to learn more about the ASM Branch Program, go to www.asm.org/branches.

Simon Knight
President, Eastern Pennsylvania Branch ASM

80th Annual Meeting of the ASM
Southern California Branch

Join your fellow microbiologists at the 80th Annual Meeting of the Southern California branch of ASM at the Hyatt Regency, La Jolla, CA, October 28–29, 2016.

We have a great line-up of speakers, starting with the ASM CEO, Dr. Stefano Bertuzzi. Topics include futures in microbiology, digital microbiology, new methods for detection, lean processes, foodborne pathogens, and case studies on cutting-edge challenges and solutions.

Up to 14 CEU units can be obtained during this two-day event, and CEU documentation is included in your registration fees. Undergraduate and/or graduate students can present their research during the poster session on Saturday.

SCASM, with support from bioMerieux, Inc., will award the top three poster presenters an all-expenses-paid, student travel award, to attend the 2017 National ASM Meeting.

You can obtain more information or register for this exciting educational event at www.scsasm.org, or email info@scasm.org or call 858–487-7759.

Obituaries

Walter Weldon Bond, Jr.

It is with deep sadness that we announce the death of Walter W. Bond, Jr., MS, on May 24, 2016 after a short but serious illness. He was 73 years old.

Walter (Walt) was a Texan, having been born in El Paso and growing up in Lubbock. He graduated from Texas Technological College (now Texas Tech University) with a BS in Bacteriology in 1964. He attended graduate school at Northwestern College of Louisiana in Natchitoches, Louisiana and received his MS in Microbiology in 1967.

Walt had an illustrious 31-year career as an indoor environmental microbiologist. He went to work for the Centers for Disease Control in 1968 where he was assigned to the Phoenix Field Station and began working in the Planetary Quarantine/Spacecraft Sterilization program in partnership with NASA for the Mariner-Mars 1969 spacecraft. While in Phoenix, he did notable research on spore-forming bacteria. During this time, he discovered a highly thermoresistant spore form of a gram-positive bacterium which was officially named Bacillus xerothermodurans. Shortly afterward, he and some of his colleagues there in Phoenix conducted ground-breaking applied research in microbial inactivation and environmental infection control. The scope of his work at this time included hepatitis B virus microbiology, sterilization and disinfection of medical instruments and health care facility surfaces, microbial quality of potable water and hemodialysis fluids, and health care worker safety. Walt and Martin Favero discovered that hepatitis B virus (HBV) could persist in an infectious state on environmental surfaces for at least seven days under ambient room conditions, a finding that underscored the importance of promptly cleaning and disinfecting blood contamination of hospital surfaces. Along with his colleague Ramon Moncada, he published some of the first applied research on the reprocessing of flexible fiberoptic endoscopes.

CDC closed the Phoenix Field Station in 1983 and moved the staff to CDC here in Atlanta. He joined the Hospital Infections Program (now the Division of Healthcare Quality Promotion) where he continued his work on the chemical disinfection of HBV, cleaning and disinfection of endoscopes, and providing microbial inactivation consultations to HIP EIS officers during outbreak investigations.

Throughout his CDC career, Walt made major contributions to the development of our current basic infection prevention principles. Walt and Dr. Favero were central to CDC’s working with Earle Spaulding in the late 1970s which led to the agency adopting and promoting the “Spaulding Classification.” The Spaulding Classification as a concept enabled health care professionals to determine the appropriate level of microbial inactivation needed for any instrument or device during cleaning and reprocessing in order to make the instrument safe for use on the next patient. The Spaulding Classification took into account the intended use of the instrument or device and the expectation of adverse outcomes if the instrument or device was contaminated at time of use. Walt was also supportive of a microbiology colleague Professor Willie Greene, University of Minnesota, in promoting the concept we know today as the “Chain of Infection.” This simple but powerful concept of infectious disease transmission helps health care professionals to determine the most effective methods for infection control and prevention for virtually every pathogen. Walt also developed the graphic that depicts the ascending level of microbial resistance to chemical disinfectants. This enabled health care professionals to determine what level of disinfectant potency was needed to inactivate bacterial, viral, or fungal pathogens whenever disinfection was indicated as the final step in instrument or surface reprocessing.

Walt made major contributions to many of CDC’s infection prevention guidelines, most notably the 1985 “Guideline for Handwashing and Hospital Environmental Control” and the 1993 and 2003 editions of the “Guidelines for Infection Control in Dental Health-Care Settings.” He authored
more than 60 journal publications and numerous book chapters. He retired as a Senior Research Microbiologist/Deputy Branch Chief of the Program’s laboratories in January 1998. He spent several years thereafter as an independent consultant in health care environmental microbiology doing business as RCSA, Inc.

Walt was a member of ASM for 50 years, and was inducted as a Microbiologist to the National Registry of Microbiologists in 1975. While in Phoenix, he served in major leadership capacities in the Arizona Branch of ASM. He received the OSAP (Organization for Safety, Aspesis, and Prevention) Dr. James J. Crawford Award for Lifetime Achievement in recognition of major contributions in science, education and public policy in 2001.

