ASM GENERAL MEETING

Studies Link Gut Inflammation, Obesity, Diabetes to Microbiome

Shannon Weiman

Specific bacterial species within the gut can influence physiology, including conditions and diseases such as inflammation, obesity, metabolic syndrome, and type 2 diabetes—but how? One key factor is gut barrier functions that keep bacteria safely within the gut in healthy individuals, but apparently fail in ways that can prove harmful to the host, according to several researchers who spoke during several sessions of the 2014 ASM General Meeting in Boston last May.

Mucus that lines the intestine is an important component of the gut barrier, keeping bacteria away from the surface of gastrointestinal (GI) epithelial cells, according to Andrew Gewirtz of Georgia State University in Atlanta. In mice with metabolic syndrome, a cluster of symptoms that includes obesity, fat mass development, and fasting hyperglycemia without affecting food intake,” he says. The levels of emulsifiers in some foods are 10 times the dose that Gewirtz finds causes metabolic syndrome in mice, suggesting that these food additives could be contributing to recent increases in obesity and type 2 diabetes in humans, he says.

Specific bacterial species that promote gut barrier functions can prevent or reverse such changes, says Patrice D. Cani of the Université catholique de Louvain in Brussels, Belgium. For example, Akkermansia muciniphila bacteria in the gut increase the number of host goblet cells, increasing the thickness of the mucosal barrier while also increasing expression of RegIIIγ, an antimicrobial peptide that helps to keep other bacteria from entering this zone. “A. muciniphila may represent 3–5% of the microbial community in healthy subjects, and its abundance inversely correlates with body weight and type 2 diabetes in mice and humans,” he says. Prebiotic agents such as oligofructose and gastric bypass surgery can increase the population of this bacterial species. “Restoration of the physiological abundance of A. muciniphila reduced diet-induced body weight gain, fat mass development, and fasting hyperglycemia without affecting food intake,” he says.

Methanogens also protect against obesity and metabolic syndrome, according to Ruth Ley of Cornell University in Ithaca, N.Y. These methane-producing bacteria are enriched in the microbiomes of lean people, while missing among the obese, she says. In mice, methanogens confer less weight gain and higher short-chain fatty acid content in stool, representing food energy that the host does not use. However, instead of mediating these effects directly, the methanogens make the gut hospitable for gram-negative Christensenella minuta, which remain after methanogens are lost to mediate long-term improvements in metabolic syndrome, she says. This species is over-represented in lean humans, she points out.

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

RESEARCH ADVANCES

Light-Harvesting Proteins in Algae May Be Part of Coherent Quantum Process

Barry DiGregorio

The light-capturing proteins from several cryptophyte algae oscillate between two quaternary structures, called open and closed, that act like an on-off switch, according to Paul Curmi of the University of New South Wales in Sydney, Australia, Gregory Scholes of Princeton University in Princeton, N.J., and their collaborators in Canada, Italy, and Germany. Their findings could mean that some steps in photosynthesis involve quantum coherence (QC), reinforcing expectations among biophysicists that “quantum processes play a nontrivial role in biology.” Details appeared 1 July 2014 in the Proceedings of the National Academy of Sciences (doi:10.1073/pnas.1402538111).

The soluble light-harvesting phycobiliproteins (PBPs) from cryptophyte algae are the focus of Curmi’s research. These proteins act as antennae, absorbing light energy that is delivered to chlorophyll, driving photosynthesis in these cells. Each PBP is a dimer of αβ subunits in which the structure of the αβ monomer is conserved. However, those subunits can assume “two dramatically distinct quaternary confor-
mations,” Curmi and his collaborators note. The second of the two confor-
mations is attributed to steric effects from an aspartic acid residue being inserted into the protein. That change disrupts the quantum coherence of the protein complex, affecting the mechanism for harvesting light, Curmi says.

“Some of these cryptophytes make light harvesting proteins where the energy absorbed from the sun is coher-
ently shared across the protein—the closed structures,” says Scholes of Princeton University. “What is re-
markable is the discovery that a whole genus of the algae, however, changed the structure of that light-harvesting protein to switch off that coherent de-
localization.” It is as if these microorga-

nisms “care about the use of coherence in light harvesting,” he adds. “Coherence matters, not because of special properties of coherence neces-
sarily, but because it is unavoidable when energy transfer is fast!”

