*Nature Reviews Gastroenterology & Hepatology* **9**, 558 (2012); published online 4 September 2012; doi:10.1038/nrgastro.2012.172

GUT MICROBIOTA

# Colorectal cancer—driven by inflammation and gut bacteria?

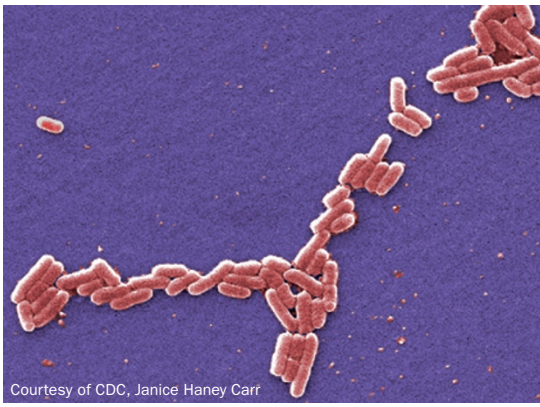
New research published in *Science* adds further weight to the role of the gut microbiota in the development of colorectal cancer (CRC). "The findings point to a novel mechanism by which intestinal inflammation promotes the development of colitis-associated CRC, by modulating the genotoxic capacity of the microbiota," explains team leader Christian Jobin, University of North Carolina at Chapel Hill, USA.

By examining mice susceptible to colitis (*Il10*$^{-/-}$ mice) and subsequent CRC (by administration of the carcinogen azoxymethane), the authors tried to piece together how inflammation and the gut microbiota contributes to carcinogenesis.

First, they found that mice with colitis had lower diversity in their gut microbiota than wild-type mice, with a shift in microbial composition towards increased numbers of commensal *Escherichia coli* (a 100-fold increase when intestinal inflammation was present).

Crucially, the authors next confirmed that *E. coli* specifically had a role in CRC development. The majority (80%) of azoxymethane-treated *Il10*$^{-/-}$ mice colonized with the mouse commensal *E. coli* str. NC101 developed invasive mucinous adenocarcinoma, whereas mice colonized with the human commensal *Enterococcus faecalis* rarely had tumours, despite similar levels of intestinal inflammation.

Upon further analyses, *E. coli* str. NC101 was revealed to produce the genotoxin colibactin—a toxin that induces DNA damage (a critical trigger of cancer)—the genes for which are encoded on the *pks* pathogenicity island. Genetic deletion of the *pks* island did not diminish the bacteria's ability to induce colitis, but did hamper the development of neoplastic lesions and invasive adenocarcinomas when tested in the colitis-associated CRC mouse model. Importantly, this *pks* island was detected in clinical isolates from patients with IBD (14 of 35; 40.0%) or CRC (14 of 21; 66.7%), demonstrating that genotoxic *E. coli* are associated with chronic intestinal inflammation and CRC in humans.



Courtesy of CDC, Janice Haney Carr

"The next frontier of medicine is to understand the interaction between host factors and the microbiome and to harness this knowledge for therapeutic purposes," opines Jobin. Targeting the microbes in our gut could be a new way to prevent CRC development. Jobin adds: "It might even be possible to utilize microbial genes as CRC biomarkers".

*Katrina Ray*

**Original article** Arthur, J. C. *et al.* Intestinal inflammation targets cancer-inducing activity of the microbiota. *Science* doi:10.1126/science.1224820

**Further reading** Tjalsma, H. *et al.* A bacterial driver–passenger model for colorectal cancer: beyond the usual suspects. *Nat. Rev. Microbiol.* **10**, 575–582 (2012)