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DNA of good bacteria drives intestinal response to infection

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A new study shows that the DNA of so-called "good bacteria" that normally live in the intestines may help defend the body against infection.

The findings, available Oct. 2 online in the journal *Immunity*, are reported by Yasmine Belkaid, Ph.D., and her colleagues in the Laboratory of Parasitic Diseases at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

A person normally has 300 to 500 species of beneficial bacteria, known as commensals, in their intestines. These bacteria are not harmful and, in fact, help an individual maintain his or her digestive health. Typically, the immune system does not attack gut commensals, even though they are bacteria.

"Within the body of a healthy adult, microbial cells vastly outnumber human cells. Research to understand these microbial communities is an exciting scientific frontier," says Anthony S. Fauci, MD, NIAID director. "Among many opportunities related to the so-called 'microbiome,' targeting beneficial bacteria may offer new avenues for therapy against infectious and immune-mediated diseases."

Just how commensals protect against harmful bacteria, known as pathogens, is a complex question. "Pathogens often behave similarly to gut commensals," Dr. Belkaid says. Because the body needs commensals but also has to rid itself of disease-causing microbes, the immune system

must distinguish the good bugs from the bad ones.

One mechanism of protection is through the interaction between the commensals and certain immune cells in the intestines. This interaction occurs through the binding of the commensals to receptors on the T cells known as Toll-like receptors (TLRs).

In healthy individuals, some intestinal T cells (known as Tregs) play a regulatory role, recognizing commensals and keeping the immune system from attacking them. During an infection, however, T cells shift into attack mode to fight the infection. The factors controlling this shift from defense to offense have not been well understood.

Dr. Belkaid's team describes a novel way in which the Tregs are regulated to facilitate an immune response to a pathogen. They found that during an infection, the DNA of the body's beneficial bacteria binds to a specific receptor on the intestinal immune cells, called TLR9. The binding of commensal DNA to TLR9 in the presence of a pathogen prevents the generation of Tregs in favor of the generation of protective T cells. These protective T cells can then clear the body of the invading pathogen.

In effect, the commensal DNA acts as a natural adjuvant by boosting the activity of T cells so they can destroy the invading pathogen.

"There is a balance of regulatory immune signals in the body," notes Dr. Belkaid. "During an infection, we've found that commensals can break this balance in favor of an infection-fighting response."

While the immune system must react to invading pathogens to maintain health, an immune response to commensals can cause problems. For example, certain inflammatory bowel diseases, such as Crohn's disease, are thought to be caused in part by immune reactions against commensal

bacteria.

Understanding how commensals interact with the immune system opens up the possibility of using beneficial bacteria as targets for future oral therapies against infections or autoimmune diseases.

Source: National Institute of Allergy and Infectious Diseases