“The timescale of the coherence is about 0.5 picoseconds, which is about 50 times longer than anyone expected,” Curmi says. “The timescale for energy transfer from the LH protein to the photosynthetic reaction center is about a picosecond. So, it seems coincidental that an unexpected quantum mechan-
ics effect is on the same timescale as a biological process. The assumption that is being made is that quantum co-
herence is therefore relevant to energy transfer. . . . People are making the as-
sumption that QC is accelerating the passage of energy from light-harvest-
ing protein to RC. This has yet to be shown.”

“This work raises many questions,” says Joseph Miller at the American University of the Caribbean School of Medicine on the Island of St. Maarten. “Undoubtedly, there is a best path which would be optimal for maximum photosynthetic efficiency. But how can such a state be ‘chosen’? The most im-
portant issue is whether this coupling is important enough to be selected for.”

Curmi agrees. For example, how does quantum coherence enable crypt-
ophytes to live under low-light situations? “What it does to cryptophyte bi-
ology is exactly what needs to be determined in future studies,” he says. “We need to figure out what QC does by comparing cryptophytes that either have or do not have coherence in their light-harvesting proteins.”

Ed Royce (R-CA), Committee Chair-
man: What is different about this out-
break? Why is it so virulent? Has there been a change in the epidemiology of the virus? If not, is it spreading because affected communities don’t have the necessary information or capacity to deal with it? If it is a capacity issue, what can the international community do to help? What measures have the governments of Guinea, Liberia, and Sierra Leone put in place to contain the outbreak? What more could they do? What is the role of the WHO, donors, and the United States Government?

I would like to get better clarity on how the embassies are communicating with American citizens in Liberia, Guinea, and Sierra Leone. We will hear today from two organizations that have

A recent colloquium report from the American Academy of Microbiology (AAM), “Viruses throughout Life & Time: Friends, Foes, Change Agents,” paints a nuanced picture of viruses, explaining that they are far more than mere agents of disease. “Vi-
ruses participate in essential Earth processes and influence all life forms on the planet, from contributing to biogeochemical cycles, shaping the atmospheric composition, and driving major speciation events,” says Marilyn Roossinck of Pennsylvania State University, a member of the steering committee that helped to organize the colloquium. “It is very important to understand the real world of viruses, as this can inform our basic understanding of life and its origins, as well as major Earth phenomena like carbon cycling.”

The report, which was released in July, is based on the deliberation of experts who met in San Francisco, Calif., a year earlier (see: http://
the U.S. government, the governments of Liberia, Sierra Leone, and Guinea, and the great work Doctors Without Borders and the many health professionals from throughout the world who are doing everything they can to help people who have contracted this awful disease. It is in America’s and the world’s interest to assist in this crisis and continue to support nations as they work to develop and strengthen their health care systems. Health care is a human right, we must ensure that countries have the ability to address this outbreak and prevent future health epidemics from occurring.

[I introduced] legislation that calls on the international community and all nations to immediately provide additional resources and services to develop the capacity of affected nations to address current and future public health crises.

Tom Frieden, Director, CDC: To stop an Ebola outbreak, we must focus on three core activities: find active cases, respond appropriately, and prevent future cases. The use of real-time diagnostics is extremely important to identify new cases. We must support the strengthening of health systems and assist in training health care providers. Once active cases have been identified, we must support patient care in treatment centers, prevent further transmission through proper infection control practices, and protect health care workers. Epidemiologists must identify contacts of infected patients and follow up with them every day for 21 days, initiating testing and isolation if symptoms emerge.

While we do know how to stop Ebola through meticulous case finding, isolation, and contact tracing, there is currently no cure or vaccine for Ebola. We need to strengthen the global response, which requires close collaboration with the WHO and additional assistance from our international partners.

Ariel Pablos-Mendez, USAID: The current total USAID funding dedicated to the Ebola response in West Africa is $14.55 million since March 2014, when the outbreak was first reported. In partnership with the WHO and UNICEF, we provided an initial $2.1 million to support the deployment of more than 30 technical experts, provide operational support for response efforts, including 35,000 sets of personal protective equipment and supplies and to distribute information on Ebola virus to the general public and health workers. This equipment provides critical protection for those working on the frontlines of pandemic outbreaks – preventing human exposure to highly pathogenic viruses and other emerging infectious diseases by limiting the risk of animal-to-human and human-to-human infections during outbreak investigations and response, human case detection and treatment, as well as other activities. The funding to the WHO builds on a $1 million annual investment that USAID has made since

