Inflammation contributes to colon cancer

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Researchers led by Drs. Lillian Maggio-Price and Brian Iritani at The University of Washington found that mice that lack the immune inhibitory molecule Smad3 are acutely sensitive to both bacterially-induced inflammation and cancer. They report these findings in the January 2009 issue of *The American Journal of Pathology*.

Bacteria contribute to the development of certain cancers, in some measure, by stimulating chronic inflammation. Absence of a molecule that inhibits inflammation, Smad3, may therefore increase susceptibility to colon cancer.

To examine whether Smad3 signaling contributes to development of colon cancer, Maggio-Price et al examined mice deficient in Smad3 that lack of adaptive immune responses. They found that these mice are acutely sensitive to bacterially-induced inflammation and cancer due to both deficient T regulatory cell function and increased expression of proinflammatory cytokines. Through increased expression of both pro-oncogenic and anti-apoptotic proteins, epithelial cells in colonic tissues underwent both enhanced proliferation and survival.

"That the inflammatory response to microorganisms is a key event in these results reveals important 'tumor-suppressive' functions for Smad3 in T effector cells, T regulatory cells, and intestinal epithelial cells, all of which may normally limit the development of colon cancer in response to bacterial inflammation," explains the groups led by Dr. Maggio-Price and Dr. Iritani.

Reference: Maggio-Price L, Treuting P, Bielefeldt-Ohmann H, Seamons A, Drivdahl R, Zeng W, Lai L-H, Huycke M, Phelps S, Brabb T1, Iritani BM: Bacterial infection of Smad3/Rag2 double-null mice with TGF beta dysregulation as a model for studying inflammation-associated colon cancer. *Am J Pathol* 2009, 174:317-329

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