Intestinal worms 'talk' to gut bacteria to boost immune system

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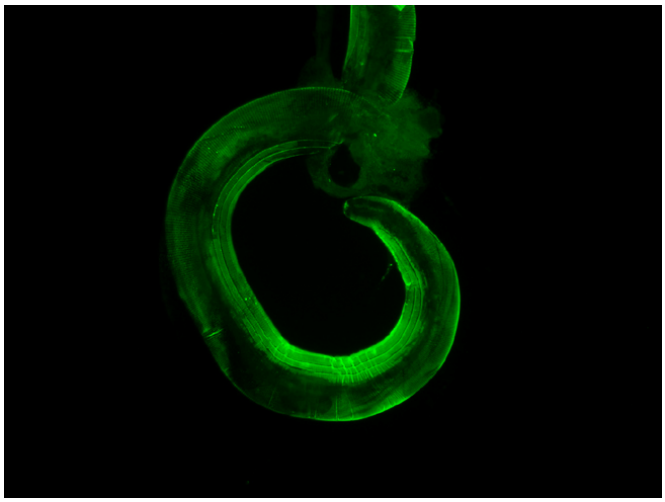

The helminth *Heligmosomoides polygyrus bakeri* (Hpb), which infects rodents. Here seen under fluorescent staining. Hpb was used in the mouse part of this study. Credit: Nicola Harris/EPFL

EPFL researchers have discovered how intestinal worm infections cross-talk with gut bacteria to help the immune system.

Intestinal worms infect over 2 billion people across the world, mostly children, in areas with poor sanitation. But despite causing serious health problems, worms can actually help the immune system of its host as an indirect way of protecting themselves. The evidence for this is so strong that we are now testing worms for clinical benefits. However, very little is known about how worms interact with the host's immune system. A new study by EPFL now shows that these effects go through the gut's bacteria that help digestion. The work is published in *Immunity*.

Intestinal worms belong to a larger family of helminths, which are large multicellular parasites that can cause chronic infections in their hosts. Virtually eradicated in industrialized areas, helminths still infect billions of people.

But because of their long co-evolution with mammals, helminths have developed a close relationship with their host's immune systems, to the point that they can regulate the host's immune system in beneficial ways. For example, helminths can ameliorate diseases such as allergic asthma. However, very little is known about how helminths modulate the immune system, and whether or not we can exploit this to fight against diseases caused by inflammation.

The lab of Nicola Harris at EPFL has now shown that the anti-inflammatory activity of intestinal helminths involves "cross-talk" with an unexpected agent: the gut's bacteria, also known as the "microbiome". These are the bacteria that have been dominating nutritional news in recent years, as we are increasingly learning how much they influence a person's metabolism, immunity, and health in general.

In this study, the researchers looked at the effects of helminths that infect pigs. After chronic infection with the helminths, they discovered that the animals' metabolism had been changed drastically; specifically, they produced increased levels of a class of fats in the gut called "short-chain fatty acids ". These fatty acids are produced by the microbiome, and can activate a family of receptors that in turn influence the immune system. The receptors are also known to contribute to certain functions - and malfunctions - of the colon, and are even involved in modulating allergic airway disease.

This is exactly what the researchers found when they also monitored cells in the immune system of mice that had been infected with a helminth. Like the pigs, the mice showed an increased production of short-chain fatty acids. Further testing showed that these acted on the same receptors to influence

specific immune cells. In short, the researchers uncovered a clear link between worm infection, microbiome, and the immune system.

The work highlights the microbiome as a new pathway through which helminths could influence the immune function of the host. "It's not the whole story," says Nicola Harris. "But it opens up an additional, intriguing way to explain - and perhaps exploit - the strategy with which intestinal worms communicate with the host's immune system."

More information: Zaiss MM, Rapin A, Lebon L, Kumar Dubey L, Mosconi I, Sarter L, Piersigilli A, Menin L, Walker AW, Rougemont J, Paerewijck O, Geldhof P, McCoy KD, Macpherson A, Croese J, Giacomin PR, Loukas A, Junt T, Marsland BJ, Harris NL. The intestinal microbiota contributes to the ability of helminths to modulate allergic inflammation. *Immunity* 27 October 2015

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