Host-Protozoan Interactions Protect from Mucosal Infections through Activation of the Inflammasome

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BACKGROUND:

- Consortium of microbes in the mammalian gut: viruses, prokaryotic bacteria, and eukaryotic microbes (fungi, helminths, and protists).

- Protists:
  - Some are pathogens of the mouse and human intestine: e.g. Toxoplasma gondii

  - Others are still neglected: commensal, pathobionts or pathogens???: stramenopiles (Blastocystis spp.), diplomonads (Enteromonas spp.), amoebozoa (Entamoeba dispar, Entamoeba coli), and parabasalids (Pentatrichomonas hominis, Dientamoeba fragilis).

  - The impact of these species on the host and host immune system is totally understudied.

  QUESTION: What is the impact of T. mu on the host and host immune system?

REFERENCES

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2. Expansion of IL-13 and IL-5 producing ILC2 in animals infected with Tritrichomonas spp, critical to restrain protozoan loads in mucosal sites. *Howitt, M.R., et al. (2016). Tuft cells, taste-chemosensory cells, orchestrate parasite type 2 immunity in the gut. Science 351, 1329–1333.*

3. *D. fragilis*, (T.mu's closest human ortholog) unicellular parasite capable of inducing gastro-intestinal symptoms in infected human individuals. *Barratt, J.L. et al(2011). The ambiguous life of Dientamoeba fragilis: the need to investigate current hypotheses on transmission. Parasitology 138, 557–572.*

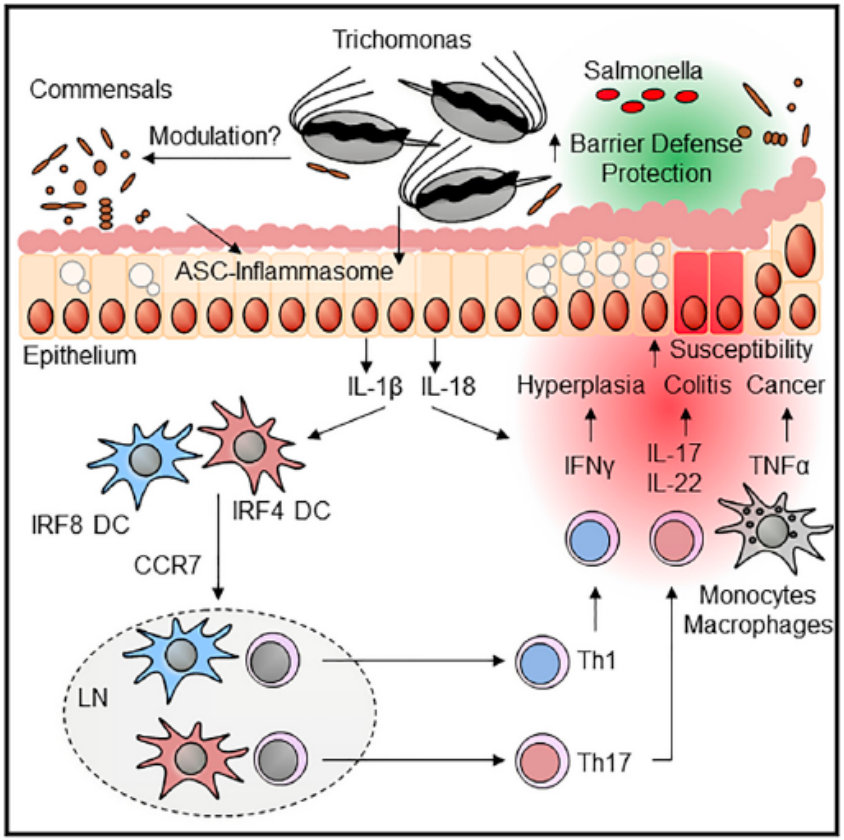
4. *D. fragilis* is an etiological agent of irritable bowel syndrome (IBS). *Stark, D., et al (2007). Irritable bowel syndrome: a review on the role of intestinal protozoa and the importance of their detection and diagnosis. Int. J. Parasitol. 37, 11–20.*

5. *D. fragilis has a* protective effect against disease flares in IBD patients. *Petersen, A.M., et al. (2013). Active ulcerative colitis associated with low prevalence of Blastocystis and Dientamoeba fragilis infection. Scand. J. Gastroenterol. 48, 638–639.*

FINDINGS:

- The murine commensal ***Tritrichomonas musculis*** **(T.mu)**, shapes the intestinal immune system:
  1. inducing **inflammasome activation** and **IL-18 release** by intestinal epithelial cells, **Th1 and Th17 response**
  2. contributing to **host protection** against mucosal bacterial infections
  3. exacerbating disease in **colitis and tumorogenesis**.

- Identification of the critical contribution of protozoa to mucosal defenses, previously unappreciated!



Stable Engraftment of *Bifidobacterium longum* AH1206 in the Human Gut Depends on Individualized Features of the Resident Microbiome

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BACKGROUND:

- Darwin's naturalization hypothesis: introduced species are more successful at surviving in communities in which their close relatives are absent.

- Introduced bacterial strains are more likely to be established in the recipient if the species are already present. *Stecher, B., et al. (2010). Likewill to like: abundances of closely related species can predict susceptibility to intestinal colonization by pathogenic and commensal bacteria. PLoS Pathog. 6, e1000711.* Li, S.S., et al. (2016). *Durable coexistence of donor and recipient strains after fecal microbiota transplantation. Science 352, 586–589.*

- Beneficial effects of of lactic acid bacteria in human clinical trials. *Ceapa, C., et al (2013). Influence of fermented milk products, prebiotics and probiotics on microbiota composition and health. Best Pract. Res. Clin. Gastroenterol. 27, 139–155.*

- Most probiotic strains show high survival rates in the gastrointestinal tract, but are detectable for less than 2 weeks following cessation of intake. *Alander, M., et al (2001). Effect of galacto-oligosaccharide supplementation on human faecal microflora and on survival and persistence of Bifidobacterium lactis Bb-12 in the gastrointestinal tract. Int. Dairy J. 11, 817–825.*

- The introduction of a live microbe does not lead to alterations of the fecal microbiota. *Kristensen, et al (2016). Alterations in fecal microbiota composition by probiotic supplementation in healthy adults: a systematic review of randomized controlled trials. Genome Med. 8, 52.*

QUESTIONS:

- How long can probiotic be established in the human gastrointestinal tract?
- What is the impact of probiotic administration on the resident bacterial community?
- What is the effect of probiotics on gastrointestinal symptoms of the subjects?
- Which are the precise community features of the resident microbiome that determine probiotic colonization?

FINDINGS:

- specific core members of the gut microbiome and functional genes associated with them can be established in humans in which they are absent.