A worm-and-mouse tale: B cells deserve more respect

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By studying how mice fight off infection by intestinal worms - a condition that affects more than 1 billion people worldwide - scientists have discovered that the immune system is more versatile than has long been thought. The work with worms is opening a new avenue of exploration in the search for treatments against autoimmune diseases like diabetes and asthma, where the body mistakenly attacks its own tissues.

The findings, reported by scientists who performed the work at the Trudeau Institute in Saranac Lake, N.Y., and who are now at the University of Rochester Medical Center, appear in the March issue of the journal *Immunity*. The article was published online Feb. 26.

The research focuses mainly on B cells, one of many types of immune cells that the body maintains to fight off invaders like bacteria, viruses, and parasites. Besides B cells, there are T cells, macrophages, neutrophils, monocytes, mast cells and others, all working in concert to keep an organism healthy. The cells cruise our bodies, looking to eliminate infectious threats before they become a serious risk to our health.

For many years, scientists believed that the major job of B cells was to identify foreign invaders and tag them with antibodies, marking the microbe for destruction by the immune system. But scientists are discovering that B cells do much more, resulting in new information about our immune system that could be useful for developing more

effective vaccines and better treatments for many types of disease.

In the past few years, Frances Lund, Ph.D., professor of Medicine in the Division of Allergy/Immunology and Rheumatology at the University of Rochester Medical Center, has found an array of unexpected functions for B cells. In the laboratory, she has found that B cells produce chemical signaling molecules known as cytokines that spur other immune cells in the body to action. Her team has also shown that B cells are crucial for presenting to T cells snippets of proteins from invaders, so that the T cells can recognize the invader, a crucial step that allows T cells to mature into useful cells which can then fight an infection efficiently.

In the new paper, Lund's team tested how the findings actually translate by watching closely as an organism - in this case, a mouse - actually fights off infection by a parasite. They chose to study the intestinal parasite *Heligmosomoides polygyrus*, a bright red worm about one-third of an inch long that infects mice.

It's a cousin of the scores of worms that infect more than 1 billion people worldwide. Roundworms, hookworms, pinworms, and others - these and other worms cause fatigue, diarrhea, nausea, and death.

"Nematodes - worms - sicken a lot of people, they can cause severe malnutrition, and they play havoc with the immune system, making many people more vulnerable to other threats, such as malaria," said Lund, whose project was funded by the National Institute of Allergy and Infectious Diseases.

The team not only verified the additional actions of B cells that they've discovered in the laboratory, but, importantly, they showed that these functions are crucial for the organism to fight off infection.

Lund's team showed that the chemical messengers produced by B cells, such as interleukin-2 and tumor necrosis factor, are necessary for the immune system to protect mice against *Heligmosomoides polygyrus*. The team also showed that B cells must be present in order for T cells to mature and operate properly.

"It's long been dogma that B cells need the help of T cells to make antibody. That's in all the textbooks," said Lund. "Now work from our laboratory and others shows that it's a two-way street, that T cells need the help of B cells also."

B cells' effects on T cells may open a new window on such diseases as lupus, asthma, multiple sclerosis, and diabetes, where doctors know that T cells are active. Maybe manipulating B cells offers a new way to affect the activity and survival of the T cells that cause disease.

The work also brings up the possibility of more targeted treatments than current treatments, which generally affect all B cells. Lund has found that different B cells produce different collections of chemical signaling molecules. Someday, instead of having a drug that simply targets all B cells, it may be possible to target a specific type of cell, cutting down side effects and making a treatment more effective.

"It may be that only certain B cells play a role in damaging immune responses. If we can narrow down the group of cells at the root of the problem, we may be able to find important new targets for improving treatment," said Lund.

Source: University of Rochester Medical Center