

MICROBIOME

The microbiota's cryptic message

The colonic crypt harbours a specialized aerobic microbiota that lives in close contact with the host epithelium. How these symbiotic bacteria influence tissue homeostasis is incompletely understood. Pédrón, Sansonetti and colleagues now find that members of the core crypt microbiota induce epithelial stem cell necroptosis and differentiation towards goblet cells.

The authors cultured microbiota from murine colonic crypts using selective medium and aeration and selected four representative strains for further experiments: *Acinetobacter modestus*, *Acinetobacter radioresistens*, *Delftia tsuruhatensis* and *Stenotrophomonas maltophilia*. Germ-free mice that were mono-colonized with each of these strains showed decreased proliferation and increased cell death in the epithelium of the proximal colon compared with non-colonized germ-free mice and germ-free mice monocolonized by *Bacteroides fragilis*. No changes were

observed in *Tlr4*-knockout mice, which indicates that the crypt microbiota modulates epithelial regeneration through lipopolysaccharide (LPS).

To determine the underlying molecular mechanisms, the authors incubated proximal colon organoids with sonicated preparations of each of the cultured crypt microbiota strains. Stimulation with the bacterial sonicates decreased survival and development of organoids, and this effect again was dependent on *Tlr4*. LPS that was purified from each of

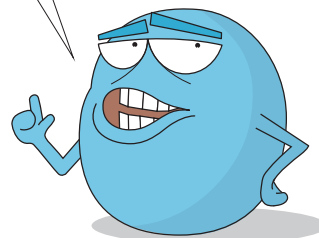
the four strains had similar effects. Interestingly, organoids from *Ripk3*-knockout mice were also protected from the deleterious effects of the purified LPS, which suggests that LPS induces necroptosis. Finally, purified LPS induced differentiation of the organoid epithelial cells towards goblet cells, although this effect varied between bacterial strains.

The crypt microbiota and the host epithelium interact closely, and LPS is one of the key bacterial molecules that regulate epithelial proliferation and differentiation. Pédrón, Sansonetti and colleagues conclude that the balance of signals that are produced by the local microbiota shape the crypt niche.

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“ the bacterial sonicates decreased survival and development of organoids ”

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ORIGINAL ARTICLE Naito, T. et al.

Lipopolysaccharide from crypt-specific core microbiota modulates the colonic epithelial proliferation-to-differentiation balance. *mBio* **8**, e01680 (2017)

FURTHER READING Donaldson, G. P., Lee, S. M. & Mazmanian, S. K. Gut biogeography of the intestinal microbiota. *Nat. Rev. Microbiol.* **14**, 20–32 (2016)