

MICROBES AND SOCIETY







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This issue of Microcosm offers a sneak preview of ASM Microbe 2023 by exploring the impact microbes have on our everyday lives—and the potentially huge impact they could have on our future.

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The Power of Microbial Sciences to Change the World

BY ASHLEY HAGEN, M.S

f the years following the emergence of SARS-CoV-2 have taught us anything, it's that microbes are everywhere and relentless in their pursuits. Microbes and humans are connected. Nothing we do takes place in a vacuum.

EMERGENCE OF A NOVEL PATHOGEN

COVID-19 came as no surprise to the microbiology community; we knew a pandemic was imminent. The only real question was which would come first, a pandemic driven by antimicrobial resistance (AMR), or one caused by a highly pathogenic respiratory virus, like influenza or a coronavirus.

The answer manifested in late 2019, when several cases of "pneumonia-like" illness of unknown etiology were reported in Wuhan, China. Less than 3 months later, on March 11, 2020, after more than 118,000 cases in 114 countries and 4,291 deaths, the <u>World</u> Health Organization declared COVID-19 a pandemic.

For many microbiologists, the pandemic instilled a unique sense of purpose—it was a chance to put our training to use on a scale unprecedented in any of our lifetimes. While the world waited with bated (i.e., masked) breath, microbiologists went to work getting acquainted with and developing a vaccine to combat this new foe, in record-breaking time.



News travels fast! Online information is easily consumable via personal devices. Source: iStock



A public health microbiologist conducting COVID-19 testing. Source: Flickr

CHALLENGES FOR THE SCIENTIFIC COMMUNITY

What we were woefully unprepared for was the manner in which fear, <u>misinformation</u> and animosity would outpace the spread of the virus. At the end of the day, in the age of 24hour news, digital publication and social media, "trust me, I'm a microbiologist," just wasn't enough to overcome fear of the unknown.

As a society, we had become lulled into a false sense of comfort with "the way things work" when it comes to modern medicine, and it was scary to confront the reality that we were more vulnerable than day-to-day operations might suggest. A deadly pathogen that we knew nothing about? That was everyone's nightmare.

Furthermore, by the time we realized that SARS-CoV-2 existed, our microscopic adversary had gained a significant head start, and humanity was forced to take a collective pause while the scientific and medical communities played catch-up. Thanks to the heroic efforts and unparalleled <u>collaboration of scientists</u> <u>around the globe</u>, pre-existing gaps in knowledge closed at breakneck speed. But in a world of instant gratification, threatened by an unrelenting opponent, the pause was taxing.

Now, a mere 3.5 years later, COVID-19 has left an indelible footprint on society, which will forever alter the landscape of individual lives, as well as local and global communities.



ASM President Colleen Kraft Source: American Society for Microbiology

WE ARE ALL CONNECTED—THE MICROBES THAT BIND US

For <u>ASM President Colleen Kraft</u>, the COVID-19 pandemic has been a pivotal time. "The last couple of years have deepened my passion not only for what I do, but also who I do it for," she explained. "Microbiology is foundational to global and public health, and it is unequivocally a social equity issue."

It is true: microbes and society are so intricately interwoven that neither can be isolated from the other, and if we are to advance professionally and personally from the past years' events, the symbolism and deeper implications of this fact cannot be overlooked.

That is why Kraft will convene a distinguished lineup of guest speakers at the <u>ASM Microbe</u> <u>2023 President's Forum</u> (June 17 in Houston, Texas) to discuss topics that are most pressing in the field of microbiology.

Pandemic Preparedness and Global Health

On the forum's roster is <u>Ambassador John Nkengasong, Ph.D.</u>, who <u>heads the U.S. President's</u> <u>Emergency Plan for AIDS Relief</u> (PEPFAR) and is the first-ever African leader to hold the position of U.S. Global AIDS Coordinator and Special Representative for Global Health Diplomacy at the U.S. Department of State. Throughout his career, Nkengasong has made significant contributions to global public health, including leading the COVID-19 response in Africa and securing 400 million doses of COVID-19 vaccines during the height of the pandemic.

In 2021, Nkengasong was recognized as one of <u>TIME magazine's 100 Most Influential People</u> and received the <u>Virchow Prize for Global Health</u> for his dedication to improving the health and well-being of the world's most vulnerable people. His work demonstrates that health equity has profound influence, and he brings a deeply informed perspective to discussions about pandemic preparedness.

"Because we are all connected, we cannot talk about pandemic preparedness without talking about global health," Kraft explained.

When it comes down to it, none of us are immune to the consequences of each other's actions because we share time and space with one another. Few things teach us as clearly as microbes that what happens to one of us ultimately happens to all of us. Simply by breathing, we are impacting our neighbors (be they human, animal, plant or microbe) and our environments.

Which means we must find a way to coexist, and to do so in a manner that considers individual processes and needs, even if they are invisible to the naked eye. These concepts can be applied to one-on-one interactions, and they can be extrapolated on a global public health scale.

"If a neighboring nation is experiencing a concerning infectious disease outbreak, alarm bells should be ringing for the rest of the world," said Kraft. "We should all be thinking, 'how can we help contain this threat?"

Stewarding Microorganisms to Change the World

Still, not all microbes are threatening. In fact, many are at the heart of our most innovative solutions and groundbreaking research. According to Kraft, from bioremediation techniques that work to create a sustainable economy, to medical and industrial applications that transform microorganisms (and their metabolites) into high-value products, microorganisms must be treated as a valuable resource.

"I believe microbes can change the world, but how we steward them will directly determine whether we are changing it for worse or for better," Kraft explained. That means keeping a handle on existing resources, protecting resources that are consumable, developing renewable options and carefully stewarding resources, like antibiotics, that if overused, underused and/ or misused can drive AMR. To speak more about stewardship, particularly as it relates to AMR, Folasade Tolulope Ogunsola, Ph.D., Vice Chancellor of the University of Lagos, Nigeria and Director of the Centre for Infection Control and Patient Safety, will also join the ASM Microbe 2023 President's Forum.



John Nkengasong, Ph.D. Source: American Society for Microbiology



Folasade Tolulope Ogunsola, Ph.D. Source: American Society for Microbiology

Ogunsola has her finger on the pulse of multiple pathogenic threats. She studies the epidemiology and ecology of antibiotic-resistant organisms in the hospital environment and how to prevent transmission of AMR pathogens to patients and staff. She also develops and executes critical infection prevention and control strategies for pathogens outside of hospital settings—e.g., Ebola, tuberculosis, polio and HIV—and is a member of the <u>Africa Task Force for</u> Novel Coronavirus (AFCOR).

Ogunsola's work demonstrates the importance of employing holistic approaches to microbiology research. "Pandemic preparedness means, to the best of our ability, <u>keeping</u> <u>tabs on (re)emerging pathogens.</u> Knowing where they are coming from, how they are evolving and what other microbes they are bringing with them," Kraft said, noting that ecologic and epidemiologic studies shed light on many of these determinants.

As ASM Microbe 2023 quickly approaches, Kraft shared that she is particularly interested in the transmission dynamics of things that "go viral." SARS-CoV-2 spread before we fully understood how it was doing so. It continued to wreak havoc, acquiring mutations that conferred varying levels of immune escape to each new variant, as the microbiology community ran experiments and conducted surveillance to trace it. And to this day, <u>the origins of the SARS-CoV-2 virus</u> remain under investigation.

Edward Holmes, Ph.D., a.k.a. the "Virus Hunter," is a world-renowned expert on virus evolution who will round out the distinguished panel of ASM Microbe 2023 President's Forum experts. Holmes researches how RNA viruses evolve and spread, often crossing species boundaries to emerge in new hosts, and he has been a key figure in the debate over the origins of SARS-CoV-2. Holmes has earned international acclaim and awards of the highest honor, including the <u>Australian Prime Minister's Prize for Science. His work demonstrates the value of metagenomic technology and phylogenetic analysis in contextualizing the processes by which outbreaks and epidemics unfold.</u>

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Kraft is excited to bring these experts together for a robust conversation that investigates the social dynamics, as well as the science, that has shaped the post-COVID-19 era. She emphasized that she is not only interested in how microorganisms spread, but also how thoughts, information and ideas are transmitted. "We have seen how quickly a pathogen like SARS-CoV-2 can spread, and we have also experienced first-hand the speed with which fear and misinformation can travel. Ideas and information can be globally transmitted; why can't hope?"

Kraft explained that she wanted to bring together leaders and subject matter experts who have global reach and influence to talk about the issues of pandemic preparedness, AMR, global health and social equity. "It is my hope that instead of driving further dissent, we can discuss ways in which the global microbiology community can use our knowledge and skillset to spark positive change."



Edward Holmes, Ph.D. Source: American Society for Microbiology

Climate Change Experts Tap Microbes to Protect the Planet

BY RACHEL BURCKHARDT, PH.D.

he <u>Earth's climate is changing</u>—oceans are warming, <u>glaciers are melting</u> and extreme weather events are increasing in frequency and intensity. These changes threaten all life, with climate change considered the "<u>biggest health threat facing</u> <u>humanity</u>" by the World Health Organization (WHO). Microbes, like humans, are not immune to these environmental changes. In fact, microbes are already adapting to a changing climate, causing serious implications for society.

Climate change can disrupt microbial community structure, perturb production of greenhouse gases and increase prevalence of plant and animal pathogens. These fluctuations can, in turn, affect food production and human health. Conversely, microbes can also be used to help mitigate the deleterious effects of climate change.

Understanding the role of microbes in climate change is therefore critical to protecting the health of the planet. Around the world, scientists from multiple disciplines, including ecology, microbial engineering and medicine, are engaging in important research and developing microbe-based techniques and frameworks to address the problem. Many of these scientists will convene in Houston, Texas, at ASM Microbe 2023 to participate in the special Climate Change and Microbes (CCM) guest track.

