MINITOPIC
Yet Another Set of Studies Involving the Gut Microbiota

Efforts to understand how microorganisms in the gut affect the host continue to fill the journals and to be part of the news. Recent examples include:

- By changing the gut microbiota, artificial sweeteners appear to accelerate the development of glucose intolerance in mice and possibly also in humans, according to Eran Elinav and Eran Segal, both of the Weizmann Institute of Science in Rehovot, Israel, and their collaborators. Details appeared 18 September 2014 in Nature (doi:10.1038/nature13793).
- Early exposure of mice to antibiotics leads to lifelong metabolic disturbances, including endowing them with a propensity to become obese, according to Martin Blaser of the New York University Langone Medical Center in New York, N.Y., and his collaborators. Details appeared 14 August 2014 in Cell (doi:10.1016/j.cell.2014.05.052).
- Mice treated with antibiotics to remove most of their intestinal bacteria or raised under sterile conditions have impaired antibody responses to seasonal influenza vaccination, according to Bali Pulendran and colleagues at Emory University in Atlanta, Ga. Details appeared 18 September 2014 in Immunity (doi:10.1016/j.immuni.2014.08.009).
- Fecal microbiota transplantation procedures proved safe for treating inflammatory bowel disease and led to improved symptoms in 70% of patients, according to David Pinn, Lawrence Brandt, and their colleagues at Montefiore Medical Center in New York, N.Y., who presented their findings during the 2014 American Gastroenterological Association James W. Freston Conference, held in Chicago, Ill., last August.
- Microbes of the gastrointestinal tract influence human eating behavior and dietary choices, according to Athena Aktipis at the University of California, San Francisco, and her collaborators. They base their conclusions on a meta-analysis of many other reports, with details appearing in the October 2014 BioEssays (doi:10.1002/bies.201400071).

constant, according to El-Naggar. Additional studies involved video observations of the bacterial membrane, periplasm, cytoplasm, and specific proteins, made possible by limiting the oxygen supply to the bacterial cells, according to his graduate student Sahand Pirbadian, a technique that dates to very early studies of these nanowires, which sprout when oxygen is in short supply.

Although simple in principle, it took a year to develop this experimental setup and to devise conditions under which the bacteria reliably produce nanowires, El-Naggar says. It took another year to analyze what happened to them and to prove that these nanowires consist of bleb extensions of the outer membrane vesicles, rather than pili, with charge transfers that occur along cytochrome proteins in the filaments, he says. Such proteins can act as electron acceptors or electron donors, moving the charge in either direction.

The wiring of S. oneidensis thus differs markedly from what occurs in Geo bacter sulfurreducens, which like S. oneidensis are also gram-negative anaerobes. “The pili of G. sulfurreducens have an intrinsic metallic-like conductivity,” says Derek Lovley of the University of Massachusetts, Amherst. That conductivity “can be attributed to overlapping pi-pi orbitals of aromatic amino acids.” Whether the newly described “wires” of S. oneidensis conduct electricity remains uncertain, according to Lovley.

“Many have argued the same for the Geobacter wires,” says Gemma Reguera of Michigan State University in East Lansing. The next stage of research in both cases would be “to show that they really function as nanowires in vivo, and evaluate their contribution to the cell’s physiology,” she continues. “In my opinion, the evidence to date provides pretty compelling arguments supporting their biological role as electronic conduits, so I remain optimistic.” Moreover, El-Naggar and his collaborators conducted “very elegant experimental approaches, with many visual experiments, including movies and the right controls.”

These two bacteria, S. oneidensis and G. sulfurreducens, carry such different mechanisms “to expand their redox-active surface beyond the confines of the cell envelope so they can access insoluble electron acceptors that would otherwise be out of reach,” Reguera says. “The ability of bacteria to produce electrically conductive filaments could be harnessed for applications in nanotechnology. It is a great time to be an electromicrobiologist.”

David C. Holzman is the Microbe Journal Highlights Editor.

NEW IN ASM JOURNALS
Sweeping Mutant Fitness Tests Help To Annotate Organism-Wide Phenotypes

David C. Holzman

“Innovations in genetic technology have allowed us to measure the contribution of every gene in an organism—specific bacteria, in our case—to its ability to survive in a given condition,” says Adam P. Arkin of Lawrence Berkeley Laboratory, in Berkeley, Calif. Details appeared online in August and in print in the October 2014 Journal of Bacteriology (doi:10.1128/JB.01836-14).
Microbes in Odd Places or with Odd Histories: Some Recent Examples

Perhaps nothing should be surprising about the whereabouts of microbes these days, but these examples seem special and deserve some attention.

