

Leishmaniasis parasites evade death by exploiting the immune response to sand fly bites

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Cutaneous leishmaniasis, a disease characterized by painful skin ulcers, occurs when the parasite *Leishmania major*, or a related species, is transmitted to a mammalian host by the bite of an infected sand fly. In a new study from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, scientists have discovered *L. major* does its damage by not only evading but also by exploiting the body's wound-healing response to sand fly bites, as reported in the August 15 issue of *Science*.

"This work changes the textbook picture of the lifecycle of the leishmaniasis parasite, identifying the inflammatory cell known as the neutrophil as the predominant cell involved during the initiation of infection," says NIAID Director Anthony S. Fauci, M.D.

Employing advanced microscopy techniques, which allowed real-time imaging of the skin of living mice infected with *L. major*, NIAID collaborators Nathan C. Peters, Ph.D., and Jackson Egen, Ph.D., found that the neutrophils—white blood cells that ingest and destroy bacteria—play a surprising role in the development of the disease.

Neutrophils were rapidly recruited out of the circulating blood and into the skin of infected mice, where they swarmed around the sand fly bite sites and efficiently engulfed the parasites. But unlike many other infectious organisms that die inside neutrophils, *L. major* parasites

appear to have evolved in a way to evade death, actually surviving for long periods of time inside the neutrophils. Eventually the parasites escape from neutrophils and enter macrophages, another immune cell population in the skin, where they can establish long-term infection.

"Parasites transmitted by sand flies to mice lacking neutrophils have more difficulty establishing an infection and surviving. This demonstrates the importance of neutrophils at the site of an infected sand fly bite and suggests the unexpected path taken by the parasite from sand fly to neutrophil to macrophage is a critical component of this disease," says Dr. Peters.

In addition, says Dr. Egen, the study reveals how neutrophils leave locally inflamed blood vessels and move into tissues; provides new information on the movement of these immune cells within damaged tissue environments and upon contact with pathogens; and provides video images revealing active neutrophil entry into areas of damaged skin.

Source: National Institute of Allergy and Infectious Diseases

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