

Coronavirus (COVID-19)

[Patient and Visitor Alerts](#) | [General Information](#) | [Self-Checker](#) | [Donate and Lend Support](#) | [Staff Appreciation](#)

Research

Home > Research > Advancements in Research > Fundamentals > In Depth

fundamentals

Sign Up for Fundamentals

Stay up-to-date with the latest research findings from the Institute for Basic Biomedical Sciences.

Sign Up

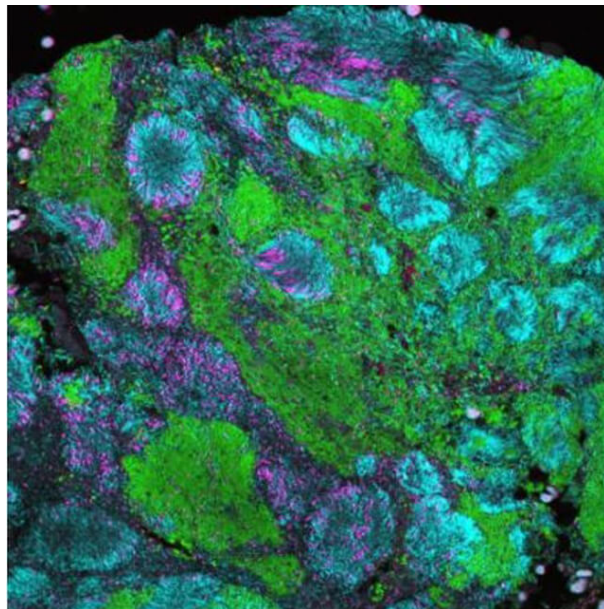
Fundamentals Topics +

IN DEPTH

[More In Depth Articles - \(http://www.hopkinsmedicine.org/research/advancements-in-research/fundamentals/in-depth\)](http://www.hopkinsmedicine.org/research/advancements-in-research/fundamentals/in-depth)

More Advancements in Research

- [Latest in Research - \(https://www.hopkinsmedicine.org/research/advancements-in-research/latest-in-research\)](https://www.hopkinsmedicine.org/research/advancements-in-research/latest-in-research)
- [Science Out of the Box - \(https://www.hopkinsmedicine.org/research/advancements-in-research/out-of-the-box.html\)](https://www.hopkinsmedicine.org/research/advancements-in-research/out-of-the-box.html)



A thick layer of bacteria growing on tumors in the colon. Several different groups of bacteria are present, each represented by a different color.

Source: Dejea C, et al. PNAS 111:18321, 2014.

The Gut: Where Bacteria and Immune System Meet

By Helen Fields

November 2015—By now, it's a familiar fact: Humans have more bacterial cells—a lot more—than human cells. Bacteria live on the skin, in the nose and ears, and, most of all, in the gut.

Until recently, if most people thought about those bacteria at all, we tended to think of them as fairly separate from us. They help with digestion, but otherwise they stay on their side of the intestinal lining, and we stay on our side. But, in fact, there is a lot of interaction between the body's immune system and bacteria in the gut. Researchers at Johns Hopkins are now in the early stages of figuring out how the composition of the gut changes in different diseases, how the body's immune system interacts with these tiny hitchhikers and particularly how that relationship may function in disease.

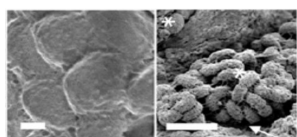
"A huge proportion of your immune system is actually in your GI tract," says Dan Peterson, assistant professor of pathology at the Johns Hopkins University School of Medicine. "The immune system is inside your body, and the bacteria are outside your body." And yet they interact.

For example, certain cells in the lining of the gut spend their lives excreting massive quantities of antibodies into the gut. “That’s what we’re trying to understand—what are the types of antibodies being made, and how is the body trying to control the interaction between ourselves and bacteria on the outside?”

Bacteria and Cancer in the Gut

[Cynthia Sears -](https://www.hopkinsmedicine.org/profiles/results/directory/profile/0002419/cynthia-sears)

(<https://www.hopkinsmedicine.org/profiles/results/directory/profile/0002419/cynthia-sears>), a professor of medicine at Johns Hopkins and member of its Kimmel Cancer Center, studies the role of the microbiome in causing colon cancer in mice and humans. Colon cancer seems to stem from an interaction among the microbiome, the immune system and epithelial cells that line the colon.



The surface of colon tumors with (right) and without (left) layers of bacteria growing on top.

Sears’ lab is using mice to study one kind of human colonic bacteria that may be a bad actor, enterotoxigenic *Bacteroides fragilis* (ETBF). ETBF makes three types of a protein called the *Bacteroides fragilis* toxin (BFT); one of which, BFT2,

has greater carcinogenic potential and is common in humans. The protein sets off a huge array of actions in the epithelial cells that line the colon. In certain mice, it can cause inflammation and cancer of the colon. Sears’ group is now trying to figure out what the receptor is that enables the protein to interact with epithelial cells. Finding that, she says, “may open our eyes to how cancer begins in the colonic epithelial cells.”