CLIMATE CHANGE AND MICROBES IMPACT EACH OTHER

In the last 150 years, the Earth's average global surface <u>temperature increased at a rate "unprecedented"</u> for at least the last 2,000 years. While <u>human activity has been a main driver of climate change</u>, microbes are also a major factor. As the <u>most</u> <u>abundant organisms</u> on Earth, microbes both affect, and are affected by a changing climate. Newly evolved microbial activities can lead to positive or negative feedback on climate change and its effects. Understanding this feedback will be vital to combat the harmful impacts of climate change on society.

Relevant research pertaining to microbes, climate change and society can be broken into the following main areas:

- Microbial influences on greenhouse gases.
- Microbial adaptation to climate change.
- Microbes, health and the environment.

MICROBIAL INFLUENCES ON GREENHOUSE GASES

<u>Greenhouse gases are atmospheric gases that emit and absorb heat</u>—trapping it in the Earth's atmosphere and leading to global warming. Such warming makes food more perishable, <u>diseases more prevalent and natural disasters more extreme, and thus more expensive</u> to clean up. Microbes found in soil and aquatic environments contribute directly to the ongoing rise in greenhouse gas emissions by <u>producing key greenhouse gases: carbon dioxide (CO2)</u>, methane (CH4) and nitrous oxide (N2O).

<u>Methane is about 25 times more efficient at trapping heat</u> than carbon dioxide. This makes lowering methane concentrations in the atmosphere a faster way to slow global warming in the short term, according to <u>Mary Ann Bruns, Ph.D.</u>, Professor of Soil Microbiology at The Pennsylvania State University. Bruns explained that understanding how microbes produce methane will aid in the development of strategies to curb emissions of this potent, heat-trapping greenhouse gas.

More than <u>50% of methane emissions come from human activities</u>—especially raising livestock, such as cattle and sheep, for meat and dairy products. <u>Bacterial</u>, <u>archaeal</u>, <u>protozoan and fungal microbes</u> live in the animal's digestive compartment called the <u>rumen</u> and <u>digest plant feedstock through fermentation</u>. The rumen microbiome converts plant sugars into energy for the animal, <u>producing methane</u> as a byproduct that is released to the atmosphere through belching. In fact, <u>rumen microbes are responsible for</u> more than 25% of anthropogenic methane emissions.



Microbes in aquatic and terrestrial environments produce and consume the greenhouse gases CO2, CH4 and N2O. Soil and aquatic microbes produce these gases when decomposing organic matter to provide nutrients for plants and marine life, respectively. Source: National Library of Medicine



Rumen microbes that live in livestock animals such as cows produce over 25% of human methane emissions each year. Scientists are working on compounds to reduce rumen methane production to slow global warming. Source: Wikimedia

Scientists are actively learning about the rumen microbiome and ways to control associated methane production. An international team of scientists found that feeding cows an inhibitor of a key archaeal enzyme responsible for methane formation decreased enteric methane emissions by 30%. Building on this observation, those researchers are using omics and models to reveal how the inhibitor affects the cattle microbiome. Bruns, who was not involved in these studies, noted that this information will be crucial in understanding how methanogens interact with the whole microbiome so that cattle feed can be modulated to reduce the production of methane during rumination. "Production and consumption of greenhouse gases occurring at the microbial level play a crucial role in determining ecosystem responses to climate changes caused by humans," Bruns said. Bruns will convene the CCM session at ASM Microbe 2023, "Microbial Technologies to Mitigate Methane Emissions," to explore additional ways microbes can be used to mitigate methane emissions.

MICROBIAL ADAPTATION TO CLIMATE CHANGE

As the environment changes, so do microbes. Microbes' fast growth rates, large population sizes and ability to share genetic information with one another allow them to adapt quickly to environmental variability. "Changes in microbial activity, diversity, community structure and interactions with other organisms are all shaped by climate change," said <u>Mengting "Maggie" Yuan, Ph.D.</u>, Assistant Project Scientist at the University of California, Berkeley, who is studying microbial communities in soil. Yuan examines how climate warming and reduced precipitation influence relationships among grassland soil microbes. "We try to find out what factors shape the below-ground microbial food web that consumes, transports and processes photosynthetic carbon," Yuan said. "Answers to these questions are fundamental to climate change predictions and potential solutions."



Cutaway view of roots of grass. Source: iStock

Microbes can adapt in a multitude of ways. <u>Bacterial respiration</u> <u>has been shown to increase</u> with warmer temperatures while <u>bacterial cell size decreases</u>. <u>Viruses found in cooler oceans</u> <u>have evolved to encode proteins related to cold shock response</u>, allowing them to survive at lower temperatures. Warmer and <u>drier soils</u>, as well as <u>warming oceans</u>, are associated with <u>shifts in microbial community composition</u>, which may result in changes to carbon and nutrient cycling in those ecosystems.

Viruses that infect <u>soil</u> and <u>aquatic microbes</u> can also promote changes in microbial activity and community structure. For instance, infection of <u>cyanobacteria by viruses called</u> <u>cyanophases can shut down carbon dioxide fixation</u> during infection, which results in greater availability of greenhouse gases to enter the atmosphere. However, more research is needed to understand the full role of the <u>virome on microbial</u> adaptation to climate change.

Understanding how microbial fluxes of carbon and greenhouse gas emissions will change over time can help scientists predict climate change's impacts for all society. "Microbes are small but mighty. They change the trajectories of climate," Yuan said.

Yuan is also a presenter for the upcoming CCM session "Ecological and Evolutionary Responses of Microbial Communities to Climate Change" at ASM Microbe 2023, where you can learn more about how grassland soil microbes are adapting to environmental change.



Consuming raw seafood contaminated with *Vibrio* spp., such as oysters, is a major source of vibriosis. Source: Wikimedia

MICROBES, HEALTH AND THE ENVIRONMENT

Pathogens must also adapt to a changing environment. Warmer temperatures and environmental shifts can <u>help pathogens and</u> <u>vector species expand their spatial range</u>. For example, <u>warmer</u> <u>oceans at higher latitudes in the North Sea are linked to a</u> <u>higher incidence of</u> infections with *Vibrio* spp. <u>Vibrio are marine</u> <u>bacteria</u> that live in warm and coastal waters and can cause diarrhea, nausea, vomiting, dehydration and fever when ingested with contaminated seafood. As global oceans have warmed, *Vibrio* spp. have expanded to these warmer waters and <u>caused</u> <u>more infections in areas not previously</u> endemic. Warmer waters are also associated with more intense hurricanes, cyclones and flooding. Such storms can lead to increased human exposure to pathogens. Warming temperatures may also select for warmadapted fungal pathogens, such as the opportunistic <u>fungal</u> <u>pathogen Candida auris</u>.

Thus, climate change-induced environmental shifts have profound impacts on animal and plant pathogens and human health. "It is increasingly evident that if we want to advance our understanding of the microbial world, and of pathogens in particular, we need to widen our span of view to include the intersection between the <u>environment</u>, the <u>animal world and humans</u>. In this regard, climate change will obviously play a major role [in] shaping the evolution of microbial organisms in the coming years," said <u>José M. Munita, M.D.</u>, who specializes in infectious diseases and antimicrobial resistance at the Clinica Alemana - Universidad del Desarrollo Faculty of Medicine in Santiago, Chile, and also holds an adjunct appointment at the University of Texas Health Science Center, Houston.

Munita explores the evolution of bacterial pathogens and their mechanisms of antimicrobial resistance and will offer the CCM talk "Environmental Pollution as a Driver of Evolution of Methicillin-Resistant Staphylococcus aureus (MRSA)." MRSA is a human pathogen that causes over <u>80,000 infections and 11,000 deaths annually</u> in the U.S. Munita hopes his research on how climate change and natural disasters, like earthquakes, have affected the evolution of MRSA will provide clues on future pathogen evolution in a changing environment. This knowledge can then inform strategies and public health measures to contain and mitigate pathogen spread.

MICROBES AS SOLUTIONS FOR CLIMATE CHANGE

Though microorganisms contribute to the negative effects of climate change, they can also help mitigate its impacts. <u>Brajesh</u> <u>Singh, Ph.D.</u>, Director of the Global Centre for Land-Based Innovation and Distinguished Professor at Western Sydney University, views microbes as solutions to the problem. "Growing evidence suggests that microbial tools can provide effective solutions for both mitigation and ecosystem adaptation to climate change," Singh said. "For successful outcomes from this line of research and innovation, studying climate change at microbial levels is critical."



Rows of plants growing out of dried soil. Source: USDA/farmers.gov

Singh studies how climate change affects the relationships between soil biodiversity and ecosystem functions. Soil microbes <u>drive nutrient turnover needed for crop growth</u> and can make <u>crops more resilient to environmental stress</u>. <u>Environmental changes like drought and heat waves threaten</u> <u>agriculture</u> and the entire food supply. In the CCM session "<u>Microbes and Climate Crisis - Problems and Solutions</u>," Singh will share how soil microbes are impacted by climate change and the consequences for the resilience of ecosystems. Singh explained that <u>soil microbes can be "harnessed"</u> to make ecosystems—especially agricultural ecosystems more resilient to the negative effects of climate change. For example, Singh reported that certain <u>microbial communities</u> provide protection against pathogens for plants or confer resilience to ecosystems and plant productivity after droughts.

Microbes can be harnessed as climate change solutions in other ways as well. Bruns, the Professor of Soil Microbiology at The Pennsylvania State University, highlighted that microbes that consume greenhouse gases are being investigated as solutions to counter rising emissions. Raising of livestock, manure management, rice paddies, landfills and <u>oil and gas operations</u> are all major sources of methane. Methanotrophs, which are bacteria and archaea that consume methane, are being investigated for their ability to reduce emissions when introduced to these methane-producing systems. By <u>facilitating methane capture and feeding it</u> to methanotrophs, scientists hope to reduce overall methane emissions into the atmosphere. Since methane traps radiative heat in the atmosphere better than carbon dioxide, these microbial solutions could be a way to help mitigate the impacts of global warming and climate change on society.

JOIN THE CLIMATE CHANGE AND MICROBES COMMUNITY AT ASM MICROBE 2023

As <u>experts in climate change conversations</u>, microbiologists have an opportunity to take action on this major threat to society. ASM Microbe 2023's special CCM guest track provides scientists the opportunity to discuss and address issues at the intersection of climate change, microbiology and human health and well-being. CCM sessions will explore the impacts of a changing climate on microbes and their relationships with humans and the environment to find effective solutions and inform policies to address climate change.

