

New study finds that inflammatory proteins in the colon increase incrementally with weight

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Studies in mice have demonstrated that obesity-induced inflammation contributes to the risk of colorectal cancer, but evidence in humans has been scarce. A new study shows that two inflammatory proteins in the colon increase in parallel with increasing weight in humans. An incremental rise in these pro-inflammatory proteins (called cytokines) was observed along the entire spectrum of subjects' weights, which extended from lean to obese individuals. In participants with obesity, there was evidence that two pre-cancerous cellular pathways known to be triggered by these cytokines were also activated.

The study, while modest in size, provides new evidence that obesity promotes cancer through inflammation. Secondary findings suggest that NSAIDS lower the levels of [pro-inflammatory proteins](#) in the colon, regardless of a person's weight. The study is published online in advance of print in *Cancer Epidemiology, Biomarkers & Prevention*.

Led by Joel B. Mason, M.D., a gastroenterologist who studies nutrition and cancer prevention at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University (HNRCA), the study included 42 Caucasian participants. Sixteen research participants were lean, with a BMI between 18.1 and 24.9, while 26 participants with obesity had a BMI ranging from 30.0 to 45.7. The participants were between the ages of 45 and 70 years of age and were undergoing routine screening colonoscopies at Tufts Medical Center.

Using blood samples and colonic biopsies, the researchers determined that the concentrations of two major cytokines rose in parallel with BMI. Cytokines are proteins that mediate and regulate immunity and inflammation, among other things. In addition to evidence that they can promote cancer risk in certain tissues, pro-inflammatory cytokines have been identified as actors in insulin resistance and diabetes, as well as inflammatory disorders such as arthritis.

In addition to the work analyzing cytokines, the research team studied differences in the mucosal transcriptome between the two sets of research participants, finding changes indicative of activation in two gene expression networks that are pivotal in the development of [colon cancer](#) in the participants with obesity.

"Our results establish, for the first time, that concentrations in the colon of two major cytokines increase in concert with increasing BMI in humans. The increased concentrations are accompanied by changes in gene activation within the lining of the colon that are pro-cancerous in

nature," said senior author Joel B. Mason, M.D., director of the Vitamins and Carcinogenesis Laboratory at the HNRCA.

In an effort to identify potential confounding factors, the research team determined that thirteen of the 42 study participants were also regular users of NSAIDs, such as aspirin and ibuprofen. The research team discovered that participants who took NSAIDs at least once per week, compared to those who did not, had lower levels of pro-inflammatory proteins in the colon. This pattern was consistent across the two BMI groups.

"Observational and clinical trials show aspirin can reduce the risk of colon cancer, but it continues to be controversial because of the risk of serious gastrointestinal bleeding. NSAIDs are probably working through multiple avenues, one of which is cytokines. Our observation underscores prior work that has suggested that some NSAIDs reduce the risk of colon cancer, presumed to occur through a reduction in colonic inflammation. Their use, however, has to be weighed against the potential adverse effects," said Mason.

The authors noted that the modest study size and the Caucasian population are limitations of the study, writing "given the cross-sectional nature of this study, the results cannot prove that the observed changes in the colonic transcriptome are due to the rise in cytokines...Observations from this study nevertheless underscore the potential contribution that the establishment of an inflammatory milieu in the colonic mucosa may play in explaining the enhanced risk of colon cancer due to obesity."

In the United States, [colorectal cancer](#) is the third most common cancer and the second leading cause of death among cancers that affect both men and women, according to the CDC. The American Cancer Society reports that the overall lifetime risk of developing colorectal [cancer](#) is about 1 in 22 for men and 1 in 24 for women.

The first author on the study is Anna C. Pfalzer, a Ph.D. graduate in biochemical and molecular nutrition from the Friedman School and former member of Mason's laboratory. Pfalzer is now at Vanderbilt University Medical Center. Joel Mason is also a professor at Tufts University School of Medicine and at the Friedman School of Nutrition Science and Policy at Tufts and a gastroenterologist at Tufts Medical Center.

More information: Anna C Pfalzer et al, Incremental elevations of TNF- α and IL-6 in the human colon and pro-cancerous changes in the mucosal transcriptome accompany adiposity, *Cancer Epidemiