Current Topics

2014 ICAAC

Unconventional Means To Combating Infections Gain Credibility, Interest

Jeffrey L. Fox

"A few years ago, a session on this subject couldn't draw flies," said symposium co-convener Steven Projan of MedImmune in Gaithersburg, Md., to a packed audience. His comments came at the start of the symposium, "Alternative Treatment Approaches to Bacterial Infections," of the 2014 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Washington, D.C., last September.

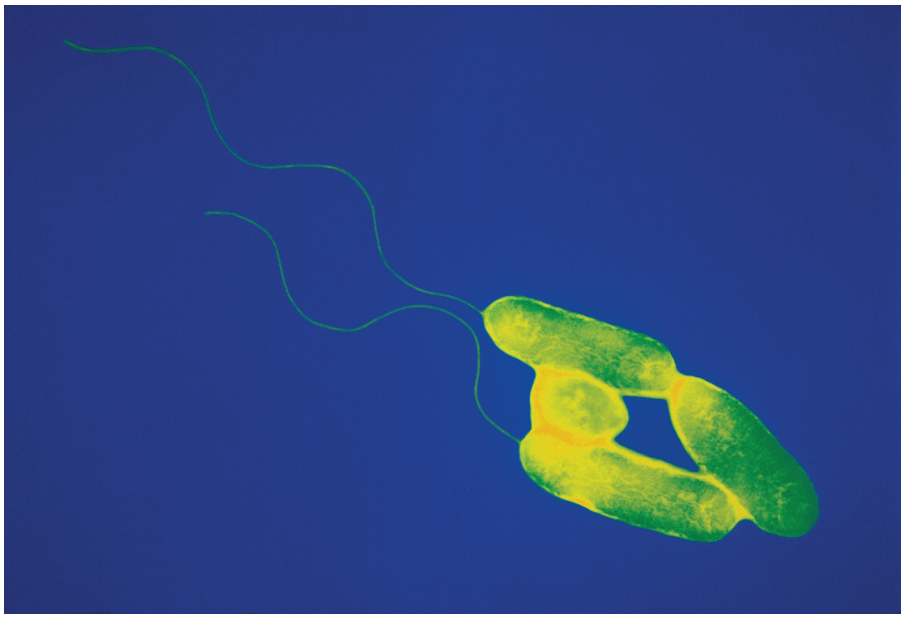
One such alternative approach to antibacterial agents involves the use of specific pathogen-targeted monoclonal antibodies (mAbs)—in general, to augment rather than outright replace conventional antibiotics, according to one of the symposium participants, C. Ken Stover, also from MedImmune. To overcome earlier failures when trying to harness mAbs into being effective agents against bacterial pathogens, Stover and his collaborators shifted strategies to take what he calls a "multifunctional approach." Taking cues from *Pseudomonas aeruginosa* being "versatile and opportunistic," that strategy entailed identifying mAbs "to several targets" on that bacterium, he says.

The development of "bi-specific" mAbs, which target two sites on that pathogen yields a product that is better than are the two single-acting mAbs used together to protect animals against *P. aeruginosa*, Stover continues. "We're not sure why." That bi-specific monoclonal was slated to begin phase 1 clinical trials "any day now," he noted in September. With that mAb plus another mAb that targets *Staphylococcus aureus*, longer-term plans call for using these or other mAbs either prophylactically or in conjunction with conventional antibiotics to treat ongoing infections. Precepts include "never treat with [mAbs] alone," and "we hope to preserve antibiotics for the longer haul," he says.

Another approach to curbing the damages inflicted during infections with *P. aeruginosa* begins with a "focus on inhibiting virulence through the target of quorum sensing (QS)," says Laurence Rahme of Massachusetts General Hospital and Harvard Medical School in Boston, Mass., another symposium participant. These bacteria have three QS systems, one of which controls dozens of small molecules that contribute to virulence, she says. She and her collaborators recently identified a series of benzamide-benzimidazole molecules that prevent the synthesis of these virulence factors—in effect, declawing this bacterial pathogen. Another set of molecules shuts down yet other virulence functions. "These inhibitors can work against chronic and acute and multidrug-resistant strains," she says. "And we've not seen the development of resistance. I'm not saying this will never happen, but clinical isolates don't have [resistance-conferring] mutations."

