SMAD4 clue to colon cancer

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Chronic inflammation is a predisposing condition for colorectal cancer, the third leading cause of cancer-related deaths in the United States.

Reporting last month in the journal *Cellular and Molecular Gastroenterology and Hepatology*, Anna Means, Ph.D., and colleagues have now linked inflammation-driven carcinogenesis in the colon to loss of an important signaling protein called SMAD4.

SMAD4 is part of the transforming growth factor beta (TGF-beta) signaling pathway that in the epithelium of the colon regulates the immune/inflammatory response to infection.

Specific deletion of the Smad4gene in normal mouse colon epithelial cells grown in vivo increased the expression of inflammatory mediators. In adult mice in the presence of inflammation, deletion resulted in tumors bearing a striking resemblance to human colitis-associated carcinoma.

Loss of SMAD4 also was observed in 48 percent of human colitis-associated carcinomas compared with 19 percent of sporadic colorectal carcinomas. "This loss may be an important factor in progression from premalignant lesions to invasive malignancy," the researchers concluded.

More information: Anna L. Means et al. Epithelial Smad4 Deletion Up-Regulates Inflammation and Promotes Inflammation-Associated Cancer, *Cellular and Molecular Gastroenterology and Hepatology* (2018). DOI: 10.1016/j.jcmgh.2018.05.006

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