Nature Reviews Gastroenterology & Hepatology **12**, 371 (2015); published online 26 May 2015; doi:10.1038/nrgastro.2015.92

GUT MICROBIOTA

Commensal bacteria and intestinal surgery complications

Enterococcus faecalis contributes to the development of anastomotic leaks after intestinal surgery in rats, reports a new study in *Science Translational Medicine*.

Resection and reconnection (anastomosis) of intestinal segments is sometimes followed by a complication in which the intestine fails to heal, ruptures and leaks internally, leading to peritonitis, sepsis or even death. The underlying cause of anastomotic leaks is unknown, although the involvement of intestinal microbes was suspected as use of antibiotics prevented anastomotic leaks in some studies.

Colon resection and anastomosis were performed in rats either with or without devascularization of a colon segment adjacent to the anastomosis. Devascularization resulted in anastomotic leaks in 50% of animals, compared with no leaks in rats with intact vasculature. Substantial collagen depletion was evident in tissue from anastomotic leaks compared with healed anastomoses, which the authors believed could be caused by microbiota. Indeed, *E. faecalis*, isolated from anastomotic tissue, was found to have high collagen-degrading activity. Colon tissue extracts exposed *in vitro* to *E. faecalis* induced matrix metalloproteinase (MMP) 9 cleavage, thereby activating it to break down extracellular matrix proteins. In addition, a specific MMP9 inhibitor prevented anastomotic leaks in the rat model. "Multiple contingencies must be met first [before commensal bacteria become harmful], such as disturbance of the normal microbiome, presence of bacteria capable of producing collagenase, and the release of host signals from tissue trauma that activate these bacteria to produce collagenase," explains corresponding author John Alverdy.

16S ribosomal RNA analysis of human colon anastomotic segments ($n = 11$) was performed to determine if humans also harbour microbial organisms capable of degrading collagen and activating MMP9. Results showed a disrupted microbial community and identified two species, including *E. faecalis* that demonstrated collagenase and MMP9-activating properties. These bacteria were not killed by the standard intravenous antibiotics given to the patients before surgery.

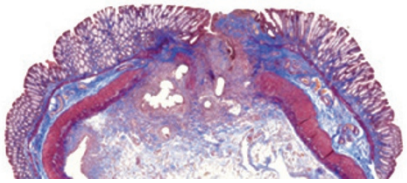

Image courtesy of J. C. Alverdy

"Now with this evidence in hand, we can do something about [anastomotic leaks]; especially since our work shows that the antibiotics we use and the way we use them is probably inadequate," emphasizes Alverdy.

Christine Weber

Original article Shogan, B. D. *et al.* Collagen degradation and MMP9 activation by *Enterococcus faecalis* contribute to intestinal anastomotic leak. *Sci. Transl. Med.* **7**, 286ra68 (2015)