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Scans show immune cells intercepting parasites

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Researchers may have identified one of the body's earliest responses to a group of parasites that causes illness in developing nations.

In a paper published online in *Public Library of Science Pathogens*, scientists report that they tracked immune cells as they patrolled the second-shallowest layer of the skin in an animal model. Injections of a genetically modified form of the parasite Leishmania major caused the immune cells to turn from their patrols and move to intercept the parasites.

The same parasites are now infecting U.S. soldiers on patrol in Iraq and Afghanistan, where sand flies, the insects whose bites spread Leishmania, are endemic. The infections normally do not cause symptoms, but the parasite can reactivate and cause complications during pregnancy or if the immune system weakens, including skin sores, fever, damage to the spleen and liver and anemia.

"This is one of our most detailed looks so far at how a first responder in the immune system scouts out pathogens," says co-author Stephen Beverley, Ph.D., the Marvin A. Brennecke Professor and head of the Department of Molecular Microbiology at Washington University School of Medicine in St. Louis. "Determining how the immune system reacts is critically important for efforts to develop vaccines that protect against these parasites."

According to Beverley, what researchers learn from Leishmania also

may have applications for controlling more harmful parasites from the same family of microbes, the trypanosomes. These include Trypanosomiasis, the cause of African sleeping sickness, which disrupts the lymph, circulatory and nervous systems and is fatal if untreated, and Chagas disease, which can damage the heart and the intestine in long-term infections.

The study began with an attempt to better understand the role of a group of immune cells known as dendritic cells in the dermis, the second layer of the skin. Scientists at the University of Pennsylvania created a line of mice genetically modified so their dendritic cells produced a yellow fluorescent protein. They used a technique called two-photon microscopy to track the movements of the cells in living mice and show that the cells were "surprisingly motile around the perimeter, moving about and doing all sorts of patrolling," according to Beverley.

One of Beverley's graduate students, Michael A. Mandell, took a strain of Leishmania genetically modified to produce red fluorescent protein and injected it into the Pennsylvania group's mice. The different colors allowed them to use two-photon microscopy to track both dendritic cells and parasites at the same time, and they found that the dendritic cells rapidly homed in on the injected parasites.

Dendritic cells are antigen-presenting cells, which means they can absorb invaders and then display bits of them on their surface to other immune system cells. This triggers a heightened counterattack against the invaders from a variety of immune cells.

Injections of latex beads did not cause the same response from the dendritic cells.

"The dendritic cells were clearly recognizing something made by the pathogen that was provoking their response, and that's one question we

will be looking to answer in follow-up experiments," Beverley says.

Beverley notes that infection with Leishmania and other parasites can cause different diseases in different people, suggesting that genetic differences in parasite and host can alter the immune response. Methods of transmission in the wild are messier than an injection and may also add variety to those responses.

"Many of the insects that pass on these parasites are not elegant eaters—they chew on skin, creating pools of many cell types," he explains. "The big question is: How do all the different immune cell types combine to orchestrate the immune system's response? What we've done is to pull out one leading player from that mix, which is an important first step to understanding the overall response."

Reference: Ng LG, Hsu A, Mandell MA, Roediger B, Hoeller C, Mrass P, Iparraguirre A, Cavanagh LL, Triccas JA, Beverley SM, Scott P, Weninger W. Migratory dermal dendritic cells act as rapid sensors of protozoan parasites. Public Library of Science Pathogens, November 30, 2008.

Source: Washington University School of Medicine