CCM track leader <u>Jay T. Lennon, Ph.D.</u>, Professor of Biology at Indiana University, is looking forward to new ideas, partnerships and integration of tools aimed at microbial solutions to climate change arising from the CCM track. "This will bring together a diverse group of scientists to use microbes to address one of the most urgent, important and complex global problems."

The CCM guest track is part of ASM's larger <u>Climate Change & Microbes Scientific Portfolio</u> initiative to provide opportunities for microbiologists to contribute their expertise and knowledge to addressing climate change. Acknowledging the strong ties between climate change and microbiology, the <u>American Academy of Microbiology</u>—the honorific leadership group and scientific think tank of ASM—established a 5-year plan in 2019 to focus on broadening scientific understanding of climate change and microbes.

You can participate in these conversations by attending ASM Microbe 2023 in Houston from June 15-19. You can also join a global community to combat climate change and <u>sign up to receive updates</u> about the latest science and resources about climate change and microbes.

Antimicrobial Resistance: Facing Tomorrow's Problems, Today

BY GEOFF HUNT, PH.D.

orldwide, the threat of antimicrobial resistance (AMR) is <u>already responsible for more than 1 million deaths every year</u>, a total that is <u>projected to grow to 10 million annual deaths by 2050</u>. Amid these growing concerns, microbiologists are looking toward something new and something old—artificial intelligence (AI) and phage therapy—to help mitigate the effects of AMR, while ensuring therapeutics are delivered equitably to patients. Here, we explore some of the unique perspectives being taken by ASM members to identify and address current and future challenges.

ARTIFICIAL INTELLIGENCE TOOLS FOR DEVELOPING ANTIMICROBIALS AND ANTIFUNGALS

Given the immediate threat posed by AMR, improving the efficiency of antibiotic discovery is imperative. Unfortunately, current efforts are not keeping pace. "Right now, we have 3 classes of drugs that are used to treat fungal infections that are life threatening," said <u>Damian Krysan, M.D., Ph.D.</u>, from the University of Iowa Carver College of Medicine. "Where is the next drug going to come from?"

That is where AI comes in. "Artificial intelligence is revolutionizing all fields, including antibiotic discovery," said <u>Silvia Cardona,</u> <u>Ph.D.</u>, from the University of Manitoba. <u>Cardona has already started applying machine learning AI in her own work</u>, which centers on developing chemogenetic profiles of essential gene knockdowns in order to better predict antibiotic activity. "How," she asked, "can we make it smarter to find new molecules?"



Only a handful of novel antifungal agents are currently under investigation. Source: Fernandes et al. (2021) doi: 10.1128/AAC.01719-20

Such development is critical. In a 5-year span (2014-2019) only 14 new antibiotics were approved for use. However, research estimates suggest that 10³⁰-10⁶⁰ drug-like molecules potentially exist—orders of magnitude beyond what humans could possibly hope to investigate using traditional methods, but well within reach of AI systems.

As Krysan explained, AI technology "is not going to help make new data, but it can take existing data and find patterns that would take a person just sitting there looking at Excel spreadsheets forever." Cardona also emphasized the benefits of AI compared to current techniques. "A high-throughput screen is expensive and takes lots of time and resources," she explained. "If we can train computers to predict which molecules have a better chance to be converted into antibiotics, then we save time."

Krysan and Cardona are co-organizing a session at ASM Microbe 2023 titled "<u>Where Will We Find the Next Generation of Antimicrobials/Antifungals?</u>" The session will explore how researchers are using AI in different ways to identify new drug candidates, including through screening chemical compounds, analysis of microscopic images and exploration of metabolic pathways.

As interest in AI has exploded worldwide, Cardona feels that exploring and learning about the benefits and limitations of the technology are critical. "I think that what matters the most is not to be afraid of AI: learn about it, learn how to use it properly," she emphasized. "If we don't educate ourselves about what it is and how to use it, then we will end up having a society that fears it. That's not how it should be."

USE OF PHAGE THERAPY TO ADDRESS ANTIMICROBIAL RESISTANCE

In addition to the decidedly 21st century approach that is AI, researchers are also exploring a much more retro technique to counter AMR: <u>phage therapy</u>.

As <u>Heidi B. Kaplan, Ph.D.</u>, from McGovern Medical School at the University of Texas Health Sciences Center at Houston explained, phage therapy "is a technology that we're re-visiting." <u>Initially developed in the early 1900s</u>, the technique fell out of favor during the second half of the 20th century. However, recent research has suggested phage therapy as a potentially effective alternative to the use of antibiotics to combat AMR.



Researchers are exploring the viability of phage therapy to combat AMR. Source: $\ensuremath{\mathsf{i}}\xspace{\mathsf{Stock}}$

The key to phage therapy is that it can be used to target multidrug-resistant infections. In contrast to broad-spectrum antibiotics, phage are "very specific for the bacteria that they kill," said Kaplan. What that means is that phage can be applied selectively and not interfere with the delicate balance that exists within established microbiomes.

Furthermore, whereas bacteria can develop permanent resistance to a static antibiotic, phage are able to keep up with an evolutionary arms race. "If bacteria develop resistance to the phage, you can evolve a related phage in the laboratory that can newly infect the resistant bacteria, or you can isolate a new phage from the environment," Kaplan said.

However, widespread implementation of phage therapy will require large-scale clinical trials to study the safety and efficacy of appropriate candidates. Clinically, "I think we're years away from

widespread use," predicted Kaplan. "In addition to the FDA approval, physicians will need to feel comfortable with this new strategy."

Kaplan will convene several leaders in the field of phage therapy for a session at ASM Microbe 2023 that will explore the current state of research, novel clinical approaches and recent commercial developments. The session is titled "<u>New Perspectives on Phage</u> <u>Therapy to Treat Multidrug Resistant Infections.</u>"</u>

EQUITY, SOCIAL JUSTICE AND ANTIMICROBIAL RESISTANCE

While addressing scientific and medical challenges related to combatting AMR is of paramount importance, if the solutions and interventions don't end up reaching patients and susceptible groups, are they truly impactful?

That is an issue that <u>Jacinda Abdul-Mutakabbir</u>, <u>Pharm.D.</u>, <u>MPH</u>, from the University of California San Diego is trying to address. "How is it," Abdul-Mutakabbir asked, "that we ensure equitable stewardship measures and policies [related to AMR]?" Such discussion is not just theoretical. The COVID-19 pandemic has laid bare significant racial and ethnic disparities in <u>virus-associated mortality</u>, along with <u>vaccination rates</u>. Hoping to prevent similar disparities from occurring in the looming AMR crisis, Abdul-Mutakabbir is working to establish "stewardship that really tries to ensure that everyone receives the most appropriate therapies, at the most appropriate time, for the most appropriate durations, and that we're making sure that all of these things are done equitably."



Speakers at the "Antimicrobial Stewardship Programs: Beyond the Looking Glass" session at ASM Microbe will explore how approaches addressing AMR can be delivered equitably. Pictured left to right: Sara Alosaimy (Wayne State University), Kierra M. Dotson (Chase Brexton Health Care), Anna Zhou (Loma Linda University), Jacinda Abdul-Mutakabbir (UCSD). Source: American Society for Microbiology

Addressing these challenges relies on improving trust, access, diversity and inclusion. "The institution of science is led by senior investigators who are typically male and/or white. When you do have diversification, it still continues to lack the representation of minoritized professionals, especially those that are at the junior and mid-career levels," said Abdul-Mutakabbir. "How is it that antimicrobial stewardship may be impacted when we don't have people at the table?" she asked.

One particular example of this problem focuses on sources of care. As Abdul-Mutakabbir explained, "People that go to federally qualified health centers (FQHCs) are more likely to be minoritized, and we don't really showcase what stewardship and antimicrobial resistance look like in these health centers."

To help address these issues, Abdul-Mutakabbir is organizing a session at ASM Microbe 2023 that will feature diverse panelists who encounter and explore these challenges from unique perspectives. The session is titled "<u>Antimicrobial Stewardship Programs:</u> Beyond the Looking Glass."

"I really wanted to see the different groups that you don't typically see having those opportunities to speak about their professions and their contributions," she explained. "I really wanted to make sure that we saw traditionally marginalized groups represented amongst the speakers."

Having diverse viewpoints included in conversations about antimicrobial stewardship will, according to Abdul-Mutakabbir, help members of the scientific and medical communities broaden their perspectives and improve the impact of their own work. "It allows for us to be able to call out some of our own biases, to get outside of what we've been taught—what has traditionally been done— and really be innovative," she said. "By calling these things out, the way that we provide care can look a lot different."

CONNECT WITH ANTIMICROBIAL RESISTANCE EXPERTS AT ASM MICROBE 2023

From tapping AI to predict antibiotic activity, to leveraging phage therapy to vanquish multi-drug resistant infections, scientists will gather at ASM Microbe 2023 to address AMR from every angle. The <u>Antimicrobial Agents and Resistance track</u> offers a hub to discuss multi-pronged strategies to tackle the grave challenge of AMR and ensure equitable health care practices are implemented.

Friends and Foes: Microbial Interactions and Infection

BY MADELINE BARRON, PH.D

f one were to write a recipe for bacterial infection, it would seem relatively straightforward: add a pathogen to a host and voilà! However, infection is not just a product of interactions between pathogens and their hosts, but also between pathogens and other microbes within and on the host.

Investigating these microbe-microbe interactions is key to understanding mechanisms of bacterial pathogenesis, as well as facilitating the development of microbe-based strategies for combatting disease. Ultimately, "we can treat infection through the lens of ecology," said <u>Joseph Zackular, Ph.D.</u>, Assistant Professor of Pathology and Laboratory Medicine at the University of Pennsylvania. "You don't have to go just for the really tough bug. If you [target] its friend or its partner, you might get an advantage."