MINITOPIC
New View on How Numbers of Endogenous Retroviruses Affect Cancer

Larger animals have edited out potential cancer-causing endogenous retroviruses (ERVs) from their genomes, possibly accounting for why such larger animals have lower rates of cancer than do smaller animals, according to Aris Katzourakis of Oxford University in Oxford, United Kingdom, and his collaborators. For example, mice have 3,331 ERVs, humans 348 ERVs, and dolphins only 55 ERVs, they find. “This is the first time that anyone has shown that having a large number of ERVs in your genome must be harmful — otherwise larger animals wouldn’t have evolved ways of limiting their numbers,” Katzourakis says. “As animals get bigger, the number of cells increases and there are more opportunities for things to go wrong, so there is an evolutionary pressure for larger animals to reduce the number of ERVs. We think this is linked to . . . how mammals have evolved to combat this risk.” Details appeared 17 July 2014 in PLOS Pathogens (doi: 10.1371/journal.ppat.1004214).
MINITOPIC

**FDA To Expand Oversight over Diagnostic Testing, Including LDTs**

Officials of the Food and Drug Administration (FDA) in July announced steps “to ensure that certain tests used by health care professionals to help diagnose and treat patients provide accurate, consistent, and reliable results.” As part of this effort, FDA plans to extend oversight to include laboratory-developed tests (LDTs), which are designed, manufactured, and used within a single laboratory—a category of diagnostic procedures that more typically falls under jurisdiction of the Centers for Medicare & Medicaid Services (CMS) under the mandate of the Clinical Laboratory Improvement Amendments (CLIA). A major focus of this new activity from FDA is the ongoing development of “companion diagnostics,” that is, tests that are paired with specific treatments. The agency says it will continue “to exercise enforcement discretion for low-risk LDTs, LDTs for rare diseases and, under certain circumstances, LDTs for which there is no FDA-approved or cleared test.”

The DART, comprising team members in Monrovia, Liberia, and Conakry, Guinea, will coordinate planning, operations, logistics, administrative issues, and other critical areas of the interagency response. CDC will staff public health and medical response positions on the DART. This week, USAID announced an additional $12.45 million of Global Health and International Disaster Assistance funding to support efforts by CDC, the WHO, and NGOs to ramp up the Ebola response. USAID also has an additional 70,000 sets of personal protective equipment already in central and southern Africa that can be deployed to West Africa for use in the Ebola outbreak.

**Ken Isaacs, Samaritan’s Purse, Boone, N.C.:** Samaritan’s Purse is an international nongovernment organization with 38 years of experience dedicated to humanitarian relief. The Ebola outbreak has had a profound impact on our organization. We had hoped not to become involved in direct clinical care but as the disease resurged in June, we had no choice.

We believe the reported numbers only show 25–50% of the cases. The ministries of Health in Guinea, Liberia, and Sierra Leone do not have the capacity to handle these crises. If a mechanism is not found to create an acceptable paradigm for the international community to become directly involved, then the world will be relaying the containment of this disease that threatens Africa and other countries to three of the poorest nations in the world.

Samaritan’s Purse and [Doctors Without Borders] continue to be the two primary caregivers... That the world would allow two relief agencies to shoulder this burden along with overwhelmed Ministries of Health in these countries testifies to the lack of serious attention the epidemic was given.

The global impact of Ebola has yet to be fully realized. In the developing world, it has the potential to destabilize entire countries while creating widespread and even regional insecurity. It will have a devastating effect on transportation hubs, economies, health care systems, and governments.

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

NEW IN ASM JOURNALS

**E. coli More Adept at Resisting Radiation Than Was Thought**

David C. Holzman

*Escherichia coli* cells carry 46 genes—many previously unrecognized—that enable it to withstand exceptionally high levels of ionizing radiation, according to Michael M. Cox of the University of Wisconsin and his collaborators. These bacteria thus encode “new pathways of cellular self-repair, including DNA pathways that [if present] in humans may help protect us from cancer,” he says. Details appear in the July 2014 *Journal of Bacteriology* (doi:10.1128 JB.01589-14).

High doses of ionizing radiation can be deadly not only to humans, plants, and animals, but also to microbial cells. “Most of the damage occurs because ionizing radiation produces reactive oxygen species in water, and these molecules cause oxidative damage to anything—cellular proteins, DNA, membranes—that they come in contact with,” Cox says.

 Nonetheless, some types of bacteria, notably *Deinococcus radiodurans*, are highly resistant to high levels of radiation. *E. coli*, which is not known for its resistance to radiation, can adapt to it under special circumstances, according to Cox and collaborators. They developed resistant strains via directed evolution, subjecting cells of *E. coli* to 20 cycles of gradually increasing levels of radiation—enough to kill 99% of the bacteria at each round—and harvesting the successive survivors.