- Seals and sea lions apparently carried Mycobacterium tuberculosis to peoples in the Americas some time less than 6,000 years ago, according to Anne Stone of Arizona State University in Tempe, Johannes Krause of the University of Tübingen in Germany, and their collaborators. Details appeared 20 August 2014 in Nature (doi:10.1038/nature13591).

- Overcoming doubts attributed to earlier contamination concerns, there is strong new evidence for a diverse community of microorganisms in a lake some 800 m below the West Antarctic ice sheet, according to Brent Christner of Louisiana State University, Baton Rouge, and many collaborators. Details appeared 20 August 2014 in Nature (doi:10.1038/nature13667).

- The fungus Cryptococcus gattii, responsible for causing sometimes fatal infections in patients with AIDS, seems to grow in several kinds of tree species, including Canary Island pine, Pohutukawa, and American sweetgum, according to Deborah J. Springer of Duke University School of Medicine in Durham, N.C., and her collaborators. Details appeared 21 August 2014 in PLOS Pathogens (doi:10.1371/journal.ppat.1004285).

- Malassezia-like fungi, linked to skin conditions such as dandruff and eczema, also are found in more exotic environments, including coral reefs, arctic soils, and deep-sea vents, according to Anthony Amend at the University of Hawaii at Mānoa and his collaborators. Details appeared 21 August 2014 in PLOS Pathogens (doi:10.1371/journal.ppat.1004277).

“Because our technology is both extremely high throughput and precise, we were able to make these measurements under hundreds of conditions,” Arkin continues. “We were able to find conditions in which nearly every gene in the organism had a relatively specific contribution. This provides a map of how every gene makes an organism more or less fit.” This analytic approach is general and should work for other types of bacteria, he adds.

These phenotype-defining experiments stem from research to understand how “non-model microbes survive in complex natural environments in community with other microbes, and in engineering microbes to live and do work in these same environments,” Arkin says. One major difficulty is that, beyond extensively studied—some might say “tamed”—species such as Escherichia coli, “the quality of information about genetic function declines rapidly,” he says. Mutation-based phylogenetic analysis “is often not even good enough to annotate ubiquitously conserved central metabolism let alone specialized functions that adapt cells to their more realistic environmental niches. So we sought a way of more rapidly annotating genetic function experimentally that could scale at a rate similar to how genome sequencing is scaling.”

Arkin considers the new analytic approach a “compromise,” but one that can prove “powerful” because it “will vastly increase the quality of annotation across the tree of life, and lead to better predictions of organisms’ function and ecology.” He and his collaborators focused on two very much “untamed” microorganisms, Shewanella oneidensis and Zymomonas mobilis, seeking to understand how mutations in hundreds of genes from either one of them affect fitness. S. oneidensis “is an organism famous for its metabolic flexibility and its ability to reduce metals,” Arkin says. “Here we used this technology to better understand genetic determinants of effectiveness of these metabolisms. We also discovered that the programs for expression regulation did not seem to be very correlated with what genes were necessary for growth in diverse conditions.”

As for the alpha-proteobacterium Z. mobilis, which produces ethanol, he and his collaborators found that 89% of assayed genes have a detectible phenotype—the highest result so far in any bacterium—and that 79 fitness experiments sufficed to find phenotypes for most of its genes. Further, 41% of Z. mobilis genes have both a strong phenotype and a similar fitness pattern (cofitness) to another gene, and are therefore good candidates for functional annotation using mutant fitness. Such findings help to establish “a blueprint for the functional annotation of diverse bacteria using mutant fitness,” they note.

“I have been working with the Department of Energy-Joint Genome Institute for years to increase the diversity of available genomes,” comments Jonathan Eisen of the University of California, Davis, who was not involved in this work. “However, for our work to be most useful we need people to study the functions of all the genes in all the diverse taxa.”

One drawback to Arkin’s approach is that it sacrifices depth for breadth, says Barry Bochner, who heads Biolog in Hayward, Calif., a company that specializes in phenotype testing. “A basic question for our field is the relative value of assessing thousands of genes ‘vaguely’ or assessing smaller numbers of genes in great detail,” he adds. “I think the latter approach moves the field ahead more quickly.”