During infection, bacterial pathogens interact with diverse types of microbes, which, in turn, interact with each other. This web of interactions influences the course and outcomes of infection. Source: American Society for Microbiology

FRIEND OR FOE? IT DEPENDS.

According to Zackular, most infections are, at some level, <u>polymicrobial</u>. The success of pathogens is intricately linked to all other microbes at an infection site. Some of these microbes may promote growth of a pathogen, while others prevent it. Whether the pathogen prevails depends on the form and function of the broader microbial community at a given time, which itself depends on numerous other factors (e.g., <u>medications</u>, diet, host responses and more). Zackular pointed to the toxin-producing, gastrointestinal pathogen *Clostridioides difficile*—a common cause of antibiotic-associated diarrhea—as a key example.

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Interactions with the gut microbiome play a central role in the pathogenesis of pathogenesis of *C. difficile*. Listen to Vincent Young, Ph.D., discuss the importance of these interactions in modulating infection susceptibility and outcomes.

The gut microbiota (i.e., the consortium of microbes inhabiting the gut) normally "does a really good job of reshaping the environment to create a hostile place for *C. difficile*," Zackular said, mainly through nutrient restriction and production of metabolites that hamper *C. difficile*'s growth. If the microbiota is perturbed (such as after antibiotic treatment, which kills many resident gut bacteria that defend against pathogens), *C. difficile* can proliferate and cause disease. In fact, recent work from Zackular's lab suggests that, after antibiotic treatment, <u>remaining members of the microbiota may facilitate *C. difficile* growth, highlighting the context-dependent role of the microbiota during infection.</u>

Zackular's lab's findings center around *Enterococcus*, a group of common intestinal bacteria often increased in the guts of people with *C. difficile* infection (CDI), in part because of *Enterococcus*' intrinsic antibiotic resistance. Through in vitro and in vivo experiments, Zackular's team discovered that *Enterococcus* promotes *C. difficile* growth by metabolizing the amino acid arginine to produce ornithine, a compound *C. difficile* readily breaks down for food. However, in the absence of arginine, *C. difficile* starts producing more toxin, which damages the host's intestine.

"Enterococcus is doing 2 things at the same time," explained Zackular, who will present in the <u>Host-Microbe Biology (HMB)</u> track session "<u>Commensal-Pathogen Interactions</u>" at <u>ASM Microbe 2023</u>. That is, it is providing *C. difficile* with a food source (ornithine) while, at the same time, restricting a metabolic signal (arginine), which consequently tells *C. difficile* to produce toxin. *Enterococcus* may, in turn, "take advantage of all the chaos that *C. difficile* causes to get an additive advantage," Zackular continued, though the details of that advantage are still under investigation.

Zackular noted that this *Enterococcus-C. difficile* interaction is just one of many relationships that modulate *C. difficile*'s pathogenesis. However, it is "proof of principle that one of the clinically relevant things we notice is, we think, pretty consequential." Still, exploring other "microbial correlates" of CDI in diverse host environmental contexts (e.g., the guts of people who are susceptible to infection in the absence of antibiotic treatment, <u>like those with inflammatory bowel disease</u>) will be important for gaining a nuanced understanding of the ecological underpinnings of disease.



Microscopy image of fluorescently labeled *Pseudomonas aeruginosa* (green), *Staphylococcus aureus* (red) and host cells (blue) interacting 4 days post-infection in a murine chronic wound model. The organisms are often found together in chronic infections. Source: Juan Barraza, Ph.D.

SPACING OUT DURING INFECTION

With that in mind, <u>Carolyn Ibberson, Ph.D.</u>, Assistant Professor of Microbiology and Plant Biology at the University of Oklahoma, underscored that understanding the ecology of infection depends not just on profiling the microbial constituents of the host environment, but also on examining their physical associations. In other words, how closely bacteria live with one another is an important, often underappreciated, aspect of microbial interactions and infection.

"We are thinking about the infection environment as its own ecosystem," said Ibberson, a presenter in the <u>Molecular</u> <u>Biology & Physiology (MBP)</u> track session, "<u>Influencing Your</u> <u>Neighbor: the Effect of Polymicrobial Interactions on Bacterial</u> <u>Behaviors," at ASM Microbe 2023.</u> "In an ecosystem, you have a biological community of interacting organisms and their environment. We could think about the microbes that live in our bodies in the same terms. So, you need to know who's there; you need to know what they're doing [and] you need to know how they're organized with each other."

The spatial organization of microbes can dictate if and how they interact. For example, *Staphylococcus aureus* and *Pseudomonas aeruginosa* are routinely <u>found together in chronic infections</u> (e.g., <u>cystic fibrosis</u> and chronic wounds), even though *P. aeruginosa* <u>generally kills *S. aureus* if they are mixed in vitro</u>. Ibberson, who studies chronic, polymicrobial infections, wanted to understand why. "We started thinking that maybe [the bacteria] are spacing themselves in a way that they <u>can benefit</u> from each other, because they do have beneficial interactions

that have been shown, like increasing each other's tolerance or virulence expression, while also not inhibiting and killing each other," she explained.

Using a mouse model of chronic wounds, Ibberson and team <u>showed that each species did, in fact, exist in distinct aggregates</u> <u>about 30 microns apart</u>—they were in the wound bed together but maintained some personal space. The separation relied on an <u>antimicrobial compound</u> produced by *P. aeruginosa*; in the absence of this compound, the bacteria intermixed. Notably, *S. aureus* became less tolerant to aminoglycoside antibiotics when mixed with *P. aeruginosa*. Though the mechanisms behind this observation are unclear, the findings indicate that the metabolic networks between bacteria, and their clinical implications, depend on their spatial orientation. To that end, Zackular's group also showed that and *Enterococcus* form mixed biofilms, which likely facilitate metabolic exchange between the organisms.

Ibberson thinks that incorporating spatial analyses into infection research, along with analyses of microbial community composition and function, is critical for taking a holistic approach to studying microbial pathogenesis. On a broader scale, she emphasized the necessity of investigating microbial interactions in their natural host environments and infection contexts, where all factors of the ecosystem are at play. This ability has become increasingly possible with the development of tools (e.g., <u>next-generation</u> <u>sequencing</u>, machine learning and more) that allow scientists to, as stated by Zackular, "embrace the complexity and study systems with so many variables." By understanding all facets of the infection landscape, researchers are better positioned to develop tactics for preventing or treating disease.



Interactions between bacterial pathogens and diverse types of microbes, including fungi, play important roles in infection outcomes. This image depicts Candida albicans, a fungus that commonly contributes to polymicrobial infections. Source: Allison D.L., et al./Microbiology Spectrum, 2016

LOOKING BEYOND BACTERIA

Adding to the complexity is the fact that the host is home to more than a few (thousand) bacterial species. For example, in the gut, "bacteria have the biggest biomass, [which] is why most research focuses on bacteria. But in terms of number, there are a lot of other nonbacterial components," said Judith Behnsen, Ph.D., Asistant Professor of Microbiology & Immunology at the University of Illinois at Chicago College of Medicine and convener of the ASM Microbe 2023 session, "Beyond Bacteria: Trans-Kingdom Modulation of Microbial Pathogenesis." She highlighted that viruses, archaea, fungi, protists and parasites are also members of the host ecosystem, not just in the gut, but throughout the body. These other microbes can influence bacterial pathogenesis to dictate the course and outcome of infection.

Behnsen's research, for instance, focuses on interactions between fungi and *Salmonella enterica* serovar Typhimurium, a major cause of gastroenteritis. Her lab recently showed that <u>commensal fungi in the gut</u>, as well as in the diet, are a <u>source of siderophores</u>, small molecules that scavenge for iron from the host environment for *S*. Typhimurium. Iron is a critical nutrient for bacteria that is limited during infection. Experiments in vitro and in mice revealed that these fungal siderophores provide *S*. Typhimurium with a growth advantage, suggesting a

potential role for "inter-kingdom cross-feeding" during infection. Behnsen noted there are also examples of <u>fungi inhibiting bacterial</u> <u>pathogens</u> (and <u>vice versa</u>), as well as competitive and cooperative interactions between pathogens and other types of microbes, <u>like viruses</u>.

However, for the most part, scientists are still in the dark when it comes to these relationships. "We do know more about what's there," Behnsen said, reiterating how advancements in technology have made it easier to study the composition of host-associated and environmental microbial communities. "But what do [those microbes] do? That [knowledge] is still lagging quite a bit. The good thing is that more and more people are starting to look." And continuing to look will be important. Knowledge of how these diverse members of the host ecosystem modulate disease could lead to novel strategies for thwarting bacterial pathogens.

CLINICALLY CAPITALIZING ON MICROBIAL INTERACTIONS: THE CASE OF PHAGE THERAPY

In fact, ecological insights into bacterial pathogenesis can inform—and have already informed—methods to combat infections. Some of these methods are broad in their microbial scope (e.g., <u>fecal microbiota transplants for treating CDI</u>) while others weaponize specific and, in some cases, nonbacterial interactions to obliterate pathogens. <u>Phage therapy</u> offers an excellent example.

Bacteriophages (phages) are viruses that bind to and hijack bacterial cells to replicate themselves, often killing the cell in the process. The bactericidal capabilities of phages have piqued interest in phage therapy for treating bacterial infections, whereby a selection of phages that specifically attack the infecting bacterium are administered to a patient. "We can use the enemy of the enemy as our friend," said <u>Jyot Antani, Ph.D.</u>, a post-doctoral researcher in the laboratory of <u>Paul Turner, Ph.D.</u>, at Yale University. Recently, scientists have focused not just on how phages attack bacteria, but also on bacterial responses to phages.

Bacteria have been locked in an evolutionary arms race with phages for eons. As a result, they have developed mechanisms to resist phages at various points in the replication cycle. "One such mechanism involves altering receptors on the cell surface," explained Antani, a presenter in the ASM Microbe MBP track session "Anti-Phage Defenses: The Battle Between Prokaryotes and Their Viruses." Often, phage resistance comes with a price. When Antani and his colleagues experimentally evolved populations of *Escherichia coli* with a flagellotropic (i.e., flagellum-binding) phage in vitro, some bacteria evolved mutations in motility-regulator genes that rendered them nonmotile. Other bacteria evolved mutations in the gene encoding the flagellar filament. These flagellar mutants were still motile but less so than the ancestral strain. In both cases, bacteria "traded" motility for phage resistance. Notably, phage-resistant bacteria can also exhibit reduced virulence or increased susceptibility to antibiotics.