“In a nutshell, three genes account for most of the new phenotype,” says Cox. However, other genes contribute to that phenotype, too, he adds. “Presumably, there were genes that were not altered in the evolution experiment, but yet were still critical to recovery from the damage inflicted by radiation. The new work is a screen to identify those genes.” Among the 46 genes, “nearly
“To follow up on that screening, Wright and his group tested AMA and meropenem on 229 strains of gram-negative pathogens. In a preliminary screening assay, AMA, which was extracted from the fungus Aspergillus versicolor, boosts the antibacterial activity of the antibiotic meropenem against several strains of Escherichia coli that produce NDM-1, they found.

The capacity of D. radiodurans to resist radiation appears ancillary to its resistance to dehydration, notes Richard Fishele of the Ohio State University in Columbus. Unlike E. coli, D. radiodurans occupies a niche where desiccation is a constant hazard. This causes massive chromosome breakage, he says. Organisms have many ways to resist or survive dehydration, including encapsulating themselves. D. radiodurans does so by ensuring that “it has multiple copies of its genome, so that no matter how badly it is thrashed, it can always reassemble it.” Some of the relevant genes are conserved, but E. coli, he says, is far less efficient at recombination than is D. radiodurans.

David C. Holtzman is the Microbe Journal Highlights Editor.
animals were treated with either AMA or meropenem alone, they died. Details appeared in the 26 June 2014 Nature (doi: 10.1038/nature13445).

These findings suggest that “natural products are a good place to find adjuvants that block bacterial resistance mechanisms and extend the life of antibiotics,” Wright says. He and his collaborators are investigating the potential of AMA for use as a co-drug, similar to clavulanic acid, which is combined with amoxicillin to overcome resistance to beta-lactam antibiotics, “Metallo-beta-lactamases destroy our best beta-lactam antibiotics and help life-threatening pathogens to spread,” says microbiologist Kim Lewis at Northeastern University in Boston, Mass. “We do not have an inhibitor against this effective resistance mechanism.” An advantage of AMA is its low molecular weight, which enables it to cross the outer membrane of gram-negative pathogens, he adds. “This formidable barrier makes it very difficult to develop drugs against this group of bacteria, making AMA a welcome addition to the arsenal of much-needed drug leads.”

**NEW IN ASM JOURNALS**

**Strategic Self-Sabotage? MRSA Inhibits Its Own Growth**

*Staphylococcus aureus*, which benignly inhabits ~30% of humanity, can turn opportunistic, in which form it represents a major, growing threat to public health on par with HIV and tuberculosis.

David E. Heinrichs, of the University of Western Ontario, London, et al., show that an enzyme, SAL2, produced by all of 63 diverse *S. aureus* strains tested, snips innocuous triglycerides in sebum secretions into compounds—fatty acids—that are toxic to itself. The universality of this action within the species suggests that it must be helping the bacteria to colonize and persist on human skin, but in the study, mutant *S. aureus* that failed to produce SAL2 grew well in the presence of triglycerides, while wild-type *S. aureus* did not. The investigators hint at the difficulty of determining how it works when they write that a variety of models will be needed to examine persistence and virulence not only on the skin, but in abscesses and in bacteremia.


**NEW IN ASM JOURNALS**

**Influenza A Potentiates Pneumococcal Co-Infection: New Details Emerge**

The high mortality in the 1918 influenza pandemic resulted not from influenza alone, but from a synergism between that virus and the respiratory disease bacterium, *Streptococcus pneumoniae*. Normally, different pneumococci specialize—some in colonizing the host, others in spreading within the host. Now W. Edward Swords of Wake Forest University, Winston-Salem, N.C., et al. show that in the presence of influenza, pneumococci become aggressive generalists. “In the presence of influenza, opaque variants [“spreaders”] can readily colonize the nasopharynx, and transparent variants [colonizers] can persist in the ear,” says Swords. “This indicates that the host environments are more permissive for infection by the entire bacterial population.” Furthermore, recent research had shown that influenza interferes with innate immunity in a way that abets the pneumococci. In the new study, that interference manifested as increased inflammatory responses at the mucosal surface in the influenza-infected mice.


