How our gut fights the intestinal parasite *Giardia intestinalis*

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Parasites are adapted to life in a host organism, where they benefit on the cost of the host. *Giardia intestinalis* is such a parasite, with a single cell that is around one tenth of a millimetre long. *Giardia* infects humans and other mammals and it lives in the host small intestines. *Giardia* infections are called giardiasis and they are a major cause of diarrhoea worldwide. Over 250 million symptomatic cases are reported every year! Mostly people in developing countries get infected due to poor hygiene, but also cases from developed countries are reported. As in so many diarrheal diseases, children are the most affected by giardiasis.

Infected hosts release *Giardia* parasites with their stool in the form of well-protected, inactive cysts, which can survive in the environment. If cysts contaminate water or food that are ingested by a host, the life cycle of the parasite continues. Once inside the new host's gut, active pear-shaped cells, called trophozoites, emerge from hatching cysts. Trophozoites swim using their flagella and attach to the intestinal cells via their adhesive disc, then divide and colonise the gut, causing diarrhoea.

In order to get rid of intruders like parasites, the host organism initiates an immune response, in which different cell types and other components are involved. In an intestinal infection, the epithelial cells of the gut - sitting on its inner surface - are an important part of this immune reaction. The intestinal epithelial cells are able to produce signal molecules, called cytokines, which are able to attract various immune cells to infection site. The parasites in turn, have developed numerous mechanisms in order to attenuate the host immune responses, allowing them to live in the host for a longer time period.

To simulate host-parasite interactions, we incubate intestinal epithelial cells with *Giardia* trophozoites and let them interact under lab conditions. This system allowed us to study cytokine production in intestinal cells and to find hints on how *Giardia* influences this.

In a first part of the project, we were able to confirm which cytokine genes in intestinal epithelial cells are activated in response to *Giardia* parasites. Next, we investigated, how our cells sense the presence of the parasites. Host cells detect microorganisms with special receptor proteins on their cell surface. In our experiments, we found that the presence of *Giardia* parasites increased the abundance of two such receptors. Then we studied, which proteins could be involved in transferring the signal within the intestinal cells, from cell surface receptors to the nucleus, leading to activation of cytokine genes. In this signalling pathway, the last protein that transmits the signal from the cytoplasm to the nucleus (where genetic information is stored) was detected with a fluorescent marker. In cells incubated with the parasites, this protein moved into the nucleus, in order to induce cytokine genes. Interestingly, in a group of three proteins that transfer external signals without moving to the nucleus, one was found to be inhibited by *Giardia*. Inhibition of this cell signalling protein had been observed in response to other parasites before. Thus, we believe that the observed inhibition in our case may be a way of *Giardia* to attenuate the host immune responses.

These results add to the picture of the immune responses of the intestinal epithelium against *Giardia* parasites. It will be particularly interesting to confirm the cell signalling inhibition and to investigate how exactly the parasite causes it.

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