"Humans are perfused with antimicrobial peptides, and some are optimized to particular [anatomic] niches," says symposium participant Michael Yeaman of Harbor-UCLA Medical Center in Torrance, Calif. Despite efforts to develop some of them as antimicrobial drugs, their "pharmacology is poorly understood" and several otherwise promising candidates failed to gain regulatory approval when reviewed by Food and Drug Administration (FDA) officials.

This outlook could be changing, particularly as the importance of using particular peptides "at sites for which



Color-enhanced transmission electron micrograph of negatively stained *Pseudomonas aeruginosa*. *P. aeruginosa* is the focus of recent research aimed at using specific pathogen-targeted monoclonal antibodies as part of efforts to treat infections. (Image © Kwangshin Kim/Science Source.)

they were evolutionarily designed" is taken into account, Yeaman says. "It's not just the molecule, but when and where they may be used." When those issues were taken into account, one such engineered kinocidin peptide, designated γ–RP-1, proved more effective than a conventional antibiotic when tested in mice infected with multidrug-resistant strains of *Acinetobacter baumannii.*

Yet another alternative approach calls for using bacterial cell wall-targeted lysin enzymes from bacteriophages as a means for combating bacterial pathogens, according to Vincent Fischetti from Rockefeller University in New York, N.Y. "Lysins have profound effects on biofilms," he says. "They are effective against drug-resistant bacteria, work synergistically with antibiotics, are new agents against gram-positive bacteria, are safe, and it's difficult to develop resistance to them." These agents "work in animals," he adds, and "clinical trials are expected soon."

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

2014 ICAAC

DNA Inhibitors, New Cephalosporins among Antibacterial Prospects

Jeffrey L. Fox

A potent new antimicrobial candidate drug that shares enzyme targets—but has alternate binding sites—with fluoroquinolones was featured during the poster summary session "Early New Antimicrobial Agents" at the 2014 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Washington, D.C., last September. Other promising drug candidates are several novel cephalosporins, including one that carries a siderophore, a β-lactamase inhibitor that helps to overcome resistance in pathogens to β-lactam antibiotics, and an antifungal agent with an unusual mechanism.

Dual targeting of bacterial topoisomerase ATPase activity is a critical component of VXc-486, a "truly novel" aminobenzimidazole antibacterial agent, according to Susan Stokes of Vertex Pharmaceuticals in Boston, Mass. Although VXc-486 targets the bacterial topoisomerase enzyme—much like fluoroquinolone (FQ) antibiotics—its binding sites are different, and "we see no cross-resistance [with FQ antibiotics], and none is expected," she says. This new antibacterial agent has a "broad spectrum," with activities against many gram-positive and "some" gram-negative pathogens. The agent, which needs to be administered as a pro-drug to gain solubility in water, is bactericidal against pathogens such as *Neisseria gonorrhoeae* and *Mycobacterium tuberculosis* that are resistant to many kinds of antibiotics, giving it good "potential for multiple applications," she says. When tested in monkeys, it shows little toxicity.

S-649266 is a novel, catechol-substituted siderophore cephalosporin that is active against gram-negative bacterial pathogens, including multidrug-resistant isolates of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, according toYoshinori Yamano of Shionogi & Co., Ltd. in Osaka, Japan. The siderophore provides this candidate drug with an efficient means for entering bacterial cells via iron-transport mechanisms, he says. It is "highly stable" against various types of carbapenemases and β-lactamases. During phase 1 clinical studies, it was "well tolerated," and there were "no significant adverse effects," he adds. This cephalosporin is excreted via the urinary tract.

