A reductionist model to study host–microbe interactions in intestinal inflammation

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Abstract

The gut microbiome is altered in patients with inflammatory bowel disease and plays an important role in colitis development in mouse models. However, the roles of host-microbe interactions in intestinal inflammation remain unclear and are difficult to study because of interindividual microbiome variability. To address these issues, researchers recently used a reductionist model and multiomics to study host-microbe interactions in wild-type and colitis-prone Was-/- mice. Was-/- mice colonized with both altered Schaedler flora (ASF) and Helicobacter developed colitis, while those colonized with either type alone did not. Bacteria also infiltrated the colon mucus layer in Was-/- mice, and Helicobacter and mucosal Mucispirillum schaedleri were positively correlated with fecal levels of the intestinal inflammation marker LCN2. Consistent with this, fitness- and immunogenicity-enhancing M. schaedleri genes were upregulated in Was-/- mice. In contrast, Parabacteroides goldsteinii was negatively correlated with LCN2.,and P. goldsteinii genes facilitating stress adaptation were downregulated in Was-/- mice. Unlike Was-/- mice, wild-type mice did not develop inflammation, and their Helicobacter abundance was negatively correlated with LCN2. Although the simplified microbiomes did not mimic real-life microbiomes, the results indicate that microbial influences on the immune system can be context dependent and emphasize the need to consider different genetic contexts, bacterial transcription profiles, and bacterial fitness levels when developing microbiota-based therapeutics