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Inflammation directly linked to colon cancer

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While chronic inflammation is widely believed to be a predisposing factor for colon cancer, the exact mechanisms linking these conditions have remained elusive. Scientists at the Melbourne Branch of the international Ludwig Institute for Cancer Research (LICR) and the Technical University Munich have jointly discovered a new piece of this puzzle by demonstrating how the Stat3 protein links inflammation to tumor development, a discovery that may well lead to the identification of new therapeutic targets for colon cancer.

Aberrant activation of the intracellular signaling protein, Stat3, has been associated with inflammation and several cancers, including those of the gastrointestinal tract. The results published on-line today in the journal *Cancer Cell* provide the first direct evidence confirming the role for Stat3 in inflammation-associated tumorigenesis. Using an inflammation-associated cancer model in genetically manipulated mice, the team identified a relationship between epithelial cell Stat3 activity and colonic tumor incidence, as well as tumor growth. They also determined that stimulation of Stat3 by the cytokines IL-6 and IL-11, chemicals produced by inflammatory and other tumor-associated cells, promotes both cell survival and growth of tumor cells.

The collaboration was sparked by discussions between Professors Matthias Ernst (LICR) and Florian Greten (Technical University Munich) at a scientific meeting, when they discovered they were both individually pursuing the mechanism by which Stat3 links inflammation to gastrointestinal cancers. Rather than compete, the two decided to join forces to discover the Stat3 connection between inflammation and colon

cancer.

"Colon cancer is the second most frequent malignancy in the developed world so it was no surprise to find another group working on the Stat3 question and trying to find new ways to target colon cancer," said LICR's Professor Ernst, the joint senior author of the publication. "Together we've been able to learn how Stat3 bridges chronic inflammation and tumor promotion by mediating cell survival during an inflammatory event and enhancing tumor cell growth. Our new findings are very much in line with our previous work on the role of Stat3 in mediating inflammation- associated gastric cancer. We expect this knowledge to strengthen efforts for the development of therapeutics that target the link between inflammation and cancer to ultimately benefit the treatment of cancer patients."

Incidentally, the group of Professor Michael Karin from the University of California at San Diego, has reached similar conclusions in paper published in the same issue of *Cancer Cell*.

Source: Ludwig Institute for Cancer Research