MedicalXpress

Intestine crucial to function of immune cells, research shows

December 12 2011

Researchers at the University of Toronto have found an explanation for how the intestinal tract influences a key component of the immune system to prevent infection, offering a potential clue to the cause of autoimmune disorders like rheumatoid arthritis and multiple sclerosis.

"The findings shed light on the complex balance between beneficial and harmful bacteria in the gut," said Prof. Jennifer Gommerman, an Associate Professor in the Department of Immunology at U of T, whose findings were published online by the scientific journal, *Nature*. "There has been a long-standing mystery of how certain cells can differentiate between and attack harmful bacteria in the intestine without damaging beneficial bacteria and other necessary cells. Our research is working to solve it."

The researchers found that some B cells—a type of white blood cell that produces antibodies—acquire functions that allow them to neutralize pathogens only while spending time in the gut. Moreover, this subset of B cells is critical to health.

"When we got rid of that B-cell function, the host was unable to clear a gut pathogen and there were other negative outcomes, so it appears to be very important for the cells to adopt this function in the gut," said Prof. Gommerman, whose lab conducted the research in mice.

Textbook immunology—based mostly on research done in the spleen, lymph nodes or other sterile sites distant from gut microbes—has

suggested that B cells develop a specific immune function and rigidly maintain that identity. Over the last few years, however, some labs have shown the microbe-rich environment of the gut can induce flexibility in immune cell identity.

Prof. Gommerman and her colleagues, including trainees from her lab Drs. Jörg Fritz, Olga Rojas and Doug McCarthy, found that as B cells differentiate into plasma cells in the gut, they adopt characteristics of innate immune cells—despite their traditional association with the adaptive immune system. Specifically, they begin to look and act like inflammatory cells called monocytes, while maintaining their ability to produce a key antibody called Immunoglobulin A.

"What intrigued us was that this theme—B cells behaving like monocytes—had been seen before in fish and in vitro. But now we have a living example in a mammalian system, where this kind of bipotentiality is realized," said Prof. Gommerman.

This B-cell plasticity provides a potential explanation how cells dedicated to controlling pathogens can respond to a large burden of harmful bacteria without damaging beneficial bacteria and other cells essential for proper function of the intestine.

It also may explain how scientists had failed to appreciate the multi-functionality of some B cells. "There are classical markers immunologists use to identify B cells—receptors that are displayed on their surface—and most of them are absent from plasma cells," said Prof. Gommerman. "So in some cases, what people thought was a monocyte could have been a plasma cell because it had changed its surface identity, although monocytes play an important role in innate immunity as well."

This transformational ability, the researchers also found, is dependent on

bacteria called commensal microflora that digests food and provides nutrients. That relationship highlights the importance of the gut in fighting infection, and begs the question of whether plasma cells trained in the gut to secrete specific anti-microbial molecules can play a role in other infectious disease scenarios, such as food-borne listeria infection.

It also opens a line of investigation into whether a systemic relationship exists between those anti-microbial molecules and healthy cells in sites remote from the intestine. Understanding the nature of that relationship could improve understanding of inflammatory mechanisms in autoimmune disorders such as lupus, rheumatoid arthritis and multiple sclerosis, in which immune cells attack and eventually destroy healthy tissue.

But the next step, said Prof. Gommerman, is to look at human samples for the same type of multi-potentiality they saw in rodent plasma cells that acquired their anti-microbial properties in the gut.

"We're really at the early stages of understanding what we call the microbiome in the gut," said Prof. Gommerman. "There is a role for plasma cells in many autoimmune diseases, and B cells can do a lot more than just make antibodies. We need to understand the full spectrum of their effects within the immune response."

Provided by University of Toronto