Antani emphasized the potential of "evolutionary medicine," in which we can use such bacterial trade-offs to our advantage. For instance, bacterial pathogens are often motile during infection, and based on Antani's findings, scientists could potentially use flagellotropic phages to hinder their motility. "If there are only a few motile bacteria remaining, then it gets easier to use other ways, in combination with the [flagellotropic] phage, to stop those bacteria from spreading," Antani said. He went on to explain that this method could make the infectious population more manageable. Ultimately, insights into bacteria-phage interactions and defenses could further inform the rational design of phage therapeutics.

THE BOTTOM LINE

Infection is complicated. Understanding the process requires delineating how bacterial pathogens organize and engage with all aspects of the host ecosystem, especially its many microbes. Doing so will allow scientists to exploit these interactions to foster human health. "Microbes are not in a vacuum," Zackular said. "The way that they interact with their environment, their ecosystem...is ultimately the thing that matters the most for [understanding] how they impact us as humans, and how they impact society."

Join us at ASM Microbe 2023 to hear from more scientists within the Host-Microbe Biology and Molecular Physiology & Biology fields as they share cutting-edge science on the interactions between microbes, human health and society at-large.

Advancing Clinical & Public Health Using Teams and Tech

BY LEAH POTTER, M.S

n the last few years, the <u>(re)emergence of several pathogens</u> has kept clinical and public health microbiologists on their toes, balancing the <u>development of rapid diagnostics</u>, therapeutics and vaccines with planning for long-term infection prevention efforts. To solve current and future health-related challenges, professionals are calling for team-based science and an interdisciplinary research approach.

Interdisciplinary investigations produce robust research that benefits patients and their environments—leading to new drugs, devices and preventive medical interventions that directly improve the health and well-being of society. "Our mission as clinical microbiologists and as public health microbiologists is to have an impact on patients and the population. This grounds us in guiding the work that we do and the innovations we try to create," said <u>Daniel Rhoads, M.D., Section Head of Microbiology for</u> <u>Cleveland Clinic.</u> "That can come across as new or better diagnostic testing or as better characterizing the infection to enable improved management of the infection."



Team science emphasizes collaboration among researchers from multiple disciplines. Source: iStock



Krishna Rao, M.D., M.S., investigated why some patients colonized with *K. pneumoniae* develop an infection, while other patients remain asymptomatically colonized by *K. pneumoniae*. Source: Wikimedia Commons

WHY TEAM SCIENCE?

Team science emphasizes collaboration among researchers from multiple disciplines and leverages the diverse strengths and expertise of scientists who may typically pursue scientific endeavors separately. In clinical and public health spheres, this might involve collaboration between clinicians, practicing physicians, medical microbiologists and pharmacists who work jointly on a research initiative and discuss subsequent implementation and best practices in health care spaces. Examples of effective partnerships of this nature might consist of scientists working on basic translational studies or microbiologists trying to understand how the microbiome relates to diagnostic and prognostic implications in clinical studies. "All of these teams include people who understand and generate the data in the lab, as well as people who see patients," said A. Krishna Rao, M.D., M.S., Associate Professor of Infectious Diseases and Internal Medicine at the University of Michigan and track lead for Clinical Infections and Vaccines (CIV) at ASM Microbe 2023. Team science will be the focus of the ASM Microbe 2023 session, "The Whole is Greater than the Sum of the Parts: Team Microbiology in Action."

Rao experienced the benefits of team science firsthand through his research on *Klebsiella pneumoniae*, a bacterium that is often the causative agent of health care-associated infections (HAIs). At the University of Michigan, Rao worked alongside <u>Michael</u> <u>Bachman, M.D., Ph.D.</u>, a trained microbiologist and pathologist, who has a particular interest in the genomics and virulence determinants of *K. pneumoniae*. Prior to teaming up with Rao, Bachman was investigating a hypothesis about the relationship between *K. pneumoniae* genetics and the outcomes of infection. "He wanted to test this [hypothesis] in patient samples, but he didn't have the necessary clinical expertise," Rao explained. "So, he partnered with me, a clinician who has training in biostatistics and clinical research, and someone who knows how to design an observational research study." Together, the research pair pursued multiple inquiries and published several papers.

"My overall strategy for success is to get people who don't have the same expertise but have a shared goal [or] interest—get them talking early, keep the lines of communication open and make it so everyone feels like they have a piece of the project," he said.



Similar collaborative efforts were leveraged to determine H. pylori is the cause of peptic ulcer disease. Listen to Robert Gaynes, M.D., reflect on the career of Barry Marshall, MBBS, and the importance of teamwork in STEM.

One paper resulting from the collaboration between Rao and Bachman <u>focused on why some patients colonized with *K. pneumoniae* <u>develop an infection</u>, while other patients remain asymptomatically colonized by *K. pneumoniae*. The team hypothesized that the genetics of the infecting *K. pneumoniae* strain played a role in this outcome—some strains harbored genes that increased virulence. With this in mind, Rao and Bachman proposed a case-control study, isolating *K. pneumoniae* from rectal swabs collected from patients. "[For the case-control study], we matched cases to controls, and adjusted for a whole bunch of clinical factors (e.g., hemoglobin level, white blood cell count) that could explain the differences between cases and controls," Rao said. "When we found the [bacterial] genes that were enriched, we could have some increased confidence that these genes were actually independently associated with the risk of infection—not just confounded by the clinical factors."</u>

Further investigation included locating 5 of these "gene hits," or bacterial loci, in *K. pneumoniae* and conducting phylogenetic analysis to determine that the hits were not just <u>lineage markers</u> but did, in fact, serve as predictors for clinical infection. The research team also knocked out *K. pneumoniae* genes of interest and, subsequently, used a mouse model of pneumonia to determine how the loss of those genes impacted the pathogen's ability to cause infection. "In the case of one [of the animal models], the severity of the infection was reduced," Rao explained. "Then, [Bachman] did a complementation assay and put the gene back in [*K. pneumoniae*] and reinfected the mouse." Sure enough, this restored the ability of the bacterium to cause disease. In clinical practice, this knowledge can help providers identify patients who are at a higher risk of *K. pneumoniae* infections. Essentially, medical microbiologists could use diagnostic assays to screen for the identified genes and, ultimately, predict which patients are most at risk for developing infection. Identifying high-risk patients would ensure that preventive interventions or rapid treatments get administered.

"What's cool about this paper is [that] not one of the authors can explain the entirety of the manuscript alone," Rao said. "It's not like I understand the nuances of the phylogenetic tree and the genomics; that's not my training and background. And it's not like Michael can explain how and why we did the matching and the additional logistic regression that we did for the case control study and analysis. But it's a classic case of the whole being greater than the sum of the parts."

BARRIERS TO COLLABORATION

Still, even with its numerous benefits, team science isn't always instinctual. Rao noted that when scientists embark upon their next clinical or public health investigation, structural barriers may hinder collaborative efforts in STEM fields. For example, promotion committees often prioritize first-author publications and last-author publications for senior and junior researchers, respectively, with authorship coming from researchers within a single institution. "There are still many institutions and many scientists who have that traditional view that the research that comes out of their lab is their lab's research. Their idea of collaboration might be, 'Hey, I'll let you use this instrument,' or 'I'll send you a strain,'" Rao said. But Rao noted some publishers, <u>including ASM Journals</u>, are starting to include co-first and co-senior authors from different institutions or departments.

EMERGING TECHNOLOGIES FUEL TEAMWORK

New technologies in clinical and public health spaces could also mean faster turnaround times for testing, improved patient care and greater opportunities for experts to collaborate, according to <u>Robert Tibbetts</u>, <u>Ph.D.</u>, Associate Director of a clinical microbiology laboratory for Henry Ford Health System and track lead for <u>Clinical and Public Health Microbiology (CPHM)</u> at ASM Microbe 2023. In particular, Tibbetts highlighted notable technologies, including new processes for automation, rapid antimicrobial

resistance susceptibility testing and <u>next-generation sequencing (NGS)</u>, all of which benefit and bring multiple professions—from medical technologists to epidemiologists—together to problem-solve.



New technologies in clinical and public health spaces can provide greater opportunities for experts to collaborate. Source: iStock



NGS—a type of DNA sequencing technology—can help answer questions using genome assembly and metagenomic analysis. Source: Flickr/NIH

"Clinical public health covers everything from veterinary sciences, environmental microbiology, global health and <u>One Health</u>," Tibbetts said. "Medical technologists, clinicians and physicians encompass infection prevention and public health—it's a collaboration with various vendors and companies that are making these tests, or that are assisting with analytics. It's not just a matter of doing a test and putting out a result; it really does encompass a large group of people working behind the scenes to get these assays developed and useful for the patients."

AN INTERDISCIPLINARY APPROACH TO NGS

NGS has grown in popularity in recent years among clinical and public health researchers, due to the technology's ability to <u>answer</u> <u>questions using genome assembly and metagenomic analysis</u>. "One of the most exciting things right now is the use of nextgeneration sequencing or whole-genome sequencing. In the clinical lab, it certainly could be a game-changer when it comes to rapid diagnostics," Tibbetts said. At ASM Microbe 2023, the session "To <u>Report or Not Report: What to do with Whole Genome Sequencing</u> <u>Results?</u>" will delve into the debate surrounding the inclusion of whole genome sequencing results in patient records and care coordination.

Jennifer Guthrie, Ph.D., Assistant Professor in the Department of Microbiology & Immunology and Epidemiology and Biostatistics at Western University in Ontario, Canada, utilizes whole-genome sequencing to understand pathogens. By combining genomic information with additional laboratory testing and clinical diagnostic information, Guthrie performs pathogen surveillance and monitoring to ascertain important information about disease

transmission and outbreaks. She can even look for antimicrobial resistance genes in bacteria. Her research benefits from an interdisciplinary approach to scientific investigation, with researchers collaborating from a variety of different fields, including epidemiology, public health, bioinformatics and genomics. The mission behind this collaborative work is rooted in providing rapid, evidence-based solutions to protect population health.