TD-1607 is a novel, "dual-mechanism," heterodimer, glycopeptide-containing cephalosporin, one that is active against a variety of gram-positive bacterial pathogens, according to Edmund Moran of Theravance in South San Francisco, Calif. The glycopeptide portion enables the compound to bind to D-Ala-D-Ala side chains along the bacterial cell wall, placing the cephalosporin portion of the molecule next to penicillin-binding proteins, he says. It is "potent" when used as a single agent, its linker is chemically "stable," and the intact molecule is 100-fold more active than are its two components separated but administered simultaneously, he adds. In phase 1 clinical studies, "all doses were well-tolerated, and there were no serious adverse effects." TD-1607 is administered as an intravenous infusion, and it is excreted (mainly intact) through the urinary tract. Food and Drug Administration officials granted it "fast-track" status.

AA139, derived from the peptide Arenicin-3, shows potent bactericidal

MINITOPIC

Federal Officials Issue Final Version of Dual Use Research Policy

Federal officials in September issued a final version of the U.S. Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (DURC), which articulates the responsibilities of institutions and investigators to identify and manage the risks associated with DURC. The policy details the necessary oversight to identify DURC and implement risk mitigation measures. The policy covers specific types of experiments, such as enhancing the harmful consequences of an agent or toxin for 15 pathogens and toxins, including avian influenza virus. For further information, please contact Andrew M. Hebbeler, Assistant Director for Biological and Chemical Threats, Office of Science and Technology Policy, Eisenhower Executive Office Building, 1650 Pennsylvania Avenue, Washington, DC 20504, DURCpolicy @ostp.gov; a detailed statement of the policy is available online at http://www.phe.gov/s3/dualuse.

MINITOPIC

One Extra-Long, Another Varied-Length Bacterium Manage To Split Evenly

Despite being varied in length in one case and extraordinarily long in the other, two different Gammaproteobacteria that live attached to the nematode worms *Eubostrichus fertilis* and *E. dianeae*, respectively, divide symmetrically, according to Silvia Bulgheresi of the University of Vienna in Vienna, Austria, and her collaborators. The crescent-shaped bacterial symbiont associated with *E. fertilis* can vary as much as 12 times in its cell length, exceeding size variations seen in many more familiar bacteria, but nonetheless divides evenly into symmetrically sized daughter cells. In like fashion, the bacteria associated with *E. dianeae*, which can grow to lengths of 120 μm, also neatly divides into equal-sized daughter cells—making it the "longest unicellular organism in which symmetric division has ever been observed," the researchers note. These findings indicate that "size is not the primary trigger of division," suggesting instead that "novel molecular machineries may time cell division and position the genome and division plane" in these bacteria. Details appeared 15 September 2014 in *Nature Communications* (doi:10.1038/ncomms5803).

activity specifically against gram-negative bacterial pathogens, according to Sergio Lociuro of Adenium Biotech in Copenhagen, Denmark. It appears to have a "dual mechanism of action," targeting protein components of the outer membrane of such bacteria, but not lipid A, he says, adding: "The mechanism looks to be more complicated. It seems we're working with multiple targets." AA139 is active in treating several types of gram-negative infections in rodents, and shows "low or no toxicity," as well as a "low propensity for resistance" to develop against it.

A diazabicyclic compound, designated OP0595, is a novel serine-β-lactamase inhibitor that acts mainly against A, B, and C-type β-lactamase enzymes, thus enhancing the activity of β-lactam antibiotics, according to Kenichiro Kondo of Meiji Seika Pharma Co. Ltd. in Tokyo, Japan. In terms of its safety, there are "no particular concerns," he says. "We are moving forward" to develop this compound.

Finally, a novel natural product hexapeptide antifungal agent, designated ASP2397, is fungicidal against *Aspergillus* spp., is "highly potent" when evaluated in animals with azole-refractory aspergillosis, and leads to 100% survival in late-treatment models of such infections, says Ikuko Nakamura of Astellas Pharma in Tsukuba, Japan. ASP2397, which chelates iron and aluminum, is "actively taken up" by fungal cells, but "we haven't identified the intracellular target within *Aspergillus*," she adds. It has a "unique mechanism," and is active against the conidial form of fungal pathogens, yielding a 3-log reduction within 8 hours.

