

Contextual effect and safety of probiotics consumption in intestinal inflammatory processes

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The intestinal mucosa is constantly exposed to various environmental antigens, originating from pathogens, or of harmless origin such as dietary components or antigens from the commensal microbiota, which affect immune homeostasis. Therefore, the immune system associated with the intestinal mucosa requires a complex cellular network of highly regulated mechanisms in order to maintain tissue balance and, at the same time, protect against the entry of pathogens. Therefore, the immune system associated with the intestinal mucosa requires a complex cellular network of highly regulated mechanisms in order to maintain tissue balance and, at the same time, protect against the entry of pathogens. Such mechanisms include specialized dendritic cells (DCs) (which express the CD103+CD11b- and CD103+CD11b+ molecules) that induce canonical responses, such as regulatory T cells (Treg) that control inflammatory responses and promote tolerance to harmless antigens, and effector cells (particularly Th17 lymphocytes) that promote tissue-specific barrier immunity. Such barrier response encompasses specialized epithelia, the production of antimicrobial molecules, antibodies, and mononuclear phagocytes. Although the intestinal mucosal immune system is constantly shaped by host genetic factors, resident microbiota, dietary habits, and exposure to environmental pathogens, the result of these interactions is usually a return to tissue homeostasis. However, disruption of the balance between tolerance and barrier immunity can lead to chronic inflammatory diseases, such as inflammatory bowel diseases (IBD). In the Mucosal Immunology Lab, we have been studying how probiotics, dietary changes, or infection episodes, shape the gut-associated mucosal immune system. We observed that, after infection clearance, *Yersinia pseudotuberculosis* (YP) causes a permanent remodeling of the immune and lymphatic systems of the gastrointestinal tract. This process, named by us “immunological scarring”, is directly related to susceptibility to experimental colitis as it compromises the migration of tolerogenic dendritic cells (DCs) to mesenteric lymph nodes. Here, we tried to reverse the immunological scarring by using two different supplements: (1) an inactivated *Saccharomyces cerevisiae* strain enriched with selenium (Se) and (2) the active yeast *S. cerevisiae* (SC) (strain UFMG A-905). Our group hypothesized that both treatments could recover the mesenteric lymphatic integrity and the migratory capacity of the CD103+ DCs, crucial for inducing tolerogenic responses in the intestine. Testing on C57BL/6 mice involved treatment 2 weeks post-infection, to reverse the immunological scar, continuing until pathogen elimination to prevent its establishment. The results obtained until now showed that post-infection treatment with the yeast SC UFMG A-905, contrary to our initial hypothesis, aggravated chronic inflammation in previously infected animals, indicated by increased recruitment of neutrophils and Th1 cells to the mesentery and mesenteric lymph nodes (MLNs) post-infection and animal mortality. We also observed that neither treatment was sufficient to restore the integrity of the mesenteric lymphatic vessels, since the treated animals also presented reduced frequency of CD103+CD11b- and CD103+CD11b+ DCs in the MLNs. Although these treatments have proven efficacy against intestinal inflammatory processes, we hypothesize that their beneficial effect on the mucosa is contextual and that probiotics consumption during immunological scarring may further weaken the intestinal barrier.

References

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