Walt lived in Lawrenceville, Ga., for many years. He was a motorcycle enthusiast and especially enjoyed units with a side car attached. He loved fishing, reading, cooking, sharing good times with friends, and listening to bluegrass music. He was devoted to all of his pets and loved animals in general.

Donations in Walt’s memory can be directed to groups who provide service dogs to disabled military veterans (e.g. PatriotPaws www.patriotpaws.org/donate.html or America’s Vet Dogs www.vetdogs.org) or to programs that rescue military service dogs and police dogs and put them up for adoption (Save-A-Vet www.save-a-vet.org/d7/donate).

Lynne M. Sehulster
Centers for Disease Control and Prevention
Atlanta, Ga.

Hubert A. Lechevalier and Mary (Midge) Pfeil Lechevalier

The world-famous academic microbiology research team of Dr. Hubert (Hugh) A. Lechevalier and his wife Mary (Midge) Lechevalier died three weeks apart in the fall of 2015. They were known for their love of actinomycetes, students, gardening, art, great French wine, French cooking, mushroom forays, and cross-country skiing. They were soul mates in so many ways and the world is a better place because they shared their knowledge and love for actinomycetes with so many students and colleagues.

Hubert A. Lechevalier, 89, died peacefully at home in Morrisville, Vt., on October 28, 2015. He was a world authority on the filamentous bacteria, the actinomycetes, which became a treasure trove for antibiotics, immunosuppressants, anthelmintics, statins, enzyme inhibitors, and growth stimulators. Mary Pfeil (Midge) Lechevalier, 87, died peacefully on November 15, 2015, while in home hospice care. She was an innovative scientist who developed new ways to isolate and cultivate rare and unusual actinomycetes.

Hubert Lechevalier, the only son of Jean Gaston Lechevalier and Maria Emile Lechevalier (Delorme) was born on May 12, 1926, in Tours, Indre et Loire, France. In the early 1930s, his family emigrated to Quebec, Canada. Midge grew up in Shaker Heights, Ohio, attended the Laurel School, where chemistry was her passion and where she was a star athlete.

Hugh attended Laval University, graduating with Licence és Sciences Naturelles (summa cum laude), 1947. While working on his graduate studies under René Pomerleau, he noticed gram-negative bacteria inhibiting the Dutch elm disease fungus, Ceratostomella ulmi (Ophiostoma). Thus was born his M.S. thesis, an evaluation of antibiotics against this fungal pathogen. His research was cutting-edge, noting that Dutch elm disease was first recorded in Canada in 1946. Hugh remained close with Pomerleau, who became the Canadian expert on Dutch elm disease.

Midge completed undergraduate education at Mount Holyoke College, Hadley, Mass., majoring in Physiology and Biochemistry and graduating in 1949. When asked of her future plans, she noted her goal was research with the recently discovered antibiotics.

Hugh continued studying antibiotics as a doctoral student under Selman Waksman, at the Department of Microbiology, Rutgers University, NJ School of Agriculture, earning his Ph.D. in 1951. In his thesis “Neomycin, a new antibiotic produced by Streptomyces fradiae,” he detailed the discovery of this new broad-spectrum aminoglycoside antibiotic. This antibiotic is effective for topical applications and in surgery and today is a key ingredient of the widely available topical product Neosporin. Neomycin has subsequently been widely used to selectively monitor gene transfer in cloning studies in combination with the aminoglycoside phosphotransferase gene.

During Hugh’s doctoral studies he maintained his interest in Dutch elm disease, leading to the discovery of a new antifungal agent from S. griseus (1953) that was especially effective on yeasts and, hence, named candidicid. In like mycological manner he later isolated an antibiotic, peniophorin, from Peniophora (1980). In 1954, Hugh moved with Selman Waksman across the Raritan River to the newly opened Waksman Institute. Here he elucidated the diversity and properties of the Actinomycetes for the next 37 years along with Midge as his co-researcher and lab director.

Midge moved to Rutgers University to study under Selman Waksman and Vincent Groupé at the Department of Microbiology, NJ Agricultural School, (Cook College), SEBS. Midge conducted a “Search for Antiviral and other Antibiotics,” addressing the antiviral properties of ehrlichin from Streptomyces lavendulae. During these studies she honed her skills in isolation of new actinomycetes, including three neomycin-producing strains that Hugh Lechevalier evaluated in his Ph.D. studies. Midge was awarded her MS in 1951. Married in April 1950 to Hugh Lechevalier, she raised their children, Marc and Paul, while also assembling data
bases for actinomycete and antibiotic
texts that Dr. Waksman and her hus-
band were producing.

