Discovery to aid in future treatments of third-world parasites

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The Trudeau Institute is an independent, not-for-profit biomedical research organization, whose scientific mission is to make breakthrough discoveries leading to improved human health. Credit: The Trudeau Institute

Schistosomiasis, one of the most important of the neglected tropical diseases, is caused by infection with parasitic helminths of the genus *Schistosoma*. These parasites are long lived (>10 years) and dwell within blood vessels, where they produce eggs that become the focus of intense, chronic inflammatory responses. In severe cases, this inflammation is associated with life-threatening liver disease.

No vaccine is currently available to prevent schistosomiasis. Options for treating the disease are largely limited to one drug, Praziquantel. Rates of re-infection in drug-treated individuals are high, and it is feared that widespread use may foster the emergence of drug-resistant variants, such as has seen with drug-resistant strains of tuberculosis.

The body's immune response to schistosome infection, as with all immune responses, is coordinated by cytokines, small proteins secreted by immune cells. Due to their fundamental importance, cytokine research is a significant focus of research at the Trudeau Institute. Because cytokines travel through the body to relay critical information, it is difficult to identify the cells that produce them and to learn about their role.

Trudeau investigators have devised cytokine "reporter mice" for tracking cells that produce the signature cytokine of the so-called "Th2" immune response mounted against infections with parasitic worms, interleukin-4 (IL-4).

While it was previously known that the complex mixture of proteins released by schistosome eggs induce Th2 responses and the production of IL-4, the specific molecule(s) responsible for these effects were unknown.

Research from the laboratories of Markus Mohrs of the Trudeau Institute and Gabriele Schramm of the Research Centre Borstel in Germany had previously shown that a protein called alpha-1 can support Th2 responses but is unable to initiate them.

However, new findings from an international study between Mohrs, Schramm, and Maria Yazdanbaksh of the Leiden University Medical Center in the Netherlands have now shown that omega-1, a single protein secreted from schistosome eggs, recapitulates the activities of the complex mixture in the test tube (in vitro).

Importantly, using IL-4 reporter mice, the researchers show that omega-1 alone is sufficient to generate Th2 responses in vivo. This identification of a single protein will undoubtedly aid in unlocking the molecular pathways inducing Th2 responses commonly elicited by infection with parasitic worms.

Ultimately, these novel insights will help researchers in the field like Dr. Yazdanbaksh, who, in addition to her laboratory research, also oversees studies in schistosomiasis patients in Africa.

These findings are reported in the current issue of the *Journal of Experimental Medicine*.

As with all basic research discoveries, incremental advances such as these may eventually lead to new treatments and therapies that will improve the day-to-day lives of the 200 million people around the globe currently afflicted by schistosomiasis. Moreover, these Th2 responses, described above in the context of worm infections, are also associated with the clinical symptoms of allergic and asthmatic disorders. Thus, understanding the immune response to infection with parasitic worms might aid in ameliorating allergy and asthma common in industrialized countries.

Source: Trudeau Institute (news : web)