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GUT MICROBIOTA

Microbiota promote gut healing

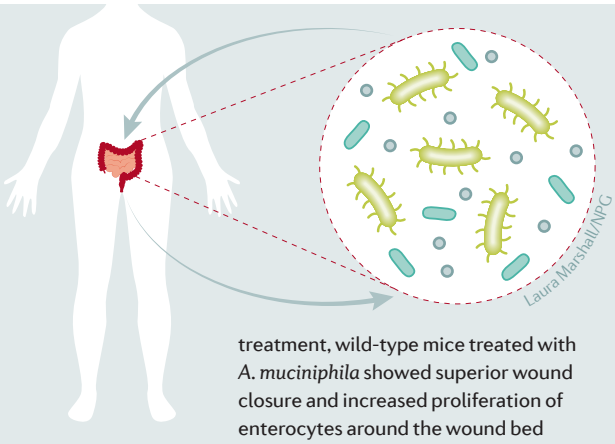
Wounds in the gut are associated with microenvironment changes that encourage the growth of microbial species that promote healing, according to new research.

Damage to the intestinal mucosa can occur as a result of physical trauma, infection or inflammatory conditions. Although the intestinal wound healing response in humans and mice is well described, the role of the gut microbiota in the process has not been investigated. "We used the mouse endoscope-wounding model we and others have used in past reports to induce a controlled and uniform lesion in the colonic mucosa of wild-type mice without associated harmful effects," explains author Andrew Neish.

Identification of wound-associated bacterial species at 0, 2, 4 and 6 days after injury showed that the abundance of anaerobic bacteria, in particular *Akkermansia* spp., increased substantially in early regenerative mucosa (between 2 and 4 days post-injury). The researchers hypothesized that changes to the tissue microenvironment after wound induction altered bacterial composition; they found that the oxygen concentration in the wounded mucosa 2 days after injury was lower than baseline concentrations.

Wound-associated neutrophils are known to deplete tissue oxygen levels through the respiratory burst. Mice lacking the gene *Fpr1*, which encodes a protein important for producing respiratory bursts in neutrophils, did not show decreased colonic mucosa oxygen concentrations after wounding, in contrast with wild-type mice. Strikingly, whereas *Akkermansia* spp. comprised ~7.8% of total wound-associated bacteria in wild-type mice at day 2, only ~1.2% of bacteria in wounds in *Fpr1*$^{-/-}$ mice at day 2 were *Akkermansia* spp.

To investigate whether *Akkermansia* spp. directly influenced intestinal wound healing, the researchers administered *Akkermensia muciniphila* or inert control intrarectally to wild-type or *Fpr1*$^{-/-}$ mice with mucosal wounds. After 6 days of treatment, wild-type mice treated with *A. muciniphila* showed superior wound closure and increased proliferation of enterocytes around the wound bed compared with wild-type control mice. By contrast, *A. muciniphila* treatment did not improve wound closure in *Fpr1*$^{-/-}$ mice, suggesting *Fpr1* is critical for the beneficial effects of the bacteria on wound healing.



> "...mice treated with *A. muciniphila* showed superior wound closure..."

"Our results show that wound-associated microbiota are not mere bystanders," enthuses Neish. "Members of these bacteria could be explored as therapeutic approaches to wound healing."

Hugh Thomas

ORIGINAL ARTICLE Alam, A. *et al.* The microenvironment of injured murine gut elicits a local pro-restitutive microbiota. *Nat. Microbiol.* **1**, 15021 (2016)