2014 ICAAC

Systems Biology Using Host Responses To Diagnose Infections

Shannon Weiman

Researchers are taking a systems biology approach to identify pathogens—diagnosing diseases by analyzing specific responses that those pathogens elicit from hosts that they infect. Gene expression signatures, particularly in immune response pathways in blood samples, point to the cause of infection, according to several researchers who spoke during the symposium, "Systems Biological Approaches to Understanding Immunity in Vaccination and Infections in Humans," convened as part of the 2014 ICAAC. These gene-expression signatures also help to predict responses to vaccines and may lead to speedier diagnoses and better patient outcomes.

"Different classes of pathogens trigger specific pattern-recognition receptors (PRRs) on peripheral blood leukocytes . . . inducing distinct gene expression profiles," says Octavio Ramilo of Nationwide Children's Hospital in Columbus, Ohio. These profiles serve as "disease fingerprints" for HIV, influenza virus, malaria, salmonella, and many other infectious agents, he says. In proof-of-concept studies, these profiles are impressively accurate in challenging circumstances, distinguishing among many different microbial causes of fever in infants with 90% sensitivity and specificity. In those cases where the patterns appeared to misdiagnose the pathogen causing symptoms, many of the patients developed the predicted infection weeks later, he adds.

Separately, Michael Levin of Imperial College in London, England, followed a similar approach to develop a point-of-care diagnostic test for tuberculosis (TB), which can be difficult to distinguish from other mycobacterial infections in patients, he says. However, a 44-transcript signature identifies *Mycobacterium tuberculosis* infections with 93% sensitivity and 88% specificity, he says.

"Functional fingerprints"—sets of transcripts indicative of responses by subsets of immune cells—can reveal pathogenesis patterns that are peculiar to specific pathogens, according to Ramilo. For example, the respiratory syncytial virus (RSV) suppresses B-cell responses, preventing them from producing protective antibodies. Vaccines to protect against this virus ought to take this suppression into account, he suggests. These patterns also provide information about individual outcomes. For example, the extent to

MINITOPIC

Ebola Takes Center Stage at Global Health Security Summit

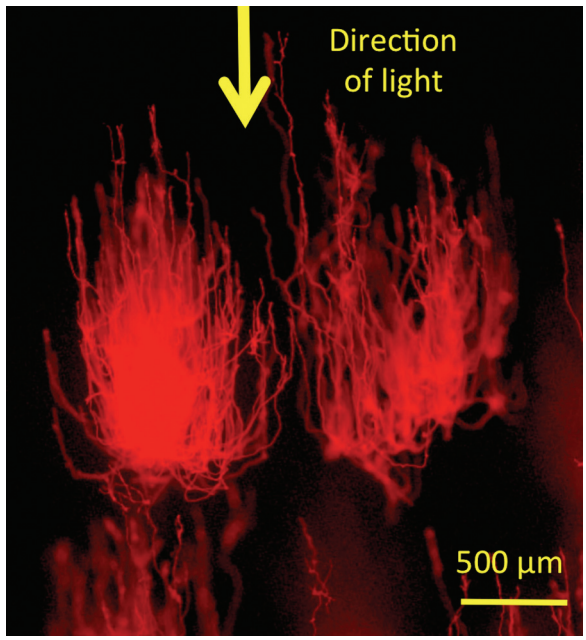
Concerns over the widening Ebola virus outbreak, which is centered in West Africa, took center stage during a Global Health Security Agenda Summit, held at the White House in September. "We have to change our mindsets and start thinking about biological threats as the security threats that they are—in addition to being humanitarian threats and economic threats," President Obama said during the summit. "We have to bring the same level of commitment and focus to these challenges as we do when meeting around more traditional security issues." Regarding the ongoing outbreak in West Africa, he added, "We're going to keep working to get new technologies to hospitals and health workers who need it so they can diagnose patients quickly and do more to save lives at the earliest stages of disease." As of early November, officials reported a total of 13,268 cases of Ebola, 4,960 of which proved fatal.

which RSV impairs immune responses significantly correlates with disease severity and length of hospitalization, he says.