In 1961, Midge joined E. R. Squibb
(now Bristol Myers-Squibb) working
on steroids. The next year, Midge went
as a Visiting Investigator with Hugh to
study at the Institute of Biology,
Czechoslovak Academy of Sciences,
Prague, for the summer. Midge contin-
ued in Europe at the Service de My-
cologie, Institut Pasteur, Paris. She re-
turned to the US in 1962 and rejoined
Rutgers first as a Research Associate at
the Waksman Institute. In 1974 Midge
was appointed to the research faculty
and rose to the upper professorial
ranks, retiring as Research Professor

Between them they published about
200 articles, with Midge individually
publishing 79 studies, 46 in association
with Hugh. They were each recognized
as world authorities on the Actinomy-
cetes. Their studies addressed the sys-
tematics of the Actinomycetes, espe-
cially based on microscopy including
elegant use of the electron microscope,
and analyses of cell wall components
(unique sugars and distinctive lipids)
thereby nurturing chemotaxonomic
identification.

Hugh was active in graduate teach-
ing. He organized the General Micro-
biology course, and taught courses on
Actinomycetes and their Antibiotics.
Hugh mentored 15 students for higher
degrees, and taught a stream of visiting
investigators from 25 countries the fi-
nesse of chemotaxonomy of the Acti-
nomycetes. He was honored with the
prestigious Lindback Award (1976) for
distinguished research, the Charles
Thom Award, Society for Industrial
Microbiology (jointly with Midge, his
wife) for contributions to Industrial
Microbiology, elected to the New Jer-
say Inventors Hall of Fame (1990), an
Honorary D.Sc. from Laval University
(1983), and as an honorary member of
the Société Française de Microbiologie
(1987) and also of the Society of Acti-
nomycetes, Japan (1997).

In addition to 200 research publica-
tions he wrote seven texts, four coau-
thored addressing the actinomycetes
and their antibiotics, Hugh was a keen
historian and served as a member of the
ASM Archives Committee. His two
texts summarized the development of
microbiology, both internationally and
at Rutgers (“Three Centuries of Micro-
biology”; “The Development of Ap-
plied Microbiology at Rutgers” plus re-
views of “The Waksman Institute of
Microbiology”, and “The search for an-
tibiotics at Rutgers University”).

Over his career he served on the ed-
itorial boards of Applied Microbiology,
Annales de Microbiologie, was coeditor
of texts on Macrophages and Cellular
Immunology, and Microbial Ecology.
With Allen Laskin he developed the
monumental Handbook of Microbiol-
ogy which in the second edition en-
compassed nine volumes. He was edi-
tor of the timely Actinomycetes
(1981–1989, published by the Waks-
man Institute). Hugh’s stature was
recognized by the many national and
international committees on which he
served.

Over the span of Midge’s career, she
received The Waksman Award of the
Theobold Smith Society; The ASM J.
Roger Porter Award for stewardship of
microbial diversity; was elected presi-
dent of the Sigma Xi Rutgers Chapter,
and as a member of the Executive
Committee US Federation of Culture
Collections, the ASM Committee on
Actinomycetes, the Advisory Commit-
tee for Bergey’s Manual of Determina-
tive Bacteriology [Muriform Actino-
mycetes (Chair)], as an Associate
member of Bergey’s Trust, and an
Honorary Member of the Society for
Actinomycetes, Japan.

Hugh was best known for his dis-
covery of neomycin, it being one of
the new broad-spectrum antibiotics
that revolutionized the practice of
medicine and world health programs,
and drove the explosive development
of the pharmaceutical industry in the
mid-20th century. Midge was most
appreciated and respected for her in-
novative laboratory methods and
mentoring of numerous students and
visiting professors. Together, they in-
fluenced many young scientists to
study actinomycetes and to continue
screening them for novel molecules
and enzymes. Many a career in mi-
crobiology was launched in the Lech-
evaliers’ laboratory. We owe them a
great debt of gratitude for all that
they taught us. Hugh and Midge will
be missed but never forgotten.

Jennie Hunter-Cevera
Douglas Eveleigh
Joachim Messing
David Pramer
Rutgers, The State University of New Jersey
New Brunswick, NJ
Microbe Mentor

Interview with a Fulbright Scholar—Dr. Luis A. Ríos Hernández

For this issue of Microbe Mentor, Eleanor Jennings interviewed Dr. Luis A. Ríos Hernández regarding his experience as a Fulbright Scholar. Dr. Ríos Hernández is currently at the University of Gdańsk in Gdańsk, Poland, working in the area of molecular biology. Before winning this award, he was an associate professor in the Biology department at the University of Puerto Rico at Mayaguez. Dr. Ríos Hernández was acting as the President of the ASM Puerto Rico branch before departing for Poland. He also served for four years as a member of the steering committee within the branch, and as the ASM representative within the Puerto Rico branch. In this interview, Dr. Ríos Hernández describes the Fulbright application process and what this award has meant for him and his family.

MM: How did you go about applying for your Fulbright Scholarship? What was the application process like?