When SARS-CoV-2 first emerged and transmission of the virus wasn't fully understood, Guthrie recalled <u>long-term care facilities</u> <u>being hit hard with high instances of infection</u>. Guthrie noted that, oftentimes, in long-term care facilities, bathrooms are shared between residents, and uncertainty regarding fomite transmission left housing setups in question. "We don't always have a lot of spare rooms to move patients into, so we wanted to [investigate risks through] genome sequencing and determine whether there was transmission [of SARS-CoV-2] between shared washroom pairs," she explained. "We determined that we could leave individuals [sharing a washroom] where they [were], whereas roommates sharing a room were obviously at risk for transmission [because of <u>exposure to respiratory droplets</u>]." Based on these findings, residents of long-term care facilities continued to share bathrooms and maintained separate bedrooms.

Typically, the order of operations for NGS for infectious disease investigation involves an initial request sent to a public health lab, followed by the collection of samples and, finally, performance of the actual genome sequencing. Guthrie pointed to the large number of professionals involved in executing these core steps. At the outset, epidemiologists are tasked with tracking and tracing a particular pathogen and entering all the contact information into a central provisional database, which can then be paired with data collected by experts in genomics. This collaboration helps determine whether transmission of a pathogen occurred in a particular area. It also provides insight into how and where the pathogen spread. Finally, that data gets sent to local public health professionals who rely on the information to develop policies to protect the health of their community.



Jennifer Guthrie, Ph.D. determined, through the use of NGS, that residents in long-term care facilities could continue sharing bathrooms safely without risking COVID-19 infection. Source: Innovative Genomics Institute

"We've got quite a system going [across multiple fields] to be able to do this work and manage an assignment and outbreak identification," Guthrie added. At ASM Microbe 2023, teams of scientists working in clinical and public health microbiology will examine how commercial sequencing technologies can be leveraged for clinical diagnostics during the session, "Integrating Commercial Sequencing Diagnostics: A Drip or a Waterfall?"

FIND YOUR TRACK AT ASM MICROBE

Join us June 15-19 at ASM Microbe 2023 in Houston, Texas, where scientists at any career stage will have the opportunity to meet professionals from multiple fields. As Rao summarized, ASM Microbe benefits society by fostering research collaboration. "[It gets] scientists out of their labs and into a conference to talk to each other," he said. "That makes for better science, and it makes for a better research community. Whenever any society invests in science, it reaps the rewards tenfold."

Part of Our World: Microbial Biodiversity Drives Innovation

BY EMILY READY

icrobes make considerable contributions to, and are greatly affected by, the environment in which they exist and function. When that environment is altered by climate change, the microbial population changes too. For example, drastic increase or decrease in temperature or moisture levels or <u>higher concentrations of toxic substances like heavy metals</u>, <u>plastics or agrochemicals</u> force microbes to evolve in order to survive. These uniquely evolved traits can help rid the environment of those substances, which might be toxic to most, if not all, other life forms.



A flooded farm in Berrigan, New South Wales, 2 months after the initial flood event. Source: Wikimedia Commons

BIOREMEDIATION APPLICATIONS FOR MICROBES ABOUND

The ASM Microbe 2023 <u>Applied and Environmental Science</u> (AES) track highlights how microbes work (and can be put to good use) in diverse environments. For example, the AES session, "<u>Environmental Biotechnology for and Biodegradation of</u> <u>Forever Chemicals: PFAS and Plastics</u>," explores new discoveries about microbial communities that possess the unique ability to degrade <u>polyfluoroalkyl substances (PFAS)</u>, plastics and other soil and environmental contaminants. PFAS, which are present in industrial processes and household items, like cleaning products, personal care products or nonstick cookware, can <u>move through soil and contaminate sources of drinking water</u>, as well as accumulate in fish and other marine life.

"Microbes are uniquely positioned with the <u>potential for degradation of emerging contaminants</u> that could negatively affect animal and human health. "This session will examine the process of how microbes act on those contaminants in the environment [and seek to] understand the process of that bioremediation, as well as ways to try to stimulate or control that process," said <u>Erica Majumder, Ph.D.</u>, Assistant Professor of Bacteriology at the University of Wisconsin-Madison and Track Leader for AES.

Another way microbiologists are using microbes to address environmental problems is by inoculating plant seeds with engineered microbes that <u>can help promote disease suppression</u>, provide a <u>buffer from stress</u> and reduce the need for agrochemical treatments. "The emphasis here is on understanding the <u>microbiome associated with plants</u> and how you might inoculate seeds to promote certain plant traits," said <u>Ariane Peralta Ph.D.</u>, Associate Professor in the Department of Biology at East Carolina University. "Helping to reduce the incidence of plant or fungal pathogens down the road can help sustain nutrient management and increase yield." The role of microbes in agriculture extends far and wide, ranging from the role of <u>microbes in crop production</u> to exploring and understanding how the <u>relationships between microbes and livestock</u> can be used to promote safety and sustainability.

MICROBES IN A CHANGING ENVIRONMENT

Microbes can subsist and even thrive in diverse environments, providing they find ways to adapt when they encounter change. The microbial environment is continuously shifting—the sudden absence or overabundance of resources, the introduction of new microbes to a community and the effects of human behavior or intervention on a given ecosystem all play a role. "Ecology, Evolution and Biodiversity (EEB) is now becoming centralized and integrated across other tracks," said <u>Britt Koskella, Ph.D.</u>, Associate Professor in the Department of Integrative Biology at the University of California, Berkeley and Track Leader for EEB at ASM Microbe 2023. "There's clearly a great deal of overlapping interest between EEB and <u>Climate Change & Microbes (CMM)</u> (the newly incorporated ASM Microbe guest track), so I'm excited to explore the topic integration across both tracks."

At the crux of that interface is the EEB track session, "<u>Microbiome Management in a Changing World</u>," which will examine applications in microbial ecology and evolution when developing or implementing solutions to environmental problems. "Microbes adapt far more quickly than plants and animals," Koskella said. "We're looking at how we might actually leverage that rapid adaptation to stay ahead of change."

Research in both EEB and AES are also relevant to <u>the emerging subfield of disaster microbiology</u>, which examines the effects of severe storms and natural disasters on microbes. Severe upheaval of microbial populations, due to tornadoes, floods, <u>fires</u>, heat waves, <u>hurricanes</u> and other natural or human-made disasters, can force microbes to further adapt to new environmental stressors. These microbial adaptions can have major impacts on human health—some microbes might become pathogenic or increase in pathogenicity, while others develop new potential for beneficial applications like <u>bioremediation</u>.

For example, soil salinity is a major agricultural issue because it inhibits or prevents crop growth. The Tohoku earthquake triggered a massive tsunami in Japan in 2011, which significantly increased salt content in the soil. Not long after, scientists demonstrated that application of halophilic microorganisms and recycled waste glass to tsunami-affected ground <u>could reduce</u> the hypersalinity of the soil. Understanding microbial adaptation and evolution becomes increasingly crucial as <u>the occurrence of</u> natural disasters grows more common with rising global surface temperatures.

"Disaster Microbiology," an EEB session at ASM Microbe 2023, will illustrate the variety of research that applies to the emerging area of study, explore the effect of natural or human-made disasters on microbes and examine the potential impact that an increasing frequency of such disasters could have on microbes and their evolution.

MICROBES AS INDICATORS AND PREDICTORS FOR PROTECTING HUMAN HEALTH

After a natural disaster, contaminated wastewater and runoff can quickly spread disease. Wastewater surveillance is a valuable tool that can be used to identify and respond to outbreaks. "Before the start of the COVID-19 pandemic, far fewer people were aware of wastewater epidemiology," AES Track Leader Majumder said. "But many microbiologists working within AES have been focused on that their entire careers."

Scientists used <u>wastewater surveillance</u> as a tool to observe and respond to outbreaks long before the emergence of SARS-CoV-2—in the 1930s, infectious poliovirus was found in the sewage of cities experiencing outbreaks. Human pathogens



COVID-19 Wastewater testing at Oregon State University. Source: Oregon State University, 2021

excreted in bodily fluids, or present on skin or hair during the period of active infection, pass into sewage systems during bathing, cleaning and waste elimination. Now, monitoring pathogen presence through wastewater surveillance can provide earlier detection of an outbreak and inform scientists of newly developed variants, including those of SARS-CoV-2, influenza, Norovirus and mpox.

This year at ASM Microbe 2023, the AES track session, "<u>Ethics, Policy and Methods in Wastewater-based Surveillance</u>," will cover new and emerging technologies within wastewater surveillance, as well as the direction of the field and ethical implications to keep in mind as those technologies and methods are developed.

EVOLUTION CAN GENERATE STRONGER PATHOGENS

Ecology and evolution constantly drive new variation in pathogens, and examining these variations can provide clues as to how we might better respond to emerging pathogens that threaten human health. "Having recently gone through the COVID-19 pandemic and seeing how a virus can shift, [this topic] is particularly relevant," EEB Track Leader Koskella said. The ASM Microbe 2023 session, "<u>Switching It Up: Viral Recombination as a Driver of Diversity</u>," will cover the mechanisms of recombination in RNA viruses and detail the best laboratory and analytical practices to detect the exchange of genetic material between microorganisms. A key concern, according to Koskella, is "how rapidly viruses can reassort their genes, pick up new genes or develop new host range." This session will look at examples from the emergence and spread of SARS-CoV-2 variants to facilitate

better understanding of the ways in which recombination can drive viral evolution and cause changes in virulence.

Evolution of parasites genes is another area of interest. Parasitic genes give no known benefit to the host but are still maintained in genomes—the question remains, what, if any, purpose do these genes serve to the organism, or is the moniker of parasite accurately bestowed? In pursuit of answers, ASM Microbe 2023 session, "<u>Parasitic Genes as Drivers of Microbial Ecology and</u> <u>Evolution</u>," will examine different classes and examples of parasitic genes and how they evolve. "These 2 sessions are really going to highlight how important microbial evolutionary change is and how rapidly it can occur," Koskella said.

