



Microbiology

Drive out the "bad bugs" to prevent colon cancers

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ABSTRACT

There is a microscopic society living within us. Many of them reside in our gut. In some colon cancers, toxin-producing bacteria invade the mucus and form a sticky biofilm in the cells that line the colon. They upend the whole biology of the system creating a little environment all their own with ill consequences for their hosts.



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There is a microscopic society living within us. Our bodies are home to more than 100 trillion microorganisms, similar to the number of human cells in the body. Many of them reside in our gut. Most of the time, this microsociety—which includes hundreds of species of bacteria—and its human host coexist harmoniously. The "bugs" aid us in digestion, metabolism, and immunity.

With such an overwhelming number of advantages, it may only take the activity of two bugs to shift this harmonious relationship in a way that can promote cancer. Our research focuses on better understanding this process. We studied how bacteria contribute to the development and growth of colon cancer. This is a very important area of investigation because colon cancer is considered a nearly completely preventable cancer if it is detected early - yet the <u>American Cancer Society reports</u> that 50,000 people will die and more than 100,000 new cases will be diagnosed in the U.S. alone this year. Globally, colon cancer rates are rising all over the world. An even more alarming report in the *Journal* of the National Cancer Institute in February 2017 reported that colon cancer rates have increased in younger people, under age 50.

The entire colon is lined with a thick protective layer of mucus, and most bacteria do not make it past this protective barrier. Our research has shown that in some colon cancers, toxin-producing strains of two kinds of common bacteria called <u>Bacteroides fragilis</u> and <u>Escherichia coli</u> invade the mucus and form a sticky biofilm in the mucus that covers the cells that





line the colon. They upend the whole biology of the system, creating a little environment all their own— complete with nutrients and everything the bacteria need to survive—causing ongoing inflammation and then DNA damage that can set cancer development in motion.

At least in some people, these bacteria appear to be picked up early in life in children less than 5-years old, sometimes without symptoms, but the bacteria can live and grow in people of all ages. We do not know precisely how they are transmitted, but person-to-person, animal-to-person, food and water are all possibilities.

To blunt the burden of colon cancer, new approaches to prevention must be developed. We think that targeting specific bacteria by administering drugs or vaccines to prevent the bacteria from living and growing in a person's colon (and potentially even probiotics to chase the bugs from the colon) could be explored to interrupt the cancer-promoting process. Our ongoing research is looking at 2,000 people to determine if colon biofilms and/or specific bacteria can be directly linked to early tumor formation. If so, we could use these drugs or vaccines to block the bacteria or their toxins in the colon or prevent exposure to the bacteria.

We found these two types of bacteria in patients with an inherited form of colon cancer and, along with other researchers, also in people who develop colon cancer with no connection to heredity (called 'sporadic colon cancer'). We have also uncovered a possible mechanism behind how one of these species spurs a type of immune response that promotes—rather than inhibits—cancer.

The coexistence of these two bacteria, how they damage DNA and the immune reaction creates the 'perfect storm' to drive colon cancer development. Both types of bugs are found to commonly live and grow in young children worldwide, potentially contributing to the rise in colon cancer rates among younger people.

The research suggests so far that only a few types of bugs of the 500 to 1,000 possibilities in the colon may be early key triggers for pushing the development of colon cancer. Our studies are still early, but we believe it may be possible to slow colon tumor development in people predisposed to colon cancer through inherited syndromes as well as those who develop it sporadically by getting rid of these bacteria in their colons.