Functional fingerprints show that *M. tuberculosis* suppresses T-cell receptor signaling and interferon production, according to Levin. "TB causes temporary acquired immune deficiency of the precise mechanisms required to contain the pathogen," he says. In yet another example involving *Salmonella typhii* infections, it appears that inflammatory and antibody responses are associated with clinical disease—more than mere exposure to the pathogen, according to Christoph Blohmke of the University of Oxford in Oxford, England.

Systems biology also helps to predict vaccine efficacy, says Helder Nakaya of Sao Paulo University in Sao Paulo, Brazil. Early innate immune system "signatures predict the immunogenicity of vaccines, and... novel mechanisms of immune regulation," he says. Vaccines to protect against meningococcus bacterial infections or the yellow fever and influenza viruses each have unique predictive profiles, he finds. These patterns could guide dosing or booster regimens, or point to strategies for improving the immunogenicity of vaccines, he says. For example, stimulating toll-like receptor 5 improves overall host responses to both influenza and polio vaccines, he adds, suggesting yet another approach for fine-tuning vaccines.

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



Fluorescence image of microcolonies of the *Leptolyngbya* sp. strain JSC-1 of cyanobacteria cells (JSC-1) collected from a hot spring near Yellowstone National Park. The image shows that the cells grow toward the light when light is provided only from above. (Image: Igor I. Brown, a research fellow at NASA JSC.)

RESEARCH ADVANCES

Some Cyanobacteria Acclimate To Using Far-Red Light for Photosynthesis

Barry E. DiGregorio

The cyanobacterium *Leptolyngbya* sp. strain JSC-1, isolated from a microbial mat from La Duke Hot Springs in Montana, not only can grow under far-red light but its photosynthetic apparatus also becomes more efficient at harvesting light energy under these ordinarily unproductive conditions, according to a team of microbiologists led by Donald Bryant of The Pennsylvania State University in University Park and collaborators from the University of California at Davis. They call this phenomenon far-red light photoacclimation (FaRLiP) and speculate that it is widespread globally and important in environments enriched in such light. Details appear in the 12 September 2014 *Science* (doi10.1123/science.1256963).

When shifted from growth under white to far-red light, gene expression involving about 40% of the genome changes by more than twofold, with about 900 genes upregulated and another 2,000 downregulated, according to Bryant and his collaborators. The cyanobacteria replace 17 proteins in three major light-using complexes while also making two new chlorophyll pigments that can capture the far-red light. The cells also use accessory pigments called bilins in new ways. A 21-gene cluster, which includes a phytochrome that is responsive to far-red light and also two response regulators, appears to control expression of some of those several thousand genes.

Leptolyngbya sp. strain JSC-1 "changes the core components of the three major photosynthetic complexes,

MINITOPIC

Micropia, a Museum about Microorganisms, Opens in Amsterdam

Queen Máxima of the Netherlands led the opening ceremonies in Amsterdam last September at Micropia, "the world's first museum of microorganisms, the invisible and most powerful life forms on Earth." The new building looms as a black box on the Artisplein, a square that is situated next to the Artis Royal Zoo, whose main attractions of course are visible without magnification. Meanwhile, Micropia is meant to inspire greater interest from the general public in microorganisms, and to serve a more general purpose by being an active "link between the general public and science," reflecting the "increasing importance of biotechnology and life sciences," museum officials note. The museum is open daily. For more information about the museum, see http://www.micropia.nl/en/about-us/how-micropia-came-about/.

so one ends up with a very differentiated cell that is then capable of growing in far-red light," Bryant says. "The organism is better than other cyanobacterial strains at producing oxygen in far-red light and, in fact, it is even better than the same cells grown under other light conditions. Cells grown in far-red light produce 40% more oxygen when assayed in far-red light than cells grown in red light."