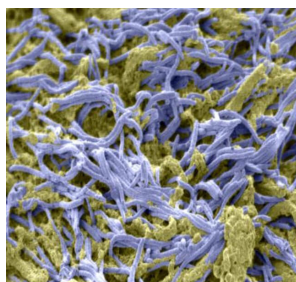
One of the actions set off by ETBF in the colon is called TH17 inflammation. This is largely thought to be useful for fighting off bacteria and fungi, but it can also turn against the body and cause cancer in the colon. Using mice, Sears’ group is trying to understand exactly what the TH17 response does to cells in the colon to promote cancer development.

No one species has been found to always cause colon cancer in humans. Instead, carcinogenesis may have to do with a shift in the ecology of the gut—that is, in the makeup of the bacterial community.

Scientists have suspected since the 1970s that bacteria contribute to colon cancer. But, as sequencing has gotten cheaper, it’s become much easier to ask questions about exactly what kind of role bacteria play in the disease. “Whether they’re the reason it starts or whether they contribute to the growth of tumors over time, I think, is a question that remains to be clearly answered,” Sears says.

From Lung to Belly

Kathryn Winglee is a graduate student in the lab of [redacted], co-director of the Johns Hopkins Center for Tuberculosis Research Laboratory. She has studied the role of the gut microbiome in another disease: tuberculosis. Winglee and Bishai thought the microbiome might provide a faster way to diagnose TB than the current gold-standard test, which takes weeks.



A mass of bacteria (purple) on the surface of colon cancer, mixed with sticky mucus (yellow).

Winglee infected five mice with TB. Then, she collected stool samples once a month until the mice died and analyzed the genetic material they contained.

She found that TB changed the bacterial communities significantly. Soon after infection, the diversity of the gut microbiota dropped off. As time went on, the samples became more diverse, but with different bacteria than were there before the mice got TB.

The TB infections were in the lungs, but these differences showed up in the gut. Winglee and her colleagues think that the immune system is sending a signal about infection from lung to gut, which appears to respond by killing off certain species. Their next step is to figure out what aspects of the immune system are contributing to the massacre.

The Parts Bacteria Play

Peterson works with mouse models of intestinal diseases like inflammatory bowel disease (IBD) and colitis. IBD is thought to be an abnormal immune response to bacteria in the gut. The IBD mice Peterson works with have a defect in the lining of the gut, the barrier that keeps bacteria from interacting with the host.



Peterson works with mouse models of intestinal diseases.

Peterson's group uses sequencing to determine which species live in the gut of a mouse in different disease states. Then, they can introduce particular species of bacteria to germ-free mice to see what effect that one species has and whether any particular species might be triggering an immune response.

For a [study published in May](#) - (<http://www.ncbi.nlm.nih.gov/pubmed/24662098>), Peterson and his colleagues studied the shift in the gut bacteria of mice that developed colitis. When they sequenced the mouse guts, they found that the bacterial species *Lactobacillus johnsonii* was common; it accounted for 30 percent of the bacteria in some of the mice. When mice got colitis, *L. johnsonii* almost doubled. The researchers thought they might have found a problematic bacterial species. They grew *L. johnsonii* in the lab, put them into germ-free mice—and found that, if anything, the mice actually got a little healthier.

This highlights one of the challenges of understanding microbiome sequencing data, Peterson says. “Just because something goes up or goes down doesn’t mean it’s bad or good.

“There are a lot of data right now on these relationships between changes in the microbial community and different diseases,” Peterson says. For example, the [Human Microbiome Project](#) - (<http://commonfund.nih.gov/hmp/overview>) has spent millions of dollars to catalog microbiome communities in people with different diseases. “The next step is the hard step: trying to figure out all that data.”

Read

[Blood Vessels 'Sniff' Gut Microbes to Regulate Blood Pressure](#)

Meet

[Jennifer Pluznick zooms in on the details to understand organisms.](#)

Support Funding

of the Institute for Basic Biomedical Sciences

- (<https://www.hopkinsmedicine.org/support/>)

- (<https://www.hopkinsmedicine.org/support/>)

Related Videos

Jen Pluznick | The Role of Smell Receptors in the Kidney

Jen Pluznick describes the research in her lab: studying olfactory and taste receptors and their role in helping the kidney maintain homeostasis.

YOU MAY ALSO LIKE

[-\(https://www.hopkinsmedicine.org/research/advancements-in-research/fundamentals/in-depth/bacterial-cytoskeleton-may-offer-new-drug-target\)](https://www.hopkinsmedicine.org/research/advancements-in-research/fundamentals/in-depth/bacterial-cytoskeleton-may-offer-new-drug-target) **Bacterial Cytoskeleton May Offer New Drug Target -**

[\(https://www.hopkinsmedicine.org/research/advancements-in-research/fundamentals/in-depth/bacterial-cytoskeleton-may-offer-new-drug-target\)](https://www.hopkinsmedicine.org/research/advancements-in-research/fundamentals/in-depth/bacterial-cytoskeleton-may-offer-new-drug-target)

Despite their ubiquity as research tools, there is still much we don't fully understand about bacteria — such as how they divide. Learning more could point the way to new desperately needed antibiotics.

Sign Up for Fundamentals

Stay up-to-date with the latest research findings from the Institute for Basic Biomedical Sciences.

Sign Up