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GUT MICROBIOTA

A protective protozoan in mucosal infection

A novel mutualistic host–protozoan interaction has been reported in a new study published in *Cell*. The findings highlight how a commensal protist *Tritrichomonas musculis* (termed *T. mu*) can modulate gut mucosal immunity in mice, protecting the host from enteric infection.

"The finding was total serendipity, we observed that wild-type C57BL/6 mice that were bred in-house had increased numbers of immune cells and increased levels of inflammatory cytokines compared to animals obtained from a commercial vendor," explains author Miriam Merad. "This phenotype was exclusively confined to the large intestine," she notes, adding that despite increased basal levels of intestinal inflammation these in-house mice did not display tissue injury. These observations prompted the researchers to find out the cause of this inflammation, suspecting that there might be a microbial component as both groups of mice had the same genetic background.

Merad and colleagues first assessed faecal material from the different mouse populations. Microscopic analysis revealed the presence of a unicellular flagellated microorganism that resembled a parabasalid protozoan parasite in the in-house mice, which closely adhered to the intestinal epithelium. Ribosomal DNA sequencing confirmed that this microorganism (now termed *T. mu*) had not been characterized previously, being similar to but distinct from *Tritrichomonas muris*. Screening of faecal samples from 188 healthy individuals from Colombia with no gastrointestinal infections and from 98 *Giardia*-positive samples from individuals from South America, Africa, Europe and Asia revealed the presence of the *T. mu* human homologue *Dientamoeba fragilis*.

Crucially, the investigators found that colonization with *T. mu* modulated gut mucosal immunity in mice, activating the host epithelial inflammasome and inducing IL-18 production. This epithelial-derived IL-18 promoted T helper (T_H)1 and T_H17 immunity via dendritic cells. Interestingly, immune modulation via *T. mu* colonization had different outcomes in different settings. *T. mu* colonization worsened T-cell-mediated colitis (more severe disease scores) and sporadic colorectal cancer (increased tumour burden in $Apc^{min/+}$ mice) in experimental settings. By contrast, the *T. mu*-modulated immune response protected mice from *Salmonella* infection.

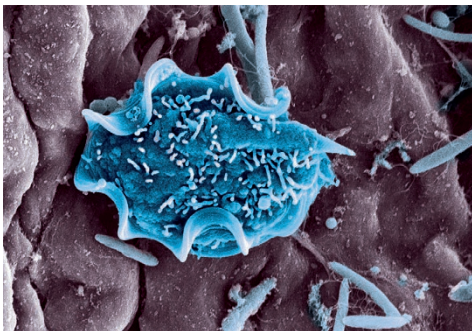

Image courtesy of A. Mortha and A. Chudnovskiy.

"These studies emphasize further the importance of nonbacterial species to our studies of the microbiome," concludes Merad. The researchers are now analysing the contributions of the human *T. mu* homologues in human gut tissue immunity.

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ORIGINAL ARTICLE Chudnovskiy, A. *et al.* Host-protozoan interactions protect from mucosal infections through activation of the inflammasome. *Cell* **167**, 1–13 (2016)