CCI-16

CCL3-CCR5 axis regulates progression of fibrosis occurring as a result of chronic colitis in mice

Soichiro Sasaki, Tomohisa Baba and Naofumi Mukaida

Div. Molec. Bioregulation, Cancer Res. Inst., Kanazawa Univ., Kanazawa

Abstract

Patients with ulcerative colitis are sometimes complicated with colon carcinoma. This carcinogenesis can be recapitulated in mice by the combined treatment with azoxymethane (AOM)-dextran sulfate sodium (DSS). Collagen type I- and α-smooth muscle actin (SMA)-positive cells accumulated in the course of carcinogenesis process of wild-type (WT) mice with intracolonal fibrocytes/fibroblasts expressing CCL3 and its specific receptor, CCR5. Moreover, *CCL3* ablation decreased collagen type I- and α- SMA-positive cell numbers and eventually reduced the numbers and sizes of colon tumors, compared with WT mice. Likewise, reduction in fibrosis and tumor incidence was observed in mice deficient in CCR5. Furthermore, WT mice transplanted with CCL3 or CCR5-deficient mouse-derived bone marrow cells, developed significantly fewer tumors after AOM/DSS treatment, compared with WT mice. Thus, chronic colitis-associated fibrosis and subsequent carcinogenesis can be regulated by the CCL3/CCR5-expressing bone-marrow-derived cells. Thus, blockade of the CCL3-CCR5 axis can be a potential therapeutic target against colon cancer, particularly one that is associated with fibrosis.