Using Immune Response against Parasites

The search for better drugs against parasitic worms and the diseases they cause matures in a lab studying a host's immune system and the parasite.

by Jackie Swift

Our bodies are invaded by pathogens regularly. To combat that onslaught, our immune system has evolved clever ways to fight foreign invaders. How it identifies pathogens and then initiates resistance is imperfectly understood, especially when it comes to parasite infections.

"It's really important to understand how mammals regulate successful immune response against parasites because that will inform the development of better drugs and vaccines against these infections," says Elia Tait Wojno, Microbiology and Immunology. "Although we currently have drugs that combat parasite infections, even after they are applied successfully,

Elia Tait Wojno
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Highlights

Diseases Caused by Parasitic Worms (Helminths) and Discovering How to Treat Them many hosts will become re-infected and the diseases associated with those infections can be severe."

[Helminth Infection and Immune Response]

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Diseases Caused by Parasitic Worms (Helminths) and Discovering How to Treat Them

Much of Tait Wojno's research focuses on helminths, parasitic worms that infect humans and other mammals. They cause debilitating diseases in humans, including schistosomiasis, gastrointestinal disease associated with intestinal infection, river blindness, and lymphatic filariasis, which affect hundreds of millions of people in tropical areas. Worms are also responsible for diseases such as heartworm in dogs and liver fluke in cattle.

Creating new vaccines against helminths would be a significant breakthrough for human and veterinary medicine. Before that can happen, much more needs to be understood about the normal interplay between a host's immune system and the parasite. "When and how does the host expel the worm with as little collateral damage as possible?" asks Tait Wojno. "Can we try to mimic that process in a vaccination scenario, or can we learn new things about how the immune system functions that will allow us to take a more creative approach as we develop a vaccine or new drugs to treat helminth infections?"

Helminth Infection and Immune Response

Tait Wojno is particularly interested in the innate immune response, made up of cells that initially recognize pathogens, then initiate the process to attack the invaders. The innate response is one of two types of immune responses in mammals. The other is the adaptive immune response made up of T and B cells that can remember a pathogen once they encounter it—an ability harnessed by vaccines that teach the body how to fight off infection.

In the case of a helminth infection, the two immune responses work together to try to make the environment for the worm so inhospitable that the parasite will want to leave. That's why helminth infection in the intestines, for instance, include diarrhea, mucus production, and gastrointestinal distress. The innate immune cells initiate and support these changes and help educate the adaptive cells.

The Tait Wojno lab is carrying out a series of research projects, using mouse models, aimed at understanding how innate immune cells' responses to pathogens shape the ultimate outcome of intestinal infection. In one project, they are looking at the role of basophils, a rare type of white blood cell. "They're like little hand grenades," Tait Wojno says. "Previous research has suggested that they develop in the bone marrow and come out into the blood and travel to the site of infection. They release all these pre-loaded toxins and poisons—things like histamines, proteases, and preformed cytokines, which are chemical messengers of the immune system—and then they die." Tait Wojno's work is now exploring whether this paradigm is indeed true in all cases, or whether these cells can change their function on the fly in response to infection.

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Tait Wojno and her colleagues looked at the role of basophils in the immune response to whip worm infections, focusing on a chemical pathway that allows cells to talk to each other, known as the Notch signaling pathway. The researchers found that basophils have a more sophisticated role to play than previously thought. "We found the Notch signaling pathway places basophils in the right area of the tissue to perform their antiparasite functions and specifically to support the adaptive T-cell response," Tait Wojno explains.

Once they are in the right place, the Notch signaling pathway also tells the basophils to change their gene expression in response to the environment, thus supporting the expulsion of the worm. The key to this communication is another cell, one that still remains a mystery.

"The basophil has the lock and the other cell has the key," Tait Wojno explains. "When they interact, that leads to very rapid signaling inside the basophil that then speaks directly to the genome, changing what genes are expressed in the basophil and what proteins are made downstream." Tait Wojno and her colleagues are pursuing ongoing studies to identify the other cell type and to understand the exact nature of that key portion of the pathway.

Intestinal Helminth Infection and Innate Immune Response

In another project, the Tait Wojno lab is investigating how innate immune responses to intestinal helminth infection direct the epithelial and smooth muscle cells of the intestine—the cells that provide the environment for the worm—to change their physiology. While the initial change alters the intestinal environment and leads to the expulsion of the parasite, Tait Wojno and her colleagues want to understand how those responses are later resolved and the intestinal environment restored to normalcy again.

A type of fatty lipid called a prostaglandin appears to be an important part of the process, acting as the key that fits the lock on a receptor present on the epithelial cells. Previous research by others had identified this chemical pathway as crucial for the initial activation of innate immune cells to begin the process of altering the intestinal environment. Tait Wojno and her collaborators, however, showed that the same pathway comes into play once the infection is over.

"The prostaglandin tells the epithelial cells to shut down some of these pro-diarrhea responses," Tait Wojno says. "Now we're exploring a hypothesis by which the same factor, depending on the timing and the environment of the response, does two different things to successfully orchestrate this response from start to finish."

Tait Wojno became interested in parasites as an undergraduate at Drew University, where she carried out a research project with noted parasitologist William C. Campbell who later won the Nobel Prize in Physiology or Medicine. "He imparted an appreciation in me of how interesting these organisms are and how much they can teach us about biology," Tait Wojno says. "Having this complex, multicelled organism living inside our bodies is an exciting example of evolution and the complexity of biology, of how communities of organisms live together. There's a lot to discover at the end of the day."

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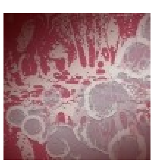

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