Bryant and his collaborators recently identified five other strains that, like strain JSC-1, are also capable of FaRLiP. "A few are soil organisms and some others come from hot spring mats as well," he says. "FaRLiP is likely to be driving a lot of terrestrial photosynthesis that otherwise would not be happening because of poor light penetration. All of the organisms to date that can do this also fix nitrogen. . . . We think this will be a globally important process."

"The retention of a set of paralogous genes for the three major light-utilizing complexes in the genome, their differential expression, and biosynthesis of the complexes illustrates the extent to which photosynthetic organisms will go to capture solar photons and compete for photochemically active radiation," says Charles Dismukes from Rutgers University of New Brunswick, N. J., referring to genes encoding proteins with similar function that likely arose via gene duplications. "This work highlights new possibilities that may be applicable to terrestrial crops to achieve improved performance."

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

NEW IN ASM JOURNALS

Microfluidics-Based Assay Identifies, Quantifies Viruses in Water Samples

David C. Holzman

By taking a microfluidics-based approach, a PCR assay was recently retailored for use in identifying and quantifying viruses in water samples, according to Satoshi Ishii of Hokkaido University in Sapporo, Japan, and his collaborators. "If we can quantify viral pathogens in hours, we can stop water distribution and disinfect drinking water before disease outbreaks occur," he says. Details appeared 26 September 2014 in *Applied and Environmental Microbiology* (doi: 10.1128/AEM.02578-14).

Traditionally, water treatment utilities and food companies rely on measurements of fecal or total bacteria to assess the presence and abundance of enteric pathogens contaminating food and drinking water supplies. However, Ishii says, these measurements sometimes miss other important pathogens, including viruses, and thus can prove unreliable. Although he and his collaborators first applied their technology to measuring bacterial pathogens, all along they planned to adapt it to measure viral pathogens, he says.

"We performed multiple quantitative PCR in parallel, in nanoliter-volume chambers that are present in high densities on a chip," Ishii continues. Although the technology was developed by other groups and is commercially available, this is the first report of its being used to detect and quantify several viral pathogens at once, he says.

Other methods for simultaneously detecting several microbial pathogens do not provide quantitative information, or are slow and not particularly

MINITOPIC

2014 Nobel in Chemistry Recognizes Super-Resolved Fluorescence Microscopy

The 2014 Nobel Prize in Chemistry is being awarded, ironically enough, to three physicists—Eric Betzig, who works on the Janelia Research Campus of the Howard Hughes Medical Institute in Ashburn, Va., Stefan W. Hell of the Max Planck Institute for Biophysical Chemistry in Göttingen and the German Cancer Research Center in Heidelberg, Germany, and William E. Moerner of Stanford University in Stanford, Calif.—for helping to develop super-resolved fluorescence microscopy, also called nanoscopy, a technology that greatly benefits research in biology. The 2014 award explicitly recognizes the following related but separate developments: Hell, for developing stimulated emission depletion microscopy, and Betzig and Moerner for separately developing the foundation for single-molecule microscopy. These developments enable biologists to peer into single microbial or other living cells with a finer resolution than the once widely accepted theoretical limit of 0.2 μm.

accurate, according to Ishii. "Our paper is the first to provide quantitative information on multiple pathogens, as accurate as those obtained by conventional qPCR, for many samples— up to 92 per run," he says. The leading competitor assay takes 20 hours, whereas the new microfluidics-based method yields results within 5 hours.

The assay covers a wide range of viruses, including adenovirus types 40 and 41, Aichi virus, astroviruses, enteroviruses, noroviruses, members of the rotavirus group, and the hepatitis A and E viruses. In one set of experiments, the investigators collected contaminated water samples downstream from a wastewater treatment plant along the Motsukisamu River to validate the new assay system under conditions in which the assay can be expected to find use, according to Ishii. "By using the method we developed, we quantitatively detected norovirus genogroups I and II and rotavirus," says Ishii. "Other viruses were below the detection limit. We obtained similar results using conventional qPCR."

