

Macrophages in distal colon form a unique type of trans-epithelial dendrites and are specialized to sample absorbed fluids

One of the main function of the colon is to harbor the largest amounts of microorganisms in the body, and at the same time to absorb fluids. Thus, the colonic mucosa is constantly facing influx of potentially dangerous metabolites locally produced by bacteria and fungi. How the peripheral immune system ensures rapid quality-check of absorbed fluids in the colon is unknown. On the other hand, there is increasing evidence that different macrophages (MFs) types populate the distinct regions of the gut and are key players in the regulation of the intestinal immune system (Mowat and Agace, 2017). We therefore hypothesized that there might be locally specialized MFs within the colonic mucosa that support the distinct functions of its proximal and distal regions. We here identify a MF population located in the distal colon, which forms a unique type of trans-epithelial dendrites referred to as "balloon-like membrane protrusions" (BLiMPs). BLiMPs cross the basal membrane to tightly contact colonocytes and sample the fluid that these cells absorb. Single Cell RNA sequencing showed that BLiMPs-wearing MFs express fungi-sensing genes, which are indeed known to be concentrated in the distal colon. Accordingly, we found that BLiMPs do not form upon fungi depletion and that their depletion results in local epithelial cell death. Interestingly, fungal overgrowth and release of metabolites can lead to epithelial cell apoptosis, leakage of fungal products into the blood stream and sepsis (Upperman, 2003). So far, our results are consistent with a model where BLiMPs-wearing macrophages control the rate of fluid absorption by epithelial cells, preventing potentially dangerous fungal metabolites from entering into the mucosa and the blood stream.

Keywords : macrophages, colon, water absorption, fungi

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