LRH: First, I would like to point out that everything started back in June 2013 at the ASM General Meeting. There, I was honored to be a lecturer presenting a talk on my experience teaching at a US territory university. At the end of that talk, an attendee introduced herself as the ASM young ambassador of Poland, and she asked me if I would be interested in giving that same talk in Poland. At the time, I said “Of course!” (while really thinking that I would never hear from her again). Later that year, however, she invited me as a guest speaker at an ASM workshop that was held in December 2013 at the University of Gdańsk. Also during that visit, I was invited to give a lecture to the molecular biology department on my ongoing research with environmental enterococci. During that seminar, a professor asked me a few questions that I was not able to answer, which then prompted me to meet with her and further discuss her research questions. From this meeting, and after her questions, I asked her if she could host me to pursue the answers together. She was very interested, but she also made it clear that I needed to bring my own funds.

Based on that necessity and my research interests, I decided to apply for a Fulbright Scholar award. This would allow me to relocate to Poland for up to nine months to do research, as well as teach at the University. The application process was simple, and the actual written proposal was short. However, it needed to fulfill the Fulbright spirit, which is to show both a cultural and scientific exchange. The evaluation process took several months, involving different evaluating panels that included one in the United States and one in Poland (with an actual interview via Skype). It should be noted that this process might be different for others, depending on the participating countries. There are more than 150 countries that participate, and I encourage the readers to visit this website (http://www.cies.org/) and become a part of the Fulbright family.

MM: So, as a Fulbright Scholar, what are you currently doing? Please describe your Fulbright research.

LRH: The name of my proposal was “The Polish Connection: A Tale of Pheromones and Addiction Modules in Enterococcus faecalis Isolates from Puerto Rico.” In this proposal, we were interested in describing the prevalence of pheromone-responsive plasmids in a population of environmental enterococci from Puerto Rico and describe the addiction modules prevalent in the population.

MM: What has been your greatest challenge regarding your Fulbright position, and how did you overcome it?

LRH: The biggest challenge was within my home institution, in part due to the financial difficulties that we were, and still are, experiencing. I have to admit that it took the support of the hierarchy of the institution, and especially that of my dean who had to defend my application against all odds. Once I was given the award, though, I was really excited to move to Poland and actually do this research. However, I was concerned with the challenge of moving
my whole family to a country that we knew little about, as well as not speaking the language. Looking for an apartment, learning how to use the public transportation system, buying groceries . . . basically we had to relearn how to live life again! Another point of concern was finding a suitable educational experience, in English, for my children.

Fortunately, my entire family was quickly adopted by parents at the International School of Gdańsk. They quickly assimilated us into, and made us part of, their community. From this group of parents, we learned key parts of the social and cultural knowledge. They showed us how they live, what they eat, their customs, their beliefs, and the significance of family. We greatly owe them for helping us transition, worry-free, into our new lives in Poland.

Also, the university students that I share office space with took it upon themselves to make sure that I knew what was happening in the department as well as in the community. For example, they keep me informed about holidays (day of the dead, independence day, mother’s day, Children’s day, Corpus Christi day, name day, etc.) and what each meant, what to do, where to go, and how to take advantage of these opportunities to learn the culture and witness Polish society. We were really fortunate to be part of this . . . I came to Poland as a US citizen born in Puerto Rico, and I will leave Poland knowing that part of the Polish culture will always be part of who I am.

MM: What do you anticipate taking away from your Fulbright experience, and how will you apply this to your career going forward?

LRH: This experience taught me that I could succeed outside the US and that I could live comfortably in Europe. Language can sometimes be a big limiting factor, but any language can be learned (some more easily than others). The reality of living outside the US and learning to enjoy every day while observing each cultural difference was priceless. The experience in the lab was outstanding, and the hospitality and the level of scientific collaboration were world class. I was able to successfully collaborate and share space in the laboratories of Dr. Barbara Kędzieraska and Dr. Obuchobski, within the Biotechnology Department of the University of Gdańsk.

Together, this significantly reinforced my scientific sense of community—as it should be! This is something that we all expect but not necessarily get to experience. I was fortunate to scratch the surface of the Polish language, and I learned that a little goes a long way. The Polish community feels very proud of how difficult their language is, and to hear you attempting to communicate in their native language fills them with joy. Thankfully, they are easily impressed with any attempt. They will actually ask why you are learning the language, as it is so difficult and it is only spoken by Poles. My answer was simple: we should never stop learning, but more importantly I want to hear your story in your own language! (I am not there yet, but it is a work in progress.)

MM: What advice would you have for somebody thinking of going through a Fulbright application? Is there anything you would do differently, or is there something you were grateful for having done?