The microfluidics-based assay "has an exquisite sensitivity and enables the simultaneous detection of a broad spectrum of viruses," says Albert Bosch of the University of in Barcelona, Spain. "On the con side, it is awfully expensive."

The cost of the assay equipment is $250,000, compared with $30,000–50,000 for a standard qPCR instrument, and the microfluidics chip, designed for one-time use, is $900 per unit, according to Ishii. However, the cost per assay can run as low as $0.10, compared to $0.40 for conventional qPCR, he says. Despite those inherent costs, however, the new assay "could both speed our analysis and reduce associated costs," points out Sudhir Murthy, who is Innovations Chief for the District of Columbia Water and Sewer Authority in Washington, D.C., referring to routine testing done at the DC water treatment plant.

David C. Holzman is the Microbe *Journal Highlights Editor.*

NEW IN ASM JOURNALS

Enterotoxigenic *E. coli* Worldwide Are Closely Related: Portent of Success for Vaccine Development

Enterotoxigenic *E. coli* (ETEC) infect 400 million people annually, or 5.3% of the world's population, killing 400,000. While ETEC were thought to vary widely from place to place, Åsa Sjöling, now of the Karolinska Institutet, Stockholm, Sweden, and collaborators of the University of Gothenburg, Sweden, and the Sanger Institute, Cambridge, UK, find that the two most potent toxins, LT1 and LT2, have changed little, but spread globally over the 30 years for which the investigators have isolates. That, says Sjöling, bodes well for a vaccine developed by the University of Gothenburg (where Sjöling did this work), which he expects "will be protective and useful globally since this vaccine is based on the toxin types and colonization factors we found to be most successful worldwide."

(E. Joffre, A. von Mentzer, M. A. El Ghany, N. Oezguen, T. Savidge, G. Dougan, A.-M. Svennerholm, and Å. Sjöling. 2014. Allele variants of enterotoxigenic Escherichia coli heat labile toxin are globally transmitted and associated with colonization factors. J. Bacteriol. Online ahead of print 10 November 2014 **(DOI?))**

NEW IN ASM JOURNALS

Salivary Mucins Play Active Role To Fight Cavities

A variety of mucins have been shown protective against certain pathogens, and defects therein have correlated with conditions such as asthma, and ulcerative colitis. Now Erica Shapiro Frenkel of Harvard University and Katharina Ribbeck of Massachusetts Institute of Technology find that salivary mucins, key components of mucus, actively protect the teeth from the cariogenic bacterium *Streptococcus mutans*. *S. mutans* attaches to teeth using sticky polymers that it produces, eventually forming a biofilm. "We found that salivary mucins don't alter *S. mutans*' growth or lead to bacterial killing over 24 hours," says Frenkel. "Instead, they limit biofilm formation by keeping *S. mutans* suspended in the liquid medium. This is particularly significant for *S. mutans* because it only causes cavities when it is attached, or in a biofilm on the tooth's surface." The research suggests that bolstering native defenses might be a better way to fight dental caries than relying on exogenous materials, such as sealants and fluoride treatment, says Frenkel. Rather than simply a catchall filter for particles, "mucus is a sophisticated bioactive material with powerful abilities to manipulate microbial behavior," says Ribbeck.

(Frenkel, E. S., and K. Ribbeck. 2014. Salivary mucins protect surfaces from colonization by cariogenic bacteria. Appl. Environ. Microbiol. Online ahead of print 24 October 2014; doi: 10.1128/AEM.02573-14.)

