How the immune system fights worm infections

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The mouse helminth H. polygyrus. Credit: 2015 Nicola Harris/EPFL

The immune system can 'remember' infectious invaders. EPFL scientists now show how immune memory triggers the body's ability to repair tissues damaged during worm infections. The work could lead to better drugs against worms, but also to treatments that actually promote wound healing.

Helminthes are parasitic worms that currently affect over 2 billion people worldwide, and also threaten agricultural livestock. Once in the body, helminthes move through the skin, lungs, liver and intestines, causing massive tissue damage in their wake. In response, the host's immune system mounts an inflammatory response that traps the migrating larvae, but this can also cause dangerous scarring of the tissue. Scientists at EPFL have now discovered that the immune system and the helminthes themselves both have the capacity to trigger a rapid wound-healing response that helps to protect vulnerable host tissues. Published in *PLoS Pathogens*, the discovery could help develop more efficient strategies for treating helminthic infections and wounds.

Helminthes cause considerable damage when worming through tissues. In response, the body begins to rapidly heal damaged tissue so as to avoid internal bleeding. Though well documented, the exact relationship between the helminth and the patient's immune system is still a mystery. But considering that helminth infections surpass both tuberculosis and malaria in numbers, understanding it better could have a tremendous impact on global health, as it could lead to new and significantly improved treatments.

The lab of Nicola Harris at EPFL has shed light on the mystery by showing that immune memory – in the form of antibodies – and the helminthes themselves work together to promote rapid wound healing. This immune memory also prevents large worm burdens that can otherwise lead to malnutrition and cognitive defects. As a model for their study, the scientists used mice that were genetically engineered to have deficient immune systems. The researchers then gave the mice a helminth that is common to rodents.

Infecting and protecting the patient

The study showed that, in mice with deficient immune systems, the

intestine failed to properly trap the migrating helminth larvae or to heal the wounds they caused. This means that the host's immune system is definitely part of the wound-repairing process that follows in the wake of helminth infections. But more fascinatingly, the team discovered that the wound-repairing process is also supported by the helminth itself. The worms release a molecule that begins a long and complex cascade of molecular events, leading to activation of immune cells that begin the wound-repairing process.

The study reveals a "dual role" that helminths and immune antibodies both play to repair damaged tissue. The question is, what does the infecting helminth gain from turning on its host's weaponry? The authors suggest that this is a textbook example of co-evolution, where infecting agent and host have evolved together to ensure each other's survival: with the helminth and patient together protecting the patient from massive tissue damage.

However, this cannot go on for long. Studies have also shown that the protective response can ultimately lead a type of liver scarring known as fibrosis. Extensive liver fibrosis can cause problems with function, leading to liver failure. What this means is that it is imperative to find effective treatments that can disrupt the relationship between helminth and host. The findings of this study could lead to an entirely new generation of medications either to treat helminth-induced scarring or to promote wound healing caused by physical damage.

More information: "Immune Antibodies and Helminth Products Drive CXCR2-Dependent Macrophage-Myofibroblast Crosstalk to Promote Intestinal Repair." *PLoS Pathogens* March 25, 2015. DOI: 10.1371/journal.ppat.1004778

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