CANCER

Human bacterium induces colon tumors in mice through activation of TH17 cells

A human commensal bacterium can promote colon tumorigenesis in a mouse model of carcinogenesis, report researchers at the Johns Hopkins University School of Medicine. "The colon tumor induction occurred, in part, through activation of specific [adaptive] immune pathways," says project leader Cynthia Sears.

Inflammation is an important factor in carcinogenesis. Several studies have highlighted the role of innate immunity in this process, but "…little information exists on how adaptive immunity, particularly T-cell responses, promote cancer," explain the investigators.

"We chose the multiple intestinal neoplasia (Min) mouse model ... because the mutation [in *Apc*] that promotes intestinal adenoma formation in these mice is common in sporadic human colon cancer and also defines the genetic defect in the familial adenomatosis polyposis syndrome," says Sears. Mice infected with enterotoxin-producing *Bacteroides fragilis* (ETBF) rapidly developed multiple colonic tumors, which were not seen in mice infected with nonenterotoxin-producing *B. fragilis* or in sham-inoculated mice. The researchers used antibody blockade and selective T-cell depletion to show that tumor formation was associated with strong local activation of Stat3 signaling, which in turn induced a T_H17 mucosal immune response accompanied by epithelial hyperproliferation and carcinogenesis. Tumor formation depended on the production of IL-17.

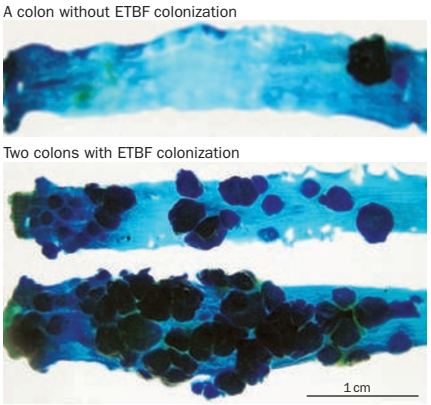

Image courtesy of C. Sears

As ETBF induces inflammatory diarrhea in human adults and children, but also asymptomatically colonizes up to 35% of adults, Sears now plans to translate this work to humans. "We hope to be able to evaluate how either microbe exposure or the host immune response relate to the epidemiology of the colon tumors and the prognosis of the patients."

Joana Osório

Original article Wu, S. *et al.* A human colonic commensal promotes colon tumorigenesis via activation of T helper type 17 T cell responses. *Nat. Med.* **15**, 1016–1022 (2009).