NEW IN ASM JOURNALS

Rapid Influenza Diagnostic Testing Reliable for Detecting Outbreaks

Timely detection of influenza in outbreak settings is key for outbreak prevention and control. Now, Adriana Peci of Public Health Ontario, Toronto, Canada, et al. show that rapid influenza diagnostic tests (RIDT), which are faster than other methods, are better for detecting outbreaks than for individual influenza cases. This is the first paper to thor-

oughly address performance of RIDT for detecting influenza outbreaks. False-negative results are common, ranging from 40% in individuals with influenza A to 42–60% for influenza B. However, false positives are less than 1% for both influenza A and influenza B. "Health care providers should use positive influenza results obtained by RIDT to guide medical care with confidence," says Peci. However, in individual testing, negatives should be followed by molecular tests such as reverse transcription polymerase chain reaction (RT-PCR), says Peci. Other findings include that RIDT detected influenza better in children and in the elderly than in nonelderly adults. The tests' performance did not vary with the amount of circulating influenza viruses, indicating that it is a useful test at any time during, or even outside of the normal flu season. The team compared two forms of RIDT to RT-PCR.

(A. Peci, A.-L. Winter, E.-C. King, J. Blair, and J. B. Gubbay. 2014. J. Clin. Microbiol. Online ahead of print 15 October 2014; doi:10.1128/JCM.02024-14.)

NEW IN ASM JOURNALS

Mussels on California Coast Contaminated with *Giardia* Transmitted from Land-Based Sources

The pathogen *Giardia duodenalis* is present in mussels from freshwater runoff sites and from areas where California sea lions lounge along coastal California, according University of California, Davis investigators. One of the *G. duodenalis* strains found is known to infect humans; the two others occur mostly in dogs and other canids. These findings imply a "potential public health risk from fecally contaminated water or uncooked shellfish," as they demonstrate that pathogens from land-based fauna are being washed into the sea, at least in the case of *Giardia*, where the same genotypes known to infect humans and canids were found in the mussels, says corresponding author Woutrina Smith. The question is still open in the case of *Cryptosporidium*, as oocysts with the correct appearance were detected in mussels via microscopy, but genotypes were not confirmed. Smith says the research reaffirms the usefulness of testing filter-feeding shellfish, that can process 2 liters of water per hour, thus concentrating pathogens in aquatic environments.

(A. D. Adell, W. A. Smith, K. Shapiro, A. Melli, and P. A. Conrad. 2014. Molecular epidemiology of Cryptosporidium *spp. and* Giardia *spp. in mussels (*Mytilus californianus*) and California sea lions (*Zalophus californianus*) from Central California. Appl. Environ. Microbiol.* **80:**24 7732–7740. Online ahead of print 3 October 2014; doi: 10.1128/AEM.02922-14.)

NEW IN ASM JOURNALS

Host Microbiota Influence Development: Another Example

Animals develop in the presence of complex microbial communities, and early host responses to these microbes can influence key aspects of development, such as maturation of the immune system, in ways that impact adult physiology. Ye Yang of the University of Oregon, Eugene, et al. previously showed that the zebrafish intestinal alkaline phosphatase (ALPI) gene alpi.1 was induced by gram-negative bacteria-derived lipopolysaccharide (LPS), a process dependent on myeloid differentiation primary response gene (88) (MYD88), and functioned to detoxify LPS and prevent excessive host inflammatory responses to commensal microbiota in the newly colonized intestine. Now they show that among the mouse ALPI genes, Akp3 is specifically upregulated by the microbiota, but through a mechanism independent of LPS or MYD88. "We showed that disruption of Akp3 did not significantly affect intestinal inflammatory responses to commensal microbiota or animal susceptibility to *Yersinia* pseudotuberculosis infection," says Ye. "However, we found that Akp3$^{-/-}$ mice acquired LPS tolerance during post-weaning development, suggesting that Akp3 plays an important role in immune education. Finally, we demonstrated that inhibiting LPS sensing with a mutation in CD14 abrogated the accelerated weight gain in Akp3$^{-/-}$ mice receiving a high-fat diet, suggesting that the weight gain is caused by excessive LPS in Akp3$^{-/-}$ mice."

(Y. Yang, J. L. Millán, J. Mecsas, and K. Guillemin. 2014. Intestinal alkaline phosphatase deficiency leads to lipopolysaccharide desensitization and faster weight gain. Infect. Immun. Online ahead of print 27 October 2014; doi:10.1128/IAI.02520-14.)