THE MATH OF MICROBES

The foundation of existing knowledge within microbiology increases scientists' ability to make more accurate predictions in commensal ecological systems, as well novel pathogens. "With the information about metabolic use and overlap, we can begin to predict and describe species coexistence, which is critical to future predictability and microbiome engineering," Koskella said. "<u>Math of Microbes: Computation and Mathematical Modeling of Microbial Interactions</u>," will highlight how data sets can be leveraged to identify what functional capabilities microbial communities have, how to distill that data into parts and how to model it to be able to make predictions.

"To me, where ecology and evolution is critical at this moment in the microbiome field, is that we can use these molecular approaches to understand what microbes are present, what they are doing and how," Koskella said. "Identifying why they are there and how we might predict who might be present in the future is a question completely rooted in ecology and evolution."



Apollo 11 astronaut Buzz Aldrin on the moon. Source: NASA

AS ABOVE, SO BELOW

AES even extends beyond Earth's atmosphere to examine microbes in outer space. This year, "The Microbiology of Human Spaceflight: Astronaut Health and Habitat Sustainability," will provide an overview of key research topics and issues that must be resolved to successfully conduct human space exploration. "Even for those who may not be specifically working in the field of space microbiology, it touches a wide variety of areas of microbial research and several AES subtracks," Majumder said. "It combines so many different aspects of health and sustainability and even agriculture." Though there are marked differences between how microbes function in space and how they function on Earth, exploring microbial resolutions for the unique challenges of space travel can support and translate into solution development in agriculture and human health—for example, identifying ways that microbes can perform processes usually performed by plants, like vitamin production, water recycling, air decontamination and waste management.

Still, how microbes behave in <u>synthetic communities</u> is not necessarily how they behave in natural communities. As best as the conditions of space can be replicated in a lab on Earth, environmental factors and members of Earth-bound microbial consortia that cannot be accounted for or incorporated in a synthetic community may mean microbes behave differently than expected outside that community.

ASM Microbe 2023's panel discussion, "<u>The Opportunities and Pitfalls of Synthetic Community Research</u>," addresses the perks and limitations of synthetic community research in developing solutions. "We can use these simplified synthetic communities to understand how microbes interact, how they work together—or don't," Koskella explained. "As you expand ecological reality, those interactions may not always be applicable." Peralta also noted the opportunity to recognize and leverage generalizable patterns, while acknowledging the variation microbes provide in ecological systems. "There's a point where oversimplifying or overengineering a system can actually make it more likely to fail more quickly in response to new stressors," Peralta said. "We're looking at how to manage microbes and microbial functions in a way that's more accurate."

JOIN A MICROBIAL COMMUNITY STRIVING FOR SOLUTIONS

Microbiologists' expertise is crucial to developing the tactics and solutions necessary to address issues that affect human life. Microbial functions and the ways in which those functions evolve are reflected in phenomena that can be witnessed on a global (and outer space) level.

Become part of the discussion about how microbiology can help address challenges facing people and our planet by attending <u>ASM Microbe 2023</u> in Houston, Texas, from June 15-19. You'll hear about new and groundbreaking research that helps further our ability to understand and address a wide variety of issues across human and animal health, agriculture and sustainability.

Microbiology Professionals Impact All Facets of Society

OURKE

hile microorganisms are amongst the world's tiniest of muses, the field of microbiology is anything but small. In fact, microbiology consists of subdisciplines that span the gamut of science and art, oftentimes intersecting, as the field's dedicated professionals work to elevate scientific discovery and benefit society.



ASM Microbe 2023 provides opportunities for scientists to network, explore innovative research and advocate for the microbial sciences. Source: American Society for Microbiology

SURVEYING THE MICROBIOLOGY WORKFORCE

In an effort to better understand the people behind the groundbreaking science (the microbiology workforce), <u>Donna</u> <u>Ginther, Ph.D.</u>, Roy A. Roberts & Regents Distinguished Professor of Economics and Director of the Institute for Policy & Social Research (IPSR), University of Kansas will present the findings from Workforce Trends: The Future of Microbial Sciences—a survey commissioned by ASM in collaboration with IPSR.

Ginther's team utilized several sources of education and employment data to paint a statistical portrait of those with microbiology degrees and those working in microbiology professions. To procure education data (2003-2021), Ginther and colleagues relied on the Integrated Postsecondary Education Data System and Survey of Earned Doctorates. For workforce data (2019-2021), the researchers leaned on the National Survey At ASM Microbe 2023, the <u>Profession of Microbiology (POM)</u> <u>track</u> is a place where everyone comes together to network, explore innovative research and advocate for the microbial sciences. POM covers topics from education and career choices to diversity and inclusion; professional development to science communication and outreach. POM is where microbiologists from all subdisciplines come to explore how to make the most of their science education, develop strategies for creating a more diverse workforce, find guidance on funding for their research and receive advice on choosing a career path and navigating application processes.

"[POM] showcases both the importance and the versatility of the microbiologist, an essential professional for the advancement of our society," said <u>Tatiana Pinto, Ph.D.</u>, Associate Professor of Microbiology at the Federal University of Rio de Janeiro and 2023 POM Track Lead. "The POM track has a lot of must-see sessions, covering topics such as how to decide on a career and apply for a job and ways to improve public communication and leadership skills." We explore some of these sessions below.



Workforce Trends: The Future of Microbial Sciences will assist ASM in designing policies and programs to attract and retain talent in the microbial sciences. Source: rawpixel.com

of College Graduates, Survey of Doctoral Recipients, ASM Survey Data and Lightcast Job Openings Data (2022).

The team's data analysis will provide a unique look at the demographic makeup, employment patterns and occupations of the discipline. For example, data revealed that more than half of microbiologists work in the private sector, while almost 30% work in government or education sectors. The project also detailed earnings, job satisfaction and reasons for leaving the field of microbiology.

Alongside employment data, the survey identified key trends in education. As of 2021, the majority of microbiology degrees were awarded to women (including bachelor's degrees, master's degrees and Ph.D.s). Rapid growth was reported in microbiology bachelor's degrees starting in 2011, with some growth in master's degrees and a decrease in doctorates since 2014.

This data collection and analysis will assist ASM in designing policies and programs to attract and retain talent in the microbial sciences. "The future of scientific discovery and combatting disease depends upon a well-trained microbiology workforce," Ginther said. "The COVID-19 pandemic increased the demand for microbiology professionals, and, as in many professions, many retired because of the pandemic. This [survey] will examine the microbiology education-workforce continuum with the goal of understanding the education, diversity, employment, earnings and job satisfaction of this workforce."

MICROBIOLOGISTS AS COMMUNICATORS

Not only did the COVID-19 pandemic highlight challenges in workforce development, it also emphasized the importance of scientists as communicators and trusted subject matter experts. At ASM Microbe 2023, the symposium, "<u>Communication Is the</u> <u>Bridge Between Confusion and Clarity: Microbiology Science</u> <u>Communication</u>," will provide an interactive discussion and key insights on science communication concepts from experts in infectious diseases, clinical microbiology/laboratory medicine and science journalism. Areas of focus will include communication during pandemics, laboratory-based education, demonstrating the value of diagnostics beyond the laboratory and science communication as a means of bridging gaps between knowledge and practice.



The COVID-19 pandemic emphasized the importance of scientists as communicators and trusted subject matter experts. Source: iStock

Andrea Prinzi, Ph.D., MPH, is a clinical microbiologist and microbiology medical liaison at BioMérieux, Inc. Prinzi will lead the symposium and said she is most excited about the collaborative nature of the session. "If anything, <u>the COVID-19 pandemic demonstrated</u> <u>the importance of multidisciplinary collaboration and the impact of communication</u>," Prinzi explained. "Hearing about science communication best practices from a variety of perspectives is not only acutely relevant, but also fascinating."

The end goal of the symposium is for attendees walk away with at least 1 skill for communicating complex scientific information across various audience types, including laboratorians, clinicians or the general public. "We hope that attendees will have learned something about how to critique the pros and cons of differing forms of academic publications, like preprint manuscripts, for example," Prinzi said. "[We also hope attendees] leave with a greater understanding of the far-reaching impact of nontraditional science publications, like blog articles or pieces produced via journalism."

In this digital age, people have tremendous access to information, and it is no longer enough to disseminate scientific findings only at conferences or through formal academic publishing. Science communication is an essential skill not only for science writers and journalists, but also for researchers, clinicians and laboratorians. "<u>In order to fight misinformation</u>, and keep clinical communities and the general public informed, we have to be able to communicate science in a way that is understandable and digestible," explained Prinzi.

BRINGING EVERYONE TOGETHER AT ASM MICROBE 2023

At ASM Microbe 2023, scientists from all backgrounds and professions will have the opportunity to convene through the POM track. "I believe ASM Microbe is a great platform to expand professional connections, and the POM track is the best place to be if you are excited about networking with your peers," shared Pinto. "POM track is especially committed to delivering the message of the importance of promoting diversity, equity and inclusion in microbial sciences."

What's Hot in the Microbial Sciences

BY ASHLEY HAGEN, M.S. & JOHN BELL

As we count down to ASM Microbe 2023, this issue of "What's Hot" explores research conducted by some of the speakers and conveners of upcoming ASM Microbe sessions. Visit the ASM Microbe page and search the scientific program to access more information and add these sessions to your itinerary.



Stages of marine plastic biodegradation. Source: Wikimedia

SYNTHETIC BIOLOGY AND OCEAN HEALTH

From shoring up the ailing oceans, to engineering synthetic gene circuits and programmable cells to produce new diagnostics and therapeutics, synthetic biology provides scientists with innovative tools to address key issues.

The world's oceans are threatened by human activities. In a recent review <u>published in *Trends in Biotechnology*</u>, researchers discussed ways to leverage synthetic biology to address issues, such as plastics pollution, that relate to ocean health.