LRH: No, I have no regrets. I have learned so much about not only Poland and its culture, but actually about myself as a scientist and more importantly as a global citizen. Teaching first-year Polish graduate students was also an adventure. Nevertheless, I really enjoyed the opportunity to challenge myself and try to overcome stylistic differences. Another gratifying experience was when I became involved in an outreach activity where I would visit different high schools to present my science and to promote the sciences in general. I took advantage of that opportunity of showcasing microbiology as a future career choice, and presented the microbiologist’s role in science and the benefits that we bring to society.

In short, I think that this type of experience is life changing, and so I would encourage all scientists and scholars to look for this or any other similar opportunity. I am sure they will not regret it!

MM: What’s next for you after your Fulbright position ends—what are your plans?

LRH: I will return to my home institution at UPR Mayaguez, and then resume my teaching and research endeavors. However, I now have a much greater international perspective to my work. I hope to continue to cultivate my international collaborations, and hopefully this experience allows me to be both a better scientist and teacher. If this was a true life-changing experience (which I think it was), then I will expect that my professional life will change soon and forever!
The ASM Microbe Mentor column would like to thank Dr. Ríos Hernandez for taking his time to provide some insight into a microbiologist’s experience with the Fulbright Scholarship program.

Dr. Luis A. Ríos Hernández is an anaerobic microbiologist who graduated from the University of Oklahoma, Department of Microbiology, and is currently an Associate Professor within the Biology Department at the University of Puerto Rico at Mayaguez. His research interests are centered in the ecology of the enterococci, with an emphasis on water quality and the anaerobic digestion of nonedible vegetative biomass to produce biogas as an alternative energy source.

ASM’s New Career Website: Cultivate Your Career

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

BOOKS

The Amoeba in the Room (Lives of the Microbes)

Although most introductory biology courses offered in high school or college contain at least one session that examines microscopic organisms, Nicholas Money feels that these small organisms deserve much more attention and research support. So he passionately and expertly goes on to demonstrate that there are all sorts of fascinating and weird microbes in the earth, in the water, in the air, and even in and on our bodies. They don’t just exist but have essential roles interacting intimately with each other, their environment, and the larger hosts that they inhabit. Over time these small organisms have even begun to share some or all of their genetic information, sometimes integrating their genetic information into the DNA of the host or existing as organelles within the host cell.

Despite our in-depth knowledge of a few model microbes such as the bacterium Escherichia coli, the fungus Aspergillus, the yeast Saccharomyces cerevisiae, and even viruses, we have barely scratched the surface of this vast and diverse group, which includes various organisms that we commonly recognize as viruses, bacteria, molds, fungi, lichens, and algae, and those less known: archaea, paramecia, diatoms, and amoebae. Many of these small organisms defy easy classification into genera, species, and kingdoms. Sequencing DNA and RNA suggests that there may be billions, or at least millions, of different organisms. They inhabit various niches, even extreme environments, and have many roles, many of them still unfathomed, in keeping our environment in balance. An important example is the sequestration of carbon dioxide on our planet. Another example is the discovery in the last few years that bacteria inhabiting the human gut are found to have immense influence not only in how we process food, but also in how we regulate our immune and neurological functions. In describing the relation between humans and their bacteria, here is a good example of the author’s unusual perspective that I quote:

“I’m captivated by the revelation that my breakfast feeds the 100 trillion bacteria in my colon, and that they feed me with short-chain fatty acids. I’m thrilled by the fact that I am farmed by my microbes as much as I cultivate them, that bacteria modulate my well being, and that my microbes are programmed to eat me from the inside out as soon as my heart stops delivering oxygenated blood to my gut.”

I wish there were more illustrations of these small organisms in the book. Line drawings and a few colored plates are shown in the first half of the book demonstrating the symmetry, beauty, or the strange constructions of these organisms. Unfortunately, the author has failed to provide some indication of size or magnification in most of them. Although most of the individual cells are invisible to the unaided eye, these organisms can vary over 1,000-fold in size.

The author demonstrates a thorough knowledge and appreciation of microbes worldwide using not just current isolates but also examples from history as well as from the fossil record. But the use of their Latin names, especially in the opening chapters, is often confusing and does not add to a better appreciation of their diversity and complexity. The writing style is a bit turgid, making the reading slow going despite the author’s attempts at literary and historical references and humorous analogies. Nonetheless, for the initiated, especially those who teach, this is a must read. It is an amazing compilation of the wide-ranging roles that these various small organisms and the variety of extreme niches that they occupy. The author is certainly successful in convincing this reviewer of the need to pay greater attention to small organisms. For students and novices, if they can slog through the first few chapters, it would be hard not to succumb to the author’s proselytizing and become an enthusiastic acolyte.

Alice S. Huang
California Institute of Technology
Pasadena, Calif.

