The Colonic Crypt Protects Stem Cells from Microbiota-Derived Metabolites

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Background

- Stem and progenitor cells located in the crypts of Lieberkühn give rise to all differentiated cell types of the intestinal epithelial layer.
- The impact of the microbiota and its metabolites is poorly understood.

Findings

- Butyrate suppresses epithelial proliferation.
- Colonocytes protect stem and progenitor cells from the butyrate by metabolizing it.
- Butyrate suppresses stem cell proliferation via a Foxo3-dependent mechanism.
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Graphical Abstract

Highlights
- Microbial metabolite screening identifies intestinal stem cell effectors
- Butyrate suppresses intestinal stem cell proliferation upon exposure
- Crypt structure and colonocytes protect stem/progenitor cells

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In Brief
The architecture of intestinal crypts protects the stem cells at their base from a growth-inhibiting metabolite derived from the gut microbiome. Might these findings suggest co-evolution of mammalian anatomy with commensal flora?

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References

Review on intestinal stem cells

Impact of the microbiota on the intestinal content metabolites

Description of the spheroid culture technique
Gut Microbiota Drive Autoimmune Arthritis by Promoting Differentiation and Migration of Peyer’s Patch T Follicular Helper Cells

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Background

- SFB drives autoimmune arthritis in the K/BxN mouse model by the induction of Th17 cells.
- T follicular helper cells can play a role in the development of rheumatoid arthritis.
- Impairment of the TFH can alter the microbiota.

Findings

- SFB drives K/BxN arthritis in SPF conditions with increased TFH and GC B cells in the spleen, lymph nodes and PP.
- TFH differentiation is induced in the PP; the generated cells migrate to systemic sites.
- PP and DCs are essential for the SFB-induced arthritis.
- SFB enhances TFH differentiation by inhibiting IL-2 signaling.
Gut Microbiota Drive Autoimmune Arthritis by Promoting Differentiation and Migration of Peyer’s Patch T Follicular Helper Cells

**Highlights**
- SFB enhance autoimmune arthritis, reflected by elevated auto-Ab, GC, and Tfh cell responses
- SFB-driven differentiation and egress of PP Tfh cells to systemic sites cause disease
- SFB induce PP Tfh cell differentiation by limiting the access of IL-2 to PP CD4^+ T cells
- DCs are required for SFB-mediated IL-2Rα suppression and Bcl-6 upregulation in PPs

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**In Brief**
The mechanism by which gut microbiota affect systemic diseases is unclear. Wu and colleagues demonstrate that a type of commensal gut bacteria, segmented filamentous bacteria, triggers autoimmune arthritis by inducing differentiation and migration of gut T follicular helper cells to systemic lymphoid sites, leading to increased auto-antibody production and exacerbation of arthritis.

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References

Review on the modulation of pro-inflammatory responses by the microbiota


Review: TFH and disease pathogenesis


SFB, arthritis and Th17 cells


Arthritis model