**NEW IN ASM JOURNALS**

**Polyester Clothes Stink After Exercise; Cotton, Not So Much**

One might cynically suggest that science has better things to do than to determine which fabric smells least offensive after a good workout. But some are so sorely afflicted with body odor that their lives are severely constrained, says Chris Callewaert, of Ghent University, Belgium, who runs the website drarmpit.com. His patients’ suffering drove him to begin investigating the problem generally. In the current research, a trained odor panel sniffed
Bacteria boost the immune system’s first line of defense against bacterial infection,” says Clarke. “Production of reactive oxygen molecules by these bacteria can actively shape the physiology of their host,” says Thomas B. Clarke, of Imperial College London, United Kingdom. Now Clarke shows that commensal bacteria boost the immune system’s ability to kill Klebsiella pneumoniae, a major pathogen of the human lung. “Alveolar macrophages are the lungs’ first line of defense against bacterial infection,” says Clarke. “Production of reactive oxygen molecules by these cells was enhanced by signals from commensal bacteria.” Specifically, when the antibacterial activity of the alveolar macrophages was compromised by the absence of commensal bacteria, Clarke was able to restore this activity, including production of reactive oxygen species, by administering bacterial NLR ligands via the gastrointestinal tract. (T. B. Clarke. 2014. Early innate immunity to bacterial infection in the lung is regulated systemically by the commensal microbiota via NLR ligands. Infect. Immun. Online ahead of print 25 August 2014; doi:10.1128/IAI.01856-14.)

NEW IN ASM JOURNALS
Commensal Bacteria Help Orchestrate Immune Response in Lung

The importance of commensal bacteria has been well-demonstrated. “What has been missing is a mechanistic understanding of how these bacteria can actively shape the physiology of their host,” says Thomas B. Clarke, of Imperial College London, United Kingdom. Now Clarke shows that commensal bacteria boost the immune system’s ability to kill Klebsiella pneumoniae, a major pathogen of the human lung. “Alveolar macrophages are the lungs’ first line of defense against bacterial infection,” says Clarke. “Production of reactive oxygen molecules by these cells was enhanced by signals from commensal bacteria.” Specifically, when the antibacterial activity of the alveolar macrophages was compromised by the absence of commensal bacteria, Clarke was able to restore this activity, including production of reactive oxygen species, by administering bacterial NLR ligands via the gastrointestinal tract. (T. B. Clarke. 2014. Early innate immunity to bacterial infection in the lung is regulated systemically by the commensal microbiota via NLR ligands. Infect. Immun. Online ahead of print 25 August 2014; doi:10.1128/IAI.01856-14.)

NEW IN ASM JOURNALS
Common European MRSA Originated in Africa

With increasing levels of community-acquired Staphylococcus aureus (CA-MRSA) reported from most of the Western world, there is great interest in understanding the origin and emergence of these epidemic lineages. Now Marc Stegger of the Statens Serum Institut in Denmark reports that the predominant strain of CA-MRSA in Europe, the Middle East, and northern Africa, CC80, derived from a single sub-Saharan ancestor. Interestingly, they also find that in the transition from a methicillin-sensitive line to a CA-MRSA clone, the bacteria simultaneously acquired two highly specific genetic elements, rendering them resistant both to methicillin and to fusidic acid. Its out-migration from its area of origin probably began in the mid-1980s, due to increased migration from sub-Saharan Africa as people sought improved economic conditions, and to increased European tourism. (M. Stegger, T. Wirth, P. S. Andersen, R.L. Skov, et al. 2014. Origin and evolution of European Community-acquired methicillin-resistant Staphylococcus aureus. 26 August 2014 mBio vol. 5 no. 5; doi:10.1128/mBio.01044-14.)

NEW IN ASM JOURNALS
Batrachochytrium dendrobatidis, has caused more than 200 mass mortality events and an increasing number of extinctions in many parts of the world. The presence or absence of skin defenses predicts whether an amphibian species or population will persist with B. dendrobatidis infection. Despite the fact that immune responses may play a major role in the survival of susceptible amphibians, very little is known about interactions between amphibian immune systems and this fungus within the skin. Now, for the first time, Louise Rollins-Smith and colleagues of Vanderbilt University provide in vivo evidence that B. dendrobatidis is capable of inhibiting local lymphocyte responses in its amphibian host to promote infection. “This adaptation by B. dendrobatidis to evade adaptive immune responses may help to explain how it is such a successful pathogen known to infect over 500 species of amphibians and why amphibians lacking robust innate immune responses are so susceptible to chytridiomycosis,” the investigators conclude. (J. S. Fites, L. K. Reinert, T. M. Chappell, and L. A. Rollins-Smith. 2014. Inhibition of local immune responses by the frog-killing fungus, Batrachochytrium dendrobatidis. Infect. Immun. Online ahead of print 25 August 2014; doi:10.1128/IAI.02231-14.)