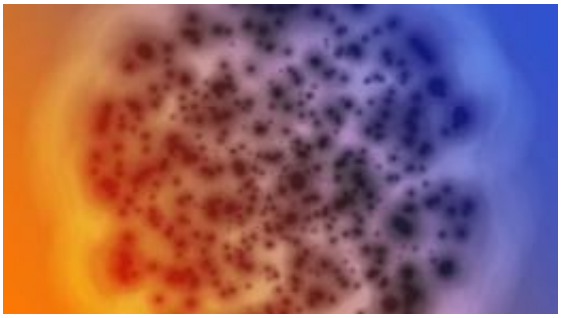
Immune cells support good gut bacteria in fight against harmful bacteria

April 21 2015



Bacteria

An immune cell protein, ID2, is critical for the maintenance of healthy gut microbiota and helps these good bacteria fight off harmful bacteria, report scientists from the University of Chicago. The study, published in *Immunity* on April 21, suggests that novel therapeutics or microbiota transplantation could be used to promote the development of good gut microbiota to indirectly kill harmful bacteria for patients with recurrent gut infection.

"Our study reveals how our body's immune system shapes the gut microbiota to naturally limit infections," says senior author Yang-Xin Fu, MD, PhD, Fanny L. Pritzker Professor of Pathology at the University of Chicago. "Given the rapid raise of harmful bacteria that are resistant to antibiotics, it is paramount that scientists find methods of limiting harmful bacterial infections without the use of antibiotics."

The human body is made up of roughly 10 times more bacterial cells than human cells. These microorganisms, collectively called the microbiota, are thought to affect health and disease, but their precise role is still poorly understood. Recent evidence has shown that gut microbiota can help protect against infections caused by harmful bacteria - for example, fecal microbiota transplantation has been used to help some patients with difficult-to-treat *Clostridium difficile* infections.

To study the interaction between hosts, gut microbiota and harmful bacteria, Fu and his colleagues focused on immune system cells known as type 3 innate lymphoid cells (ILC3s), which are essential for infection resistance in the gut. They found that the protein ID2 is central to this protective effect. ILC3s that are missing ID2 have a diminished ability to respond to harmful bacterial infections.

To test how ID2 affected healthy gut microbiota, the team transferred microbiota from a mouse with ILC3s that lacked ID2 into a completely germfree mouse. These mice were highly susceptible to harmful bacterial infection. However, germfree mice that received microbiota from normal mice had dramatically reduced harmful bacterial populations.

The researchers found that mice with ILC3s that lacked ID2 were unable to produce the cytokine IL-22and subsequently induce antimicrobial peptides (AMPs) by intestinal epithelial cells,. This disrupted the health of the native gut microbiota, which then allowed harmful bacteria to colonize the gut.

"The body's immune system is needed to help shape our gut microbiota, which is the first line of protection against harmful bacteria," Fu said. "Without the presence of IL-22 and AMPs from ILC3s, the normal gut microbiota is not properly developed and thus harmful bacteria can more easily infect the body."

Fu and his colleagues believe the discovery of this mechanism could lead to novel therapeutic options to help prevent harmful infections, instead of just responding to them. The findings better inform microbiota transplantation research, and have the potential to aid in the development of new drugs or probiotics that promote good microbiota or mimic their products against various pathogens.

The team are now focusing on isolating specific microbiota species that can help prevent bacterial infections, as well as another intriguing question: how do immune cells distinguish between beneficial and harmful bacteria to maintain a healthy microbiota? Although this is still unclear, Fu notes that the human body and its microbiota have evolved to live in harmony over millions of years.

"This mutual beneficial relationship provides us with the ability to properly receive all of the nutrients from our food, and as shown with this study, the ability to limit harmful bacterial infections," he says.

More information: "Innate Lymphoid Cells Control Early Colonization Resistance against Intestinal Pathogens through ID2-Dependent Regulation of the Microbiota", *Immunity*, 2015. dx.doi.org/10.1016/j.immuni.2015.03.012

Provided by University of Chicago Medical Center