Aspirin's ability to protect against colorectal cancer may depend on inflammatory pathways

March 9 2011

The reduced risk of colorectal cancer associated with taking aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs) may be confined to individuals already at risk because of elevations in a particular inflammatory factor in the blood. In a paper in the March issue of *Gastroenterology*, investigators from Massachusetts General Hospital (MGH) and Dana-Farber Cancer Institute report finding that higher baseline levels of a novel inflammatory marker indicated increased risk of developing colorectal tumors and also predicted who might benefit from taking aspirin or NSAIDs.

"These findings suggest that a blood biomarker may be helpful in deciding whether individuals should take aspirin or NSAIDs to reduce their cancer risk," says Andrew Chan, MD, MPH, of the MGH Gastrointestinal Unit, the paper's lead author. "They also indicate that chronic inflammatory pathways are quite complex and further studies are needed to understand which facets of the inflammatory response are most associated with the development of colorectal cancer."

In recent years, considerable research has supported the importance of inflammation in the development of chronic conditions such as cardiovascular disease and several forms of cancer. Many studies have found reduced incidence of colorectal cancer among individuals who regularly take aspirin or other NSAIDs, and disorders such as colitis and inflammatory bowel disease are known to increase the risk. To

investigate whether moderately elevated levels of chronic inflammation also raise the risk of colorectal cancer, the investigators analyzed data from the Nurses Health Study (NHS), which has followed more than 120,000 female registered nurses since 1976, gathering comprehensive health information from its participants every two years.

The current study analyzed data from NHS participants who had provided a blood sample in 1989 or 1990 and were cancer-free at that time. After identifying 280 participants who developed colorectal cancer during the subsequent 14 years and 555 age-matched controls who did not, the research team analyzed their baseline levels of three inflammatory factors – C-reactive protein (CRP), interleukin-6 (IL-6) and soluble tumor necrosis factor receptor-2 (sTNFR-2). Although no association was seen between levels of CRP or IL-6 and risk of developing colorectal cancer, participants with the highest levels of sTNFR-2 had a 60 percent greater risk than did those with the lowest levels of the factor. In addition, the reduced risk of developing colorectal tumors associated with regularly taking aspirin or NSAIDs was primarily seen among participants with high baseline sTNFR-2 levels.

"Our results suggest that, even though chronic inflammation may increase colorectal cancer risk, not all blood markers of inflammation are markers of that risk," says Chan. "The most common blood biomarkers of inflammation – CRP and IL-6 – do not appear to be relevant, while sTNFR-2 does. A better understanding of the significance of these markers will help us identify individuals most likely to benefit from chemoprevention using aspirin or NSAIDs."

Charles Fuchs, MD, MPH, of Dana-Farber, the study's senior author adds, "Understanding the specific inflammatory pathways that influence risk for colorectal cancer will be critical. While there is widespread agreement that inflammation is broadly related to cancer risk, some pathways may be protective while others are detrimental. More clearly

defining the relevant pathways should help us better tailor therapies and interventions that will reduce cancer risk."

Provided by Massachusetts General Hospital