Bacteria contribute to immune suppression in skin after repeated schistosome exposure

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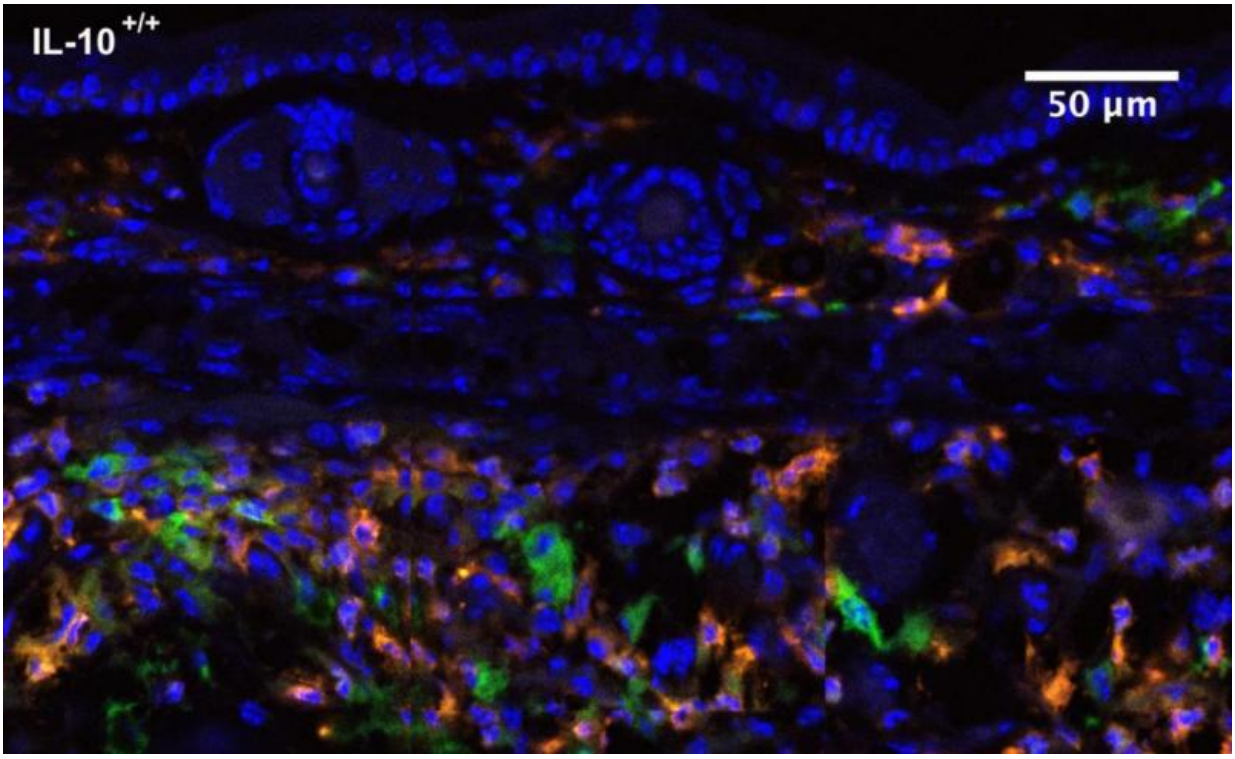

Skin of normal mice. IL-10 production by CD4+ T cells (green) following infection of the skin with Schistosoma mansoni cercariae, prevents excessive inflammation of the epidermis and dermis, and limits the influx of myeloid cells (CD11b+ (yellow); MHC-II+ (red)). IL-10 is triggered by commensal microorganisms that gain entry to the host during percutaneous infection with schistosome larvae infection, which subsequently sustains the production of IL-10. Credit: Mountford et al., CC-BY

Our two square meters of skin act as a defensive barrier against environmental pathogens but is also covered by beneficial commensal bacteria. We live alongside these bacteria without excessive and unnecessary immune responses, which could destroy the skin's function as a barrier and so make us more vulnerable to infections. However, we must also be able to establish a robust immune response to invading pathogens. A study published on May 14th in *PLOS Pathogens* explores that delicate balance and reports that when schistosome parasites repeatedly penetrate the skin they are cloaked in skin bacteria, leading to a tightly controlled and limited immune response, due in part to this cloaking mechanism.

Schistosomiasis, the most common parasitic disease after malaria, is transmitted directly through the skin when people are exposed to fresh water contaminated with larvae of the schistosome parasites. Despite the fact that many residents of schistosome-endemic regions experience repeated exposure to the parasite larvae during regular contact with contaminated water sources, most experimental studies of schistosome infection focus on immune events after a single infection. To address this gap in our knowledge, Adrian Mountford, from the University of York, United Kingdom, and colleagues have established a mouse model that recapitulates the more realistic scenario of repeated skin infection.

The researchers report that both after a single but particularly after repeated (four times) penetration by schistosome larvae, the skin at the infection site becomes rich with a molecule called IL-10, which is known to dampen the immune response. The presence of IL-10 was important in limiting the extent of inflammation at the site of infection by reducing skin thickening and preventing recruitment of other immune cells called neutrophils, which can cause damage to the tissue.

The researchers determined that the source of IL-10 are immune cells of the CD4+ T cell type in the skin, which were responding to both the

schistosoma parasite and surprisingly skin bacteria. They also found that these T cells have different molecular characteristics than conventional regulatory T cells known to secrete IL-10 in other situations. In addition to being able to limit the local immune response in the skin, the suppressive CD4+ T cells were able to prevent the proliferation of parasite-specific immune cells isolated from local lymph nodes, which would normally multiply after a single contact with the pathogen. As lymph nodes are the relay stations of the immune system, this could explain how immune hypo-responsiveness to the parasite is initiated in individuals infected multiple times.

The researchers conclude that their work "highlights a possible role for unconventional IL-10 producing CD4+ T cells which are functionally suppressive in maintaining host fitness in populations that inhabit areas endemic for schistosomiasis and other helminth larvae that penetrate via the skin". Moreover, they say, their work suggests a "previously unknown interaction between skin invading helminths and normal skin bacteria, which benefits both the host which experiences less immune-mediated pathology, and the parasite which is not killed by the immune response".

More information: Sanin DE, Prendergast CT, Bourke CD, Mountford AP (2015) Helminth Infection and Commensal Microbiota Drive Early IL-10 Production in the Skin by CD4+ T Cells That Are Functionally Suppressive. *PLoS Pathog* 11(5): e1004841. DOI: 10.1371/journal.ppat.1004841

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