Houston, We Have a Narrative: Why Science Needs Story

Randy Olson gives us yet another tool for our communication belts. . .and I’m glad to say my pants are beginning to sag! We are blessed to have excellent books, videos, podcasts, blogs, online training, and workshops available to help us improve our communication skills. One of the best books I’ve come
across recently is Olson’s *Houston, We Have a Narrative: Why Science Needs Story*. Following his popular book, *Don’t Be Such a Scientist* (2009), Olson takes a deeper analysis of the substance (not style) of science communication, which remains shamefully in need of improvement. I am delighted to report that by applying some of the methods explained in this book, Olson is helping me and many other emotionally stingy scientists, engineers, and technicians better connect with fellow humans.

Olson, a former tenured professor and current documentary filmmaker, has spent 25 years trying to figure out how to communicate science in a way that is interesting, entertaining, and informative. To do this, he immerses himself in the world of Hollywood entertainment and learns from the best how to connect with mass audiences. Scriptwriters tell us mastering the narrative process (i.e., storytelling) is “the soul of good communication.” Olson cautions us that learning narrative is not easy, takes time, and demands a mindset based not on cerebral thinking but rather on human emotions. Mastering narration in a single seminar or weekend workshop is unrealistic. However, through repetitive practice, we will improve...dramatically, as he and successful screenwriters have.

Olson describes a basic tool for writing good narration: a simple, one-sentence story template, called ABT. Begin your talk with a collection of necessary facts connected by the conjunction AND. (Example: I work on protein folding AND in a lab in New York AND I'm a postdoc AND...). Next, insert a BUT statement that says how your story is about to deviate from normal and add tension. (Our lab realized that our research could be used to make a drug to treat dementia. BUT, we first had to overcome a lot of problems, such as...). Finally, bring the story back home with a THEREFORE statement. (We are working hard to take our drug into clinical trials next year.)

I have found the ABT template easy to remember and can be used in drafting scripts for talks to students, media, funding agencies, general lay audiences, as well as scientific colleagues. Even elevator pitches follow the ABT format. Olson gives multiple examples of how ABT has been used in real-world situations.

ABT is one of several templates Olson and other storytellers use to help them write better script for their talks. Regardless of what template we use, Olson urges us to make narrative “one of the highest priorities for all science programs and agenda. If many of us do this, we can establish a self-perpetuating narrative culture that raises the expectations and standards for good presentations.” No longer will dull, boring, disjointed talks with complex slides be considered acceptable. Olson devotes the last chapter to ways to build a narrative culture at your university or organization. Abandon the lousy PowerPoint talks and be kind to your listeners.

**Dennis F. Mangan**  
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Application Deadlines

ABRCMS 2016. The 16th Annual Biomedical Research Conference for Minority Students (ABRCMS) will take place 9–12 November 2016 in Tampa, Fla. Register early (by 12 October) to receive a $100 discount off the onsite registration fee. ABRCMS 2016 attendees will benefit from a distinguished roster of speakers, along with numerous workshops, scientific presentations, professional development opportunities, networking events, and more. ABRCMS is managed by ASM and supported by the National Institute of General Medical Sciences of the National Institutes of Health under award number T36GM073777.
Deadline: 12 October for early registration discount.

Scientific Writing and Publishing Online Course (SWP Online). SWP Online is a four-month overview of scientific writing and publishing concepts. Geared to ASM members who are graduate students, postdoctoral fellows, and early-career scientists, the course includes seven 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 2017 program takes place from January through April, and registration for the course will be accepted until 1 December 2016.
Deadline: 1 December 2016.

ASM Science Teaching Fellowship. The ASM Science Teaching Fellows Online Course is a five-month professional development opportunity that prepares doctorally-trained students for science teaching positions at a variety of nondoctoral institutions. The course will develop introductory teaching skills on course design, student-centered learning strategies, and career preparation. Participants will be part of an online community of fellows, mentors, and facilitators with exclusive access to interactive webinars, readings, and skill-building activities presented by experts in the field.
ASM Meetings Calendar

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

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

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

6–8 February 2017.
ASM Biothreats Conference: Research, Response and Policy.
Washington, D.C.
http://conferences.asm.org/

33rd Clinical Virology Symposium.
Savannah, Ga.
http://conferences.asm.org/

1–5 June 2017.
ASM Microbe 2017.
New Orleans, La.

March 2017.
ASM Conference on Innovative Microbial Ecology for Mitigation of Antibiotic Resistance and Bacterial Diseases.
www.asm.org/conferences

March 2017.
ASM Conference on Mechanisms of Intercellular Cooperation and Competition.
www.asm.org/conferences

April 2017.
ASM Conference on Tuberculosis: Past, Present and Future.
www.asm.org/conferences

May 2017.
ASM Conference on Interplay of Viral and Bacterial Pathogens (ASM-ASV collaboration).
www.asm.org/conferences

September 2017.
2nd ASM Conference on Rapid Applied Microbial Next-Generation Sequencing and Bioinformatic Pipelines.
www.asm.org/conferences

October 2017.
6th ASM Conference on Cell-Cell Communication in Bacteria.
www.asm.org/conferences

November 2017.
ASM Conference on Vibrio2017: The Biology of Vibrios
www.asm.org/conferences

December 2017.
4th ASM Conference on Viral Manipulation of Nuclear Processes.
www.asm.org/conferences

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

Assistant Professor, Food Safety Epidemiology/Bioinformatics

Assistant Professor of Food Safety Epidemiology/Bioinformatics, Center for Food Safety, Griffin, Ga.; 100% research (12 month, Tenure Track).