Plastics pour into the seas from landfills and river systems. Weathering and churning seas grind the large plastic into smaller components, including tiny bits called microplastics. The tissues of marine organisms become home for the smallest microplastics, which exert toxic effects. Bigger plastics choke large areas of open ocean, where some sea life ingest or become entangled by them. Preventing land-based plastics from entering waterways represents one upstream way of

safeguarding oceans. However, much plastic already resides there. Scientists envision the selective isolation of microorganisms that degrade plastics naturally (biotransformation) to inform strategies for engineering more robust plastic-degrading strains.

For example, one study, <u>published in Archives of Microbiology</u>, examined the natural potential of communities of bacteria living in sediment found in Manila Bay, Philippines (<u>an area that suffers from severe plastic pollution</u>) to degrade low-density polyethylene (LDPE)—a soft, flexible, lightweight plastic material. First, scientists quantified plastic composition in selected sites of the bay. Then they collected sediment samples for further experimentation from sites that registered the highest and lowest concentrations of plastic. In the laboratory, sediment samples were incubated for 91 days with LDPE then examined by <u>fourier transform infrared</u> <u>spectroscopy (FTIR)</u>. Researchers observed structural modifications (i.e., carbonyl and vinyl products) that were considered signs of polymer degradation on the surface of the LPDE. High-throughput sequencing further revealed that the dominant phylum in the microbial sediment consortium was Proteobacteria.

Other bacterial taxa that are associated with hydrocarbon degradation were also identified and thought to be playing active roles in partial biodegradation of the plastic. Researchers hypothesized the remaining microbial taxa were consuming byproducts, or providing nourishment for other groups in the consortia, and collectively creating a synergistic biofilm-associated microenvironment, which utilized plastic as its main carbon source.

In pursuit of scalable bioremediation techniques to address plastic pollution, researchers associated with the *Trends in Biotechnology* review proposed a multi-step synthetic approach to leverage knowledge gleaned from microenvironments within plastic biofilms, like those in Manila Bay. First, scientists called for a compilation of datasets pertaining to microbial communities that naturally degrade plastic. From there, genetic toolkits and engineering strategies could be developed to augment the pool of microorganisms that degrade plastics. Protein engineering could be explored to improve the effectiveness of plastic-degrading enzymes, with the downstream goal of constructing synthetic microbial consortia that degrade, and perhaps even biosynthesize value-added products from, the degraded plastic (e.g., carbon sources as added nutritional fodder for the engineered microorganisms themselves).

James J. Collins, Ph.D., one of the authors of the *Trends in Biotechnology* study will be presenting at ASM Microbe 2023 about harnessing synthetic biology and deep learning to fight pathogens in a session titled "<u>Synthetic Biology Tools and Emerging</u> Environmental Organisms for Antibiotic and Natural Product Discovery and Synthesis."

NOVEL ANTIBIOTIC MOUNTS A 2-PRONGED ATTACK ON CELL ENVELOPE

Bacteria that are resistant to multiple antibiotics continue to be a grave threat to human health. Equally concerning is the dearth of new antibiotic development to combat them. Teixobactin, a <u>novel antibiotic that came to light in 2015</u>, fared well in animal models of infection, providing evidence of its potential as a human antibiotic agent. Recently, a <u>paper published in Nature</u> explored 2 modes by which teixobactin exerts activity against multidrug-resistant (MDR) gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus pneumoniae* and drug-resistant enterococci.



Chemical structure of texiobactin. Source: PubChem (ID: 86341926)

One mode of action involved teixobactin targeting lipid II, a peptidoglycan precursor, which led to interference with peptidoglycan biosynthesis and contributed to defects in the bacterial cell membrane. Finding antibiotics that act on prokaryotic membranes, but leave human cells unharmed, has been challenging. However, teixobactin damages only membranes that contain lipid II—which human cells do not possess. This microbial-specific targeting eliminates the threat of toxicity for human applications.

In addition to lipid II targeting, teixobactin was shown to possess a supramolecular structure that sequesters lipid II into <u>supramolecular fibrils</u> (multi-protein complexes that polymerize into fiber-shaped structures) and displaces phospholipids. The result? Thinning and disruption of the bacterial cell membrane. Teixobactin's 2 modes of action, (i.e., inhibition of cell wall synthesis and weakening of cytoplasmic membrane), produce an effective compound for targeting the bacterial cell envelope. Very few new classes of antibiotics have been created in the past 30 years, yet teixobactin shows promise for targeting bacterial pathogens while sparing mammalian cells.

Kim Lewis, Ph.D., one of the authors of the *Nature* study referenced above will be presenting about antibiotics from unusual microorganisms and "undruggable" targets at the ASM Microbe 2023 session titled, "<u>Synthetic Biology Tools and Emerging</u> Environmental Organisms for Antibiotic and Natural Product Discovery and Synthesis."

PHAGE THERAPY TO TREAT MULTIDRUG RESISTANT INFECTIONS

Not surprisingly, MDR bacterial pathogens are also emerging as a major threat in common infections like <u>urinary tract infections</u> (UTI)—one of the most frequent infections for which antibiotics are prescribed. As antimicrobial resistance (AMR) continues to increase in uropathogenic *Escherichia coli* (UPEC), a primary agent of UTIs, new antibiotics and therapies will be critical to maintain ability to control infections.



Bacteriophage coming in contact with cell surface. Source: iStock

New developments in <u>bacteriophage (phage) therapy</u> are showing promise to combat AMR UTIs. However, bacteria also develop resistance to phages, which could impact the efficacy of this treatment. In a <u>recent *mSphere* paper</u>, researchers evaluated the costs of the development of phage resistance during UPEC infection.

To gauge phage activity in a simulation of the human urinary environment, scientists compared susceptibility of UPEC strains to 2 distinct phages (HP3 and ES17), using both in vitro and in vivo models. Researchers found that development of phage resistance in UPEC strains began within the first 6-8 hours postphage introduction in both pooled human urine and bacterologic medium. Phage-resistant UPEC strains demonstrated some distinct genotypic and in vitro phenotypic changes. Namely, these strains possessed mutations in genes involved in lipopolysaccharide (LPS) biosynthesis and demonstrated altered adherence to and invasion of human bladder epithelial HTB-9 cells. Furthermore, resistant strains demonstrated reduced growth in vitro and reduced ability to colonize the mouse urinary tract in vivo, compared to parental strains.

Overall, researchers observed that phage resistance is accompanied by fitness costs. They concluded that phage therapy for UTIs will succeed when the development of said resistance decreases UPEC fitness to the extent that it causes phage-resistant bacteria to become less virulent—promoting immune clearance and resolution of infection. Finally, researchers noted that phage-resistant bacteria may also become more sensitive to other antibacterial treatments, suggesting that phage resistance could bolster efficacy of antimicrobial agents against MDR pathogens.

Barbara Trautner, M.D., Ph.D., one of the authors of the *mSphere* study referenced here will be convening a session about phage therapy at ASM Microbe 2023 titled, "New Perspectives on Phage Therapy to Treat Multidrug Resistant Infections."



Young sprouts of mung bean seeds. Source: Flickr

LESSONS FROM THE ASSEMBLY AND TRANSMISSION OF SINGLE-SEED MICROBIOTA

Climate change is driving further adaptation in an already incalculably diverse microbial world, suggesting that when it comes to microbiome management of synthetic and natural communities, the principles of ecology and evolution are critical.

The microbiota within seeds of agriculturally important plants exhibit roles in ending seed dormancy, improving seed germination and helping ward off certain plant pathogens, thus influencing a plant's potential to grow and thrive. Evidence further indicates that the seed microbiota may also have an impact on soil microbiome establishment and, as a result, confer longer-term consequences on crop development. Characterizing seed microbiota may, therefore, permit improvement in plant phenotypes, which could have important ramifications on agricultural practices. With this in mind, scientists <u>published</u> an <u>mBio</u> paper in which they examined the diversity of bacteria associated with individual seeds during development and sought to understand how plant phenotype was influenced by variations in seed microbiome composition.

Using common bean and radish seeds, researchers estimated the microbiota structure and assembly of 1,000 individual seeds during seed development and maturation. To account for the low microbial biomass presented at the single-seed level, scientists employed a culture-based enrichment strategy prior to DNA extraction and sequencing.

Overall, researchers reported that individual seeds were associated with low bacterial richness. In fact, more than 75% of reads were associated with only 1 dominant taxon, the identity of which varied greatly between plants and even between individual seeds of the same plant. Fifteen bacterial orders were represented in these dominant taxa. Authors noted that these results aligned with previous reports that the <u>plant microbiome might be bottlenecked at the individual seed level</u>, as a result of plant defenses and <u>microbial interactions</u>, which supports the primary symbiont hypothesis.

Next, researchers sought to identify the origins and changes in community composition of seed-associated microbial taxa after colonization (succession). Scientists discovered that initial seed colonizers arrived by 1 of 2 primary methods: internally (through the vascular tissue) or externally (through the colonization of reproductive tissues via airborne organisms or pollinators). However, succession profiles differed amongst plants. In radish seeds, bacterial diversity and taxonomic composition remained stable, suggesting that the original bacterial settlers persisted during seed maturation. Whereas, in bean seeds, the original bacterial taxa were replaced with new microbial residents during seed development.

When it came to seed microbiota assembly, researchers reported that local processes were more impactful than seed dispersal, indicating that selection of microbial taxa is, at least partially, dependent upon host defenses. Authors therefore suggested that the differences in succession profiles might be driven by a variability in available resources amongst bean and radish plants but acknowledged that this hypothesis required further testing. Differences in fitness between taxa exerted the most influence on transmission of seed-borne microbes to seedlings for bean and radish seeds alike. Bacterial population size was not significantly impactful.

Overall, this study provided insight into the origin, composition, assembly and transmission of the seed-microbiota. Developing a more robust understanding of how these factors impact seed phenotype and vitality will inform possible avenues for seed microbiome manipulation to increase crop productivity and sustainability.

Marie Simonin, Ph.D., one of the authors of this mBio study will be speaking about plant microbiota engineering at ASM Microbe 2023 in the session titled, "Microbiome Management in a Changing World."