INVESTIGATING THE ROLE OF THE INTERCRYPT GOBLET CELLS IN INFLAMMATORY BOWEL DISEASES

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Objectives: The intestinal mucus layer secreted by specialized secretory cells, called goblet cells (GCs) covers the intestinal epithelium to provide lubrication and protection against the luminal material and the microbial community living in our gastrointestinal tract. GCs are a heterogeneous cell population, and the ones located at the surface epithelium of the colon between crypts, denoted intercrypt GCs (icGCs) secrete mucus with different properties compared to the mucus secreted by the crypt-residing GCs. A reduced icGC number leads to a deficient intercrypt mucus secretion and disruption of the mucus layer. These alterations correlate with increased colitis susceptibility in murine models and are found in patients with both active and remission ulcerative colitis (UC). However, the mechanism behind the impairment of such GCs population is still unknown and needs further investigation.

Methods: Co-housed and non-cohoused mice lacking the gene interleukin-10 (IL-$10^{-/-}$), a common genetic IBD mouse model, and their respective control littermates were sacrificed at different ages. The number and the distribution of icGCs were evaluated by *in-situ* hybridization RNAscope and mucus barrier integrity was assessed ex-vivo by assessment of mucus penetrability using bacteria-sized beads.

Results: The number and distribution of the icGCs are affected during disease progression, strengthening our hypothesis that the fate of these cells is under inflammatory control. Additionally, the disease progression in IL-$10^{-/-}$ mice was associated with an increased mucus layer permeability to bacteria-sized beads when compared to their respective controls. Furthermore, the first pilot study in co-housed and non-cohoused IL-$10^{-/-}$ mice and their respective controls underlined that co-housing also affected mucus properties in the control mice as compared to the IL-$10^{-/-}$ further underlying the importance of the microbial communities as a pivotal modulator of the mucus properties.

Conclusion: Taken together, our preliminary results elucidate potential mechanisms implicated in the regulation of the icGCs population as well as of the mucus properties in a genetic IBD mouse model. We propose that these differences could be related to changes in both the inflammatory state and the composition of the microbial communities occurring during disease progression.