Date position available: March 1, 2017 or as soon as possible thereafter. Applications received by October 10, 2016 are assured of consideration. The successful candidate will develop a research program in the area of food safety epidemiology/bioinformatics and contribute to outreach programs of the Center for Food Safety. A Ph.D. in Epidemiology, Bioinformatics, Food Microbiology, or closely related field is required. At least 1 year of postdoctoral or prior academic experience with microbial genetics or bioinformatics is desired. Candidates should show the potential to obtain external funding to support their research program. Candidates must demonstrate excellent oral and written competencies, interpersonal skills, and willingness to work in multidisciplinary teams. Specific responsibilities include: (1) conduct research on food safety epidemiology and/or bioinformatics; (2) establish an extramurally funded research program; (3) establish a strong record of scholarly activity; (4) direct Ph.D. and M.S. degree students and postdoctoral associates; and (5) work cooperatively with other faculty and staff and with food industry personnel. The selected candidate will also be a member of the Department of Food Science and Technology. The individual in this position will be expected to achieve a record of scholarly activity as evidenced by peer-reviewed publications, successful extramural funding, and success in mentoring graduate students. Applicants must send (1) letter of application; (2) a curriculum vitae detailing background and capability to conduct research and outreach; (3) undergraduate and graduate transcripts; and (4) names, addresses, telephone numbers; and e-mail addresses of four professional references that the search committee may contact. Application materials and unofficial transcripts should be sent electronically to bbanist5@uga.edu or to Food Safety Epidemiology/Bioinformatics Search Committee, Cen-

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 September 2016 issue, your ad must be received by 1 August 2016). Classified ads should be sent (with payment) to Walchli-Tauber Group, 2225 Old Emmorton Road, Suite 201, Bel Air, MD 21015, attn: Rhonda Truitt, tel. (443) 512-8899x106; fax, (443) 512-8909; e-mail, rhonda.truitt@wt-group.com.

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1–50 words $185
50–100 words $350
101–150 words $535
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For display ad Internet posting costs, please contact Rhonda Truitt 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 Truitt at the address given above.
ter for Food Safety, University of Georgia, 1109 Experiment Street, Griffin, Georgia 30223–1797 Tel: 770–228–7284; Fax: 770–229–3216. Inquiries about this position should be directed to Dr. Ynes Ortega at Ortega@uga.edu. Candidates will have the opportunity to work on collaborative projects with a wide variety of groups including those on campus and some federal agencies. Selected candidates will be required to submit to a background investigation demonstrating eligibility for employment with the University of Georgia. The University of Georgia (http://www.uga.edu/) a land-grant/sea-grant university, is ranked among the top 20 public universities in U.S. News & World Report’s 2015 edition of America’s Best Colleges. The university is recognized as a research intensive and community engaged institution by the Carnegie Foundation. The Department of Food Science and Technology (http://www.foodscience.caes.uga.edu/) and the Center for Food Safety (www.caesarcs.org) are units of the College of Agricultural and Environmental Sciences. The University of Georgia is an EEO/AA/Vet/Disability Institution. As such, we are especially interested in candidates who can contribute to the diversity and excellence of the academic community. We not only strongly encourage women, minorities and other diverse candidates to consider applying for this position, but we also maintain that all candidates should share our commitment to diversity and inclusion. All consideration for employment without regard to race, color, religion, sex, national origin, disability, gender identity, sexual orientation, or protected veteran status.

Tenured Faculty Position in Virology

The Microbiology Program in the Indiana University Department of Biology (http://www.bio.indiana.edu) invites applications for the Lawrence M. Blatt Chair, an endowed faculty position in Virology at the level of Associate Professor with Tenure. More senior candidates with exceptional credentials will also be considered. We are particularly interested in scientists examining the interaction between viruses and host cells at the molecular and cellular level. Applicants working on virus structure and assembly, and virus evolution will also 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 linked with Programs in Molecular and Cellular Biochemistry, Cell and Developmental Biology, Biotechnology, the Medical Sciences and a Precision Health Initiative. The successful candidate will be provided with a generous 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 cryo-electron microscopy. Successful candidates must hold a Ph.D. and have demonstrated exceptional leadership roles and scholarly success in their field, will have an outstanding track record in research including peer-reviewed publications and external funding, and will have excellent teaching credentials at the undergraduate and graduate levels. Applications received by October 7, 2016 will be assured of full consideration. Applicants should submit a cover letter, a CV, three letters of recommendation, and up to 3 pdfs of published and/or submitted manuscripts using the online submission link at http://indiana.peopleadmin.com/postings/2541. For questions about the application procedure please contact Jennifer Tarter (jenjonesindiana.edu) or by mail at 1001 E. Third Street, Bloomington, IN 47405–7005, and for all other questions please contact Pranav Danthi (pdanthi.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.

Professor, Associate Professor or Assistant Professor without Tenure

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

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Formerly known as the ASM Biodefense and Emerging Infectious Diseases Research Meeting, the 2017 ASM Biothreats meeting will discuss a wide-range of biological threats and emerging infectious diseases to stimulate knowledge-sharing amongst stakeholders in academia, industry and government; and to help the overlapping communities prepare for, mitigate, and prevent these global threats.

**Important Dates**

- Abstract submission opens: September 1, 2016
- Abstract submission closes: October 27, 2016
- Registration opens to ASM Premium Members: November 3, 2016
- Registration opens to all: November 10, 2016
- Early Bird deadline: January 12, 2017

For more information, please visit

[www.asm.org/biothreats](http://www.asm.org/biothreats)
Small Things Considered

Your Operating System on a Thumb Drive
http://schaechter.asmblog.org/schaechter/2015/11/your-operating-system-on-a-thumb-drive-a-snippet.html

by Christoph Weigel

At the heart of every cell’s “operating system” are the ribosomes: ingenious nanomachines that translate messenger RNA (mRNA) into proteins that cells need to build and maintain themselves. Ribosomes were first described by the electron microscopist George Palade in a 1955 paper, in which he contemplated the electron dense particles lining the endoplasmic reticulum of rat pancreas cells: “The relationship between the membrane of the endoplasmic reticulum and the small granules deserves special consideration.” Indeed, they deserved and got consideration: today PubMed lists over 50,000 papers dealing with ribosomes—comparable to the number of ribosomes in rapidly growing E. coli cells. With such numbers, it’s no wonder cells spend roughly 2/3 of their energy budget on the synthesis of ribosomes and translation!

Ribosomes are composed of ~50 proteins and three RNAs, termed ribosomal RNA (rRNA), and arranged in two subunits, with the sites of protein synthesis and mRNA-binding at their interface. It was assumed for decades that the rRNA provides a scaffold on which the ribosomal proteins join amino acids to a growing peptide chain. The first hint that this might be less than half the truth came from the deciphering of the genetic code, when it was shown that the codon-anticodon interactions of ribosome-bound tRNA and mRNA drive translation, with proteins being causal bystanders. But it was still surprising when the elusive ribosomal “peptidyl-transferase”—the enzymatic reaction that joins amino acids by a peptide bond—turned out to be a ribozyme-type activity located in the rRNA moiety of the large ribosomal subunit. So a remnant of the “RNA world” seems to be a key component of the cell’s “operating system.”

Intuitively, one would guess that, in prokaryotes, the genes encoding such vital parts of the operating system are encoded on the hard drive: the chromosome. Indeed, the three bacterial rRNAs (16S, 23S, and 5S) are encoded by “rDNA” genes that are organized as an operon and transcribed from a common promoter. A long primary RNA transcript (~4,600 nt) is processed by specialized RNases to yield the individual rRNA species that are then assembled with the ribosomal proteins into precursor ribosomal subunits. However, it turns out that some prokaryotes encode their rRNA genes on “thumb drives” rather than hard drives.

Enter Aureimonas sp. AU20 and its cousins, humble members of the Rhizobiales subfamily of the ubiquitous Alphaproteobacteria. Recently, Hisayuki Mitsui and coworkers sequenced an Aureimonas genome from the stem of a soybean plant and found that it lacked rRNA genes on its chromosome. Instead, the rRNA operon was carried on a small, (9.4-kb) multicopy plasmid (18-34 copies/cell) that was also present in the 4 cousins (out of 12) of Aureimonas that also lacked chromosomal rRNA genes. The rRNA-carrying plasmid is the normal state of affairs in biology. Nevertheless, the authors could not detect any of the plethora of known addiction modules that usually ensure plasmid maintenance. Most likely, the selective pressure to stably maintain the rRNA-encoding plasmid is sufficiently high in this case: you better keep your thumb drive plugged in!

If you’re a frequent reader of STC, you won’t be surprised to find out that there are viruses lurking here as well. Virus DNA recently isolated from the marine sponge Hymeniacidon perlevis contained a bacterial 16S rRNA gene. Since marine sponges usually live with bacterial epibionts and symbionts, it is still unknown whether this 16S rRNA gene was carried by a bacteriophage or by a virus of the eukaryotic sponge. In any case, this provides another example for an “operating system on a thumb drive,” and suggests that rRNA genes can be transferred horizontally. Therefore, rRNA-based phylogenetics—the marvelous idea that allowed Carl Woese to propose his three-domains model—may turn out to be really messy in some niches at least. Then again, that would be the normal state of affairs in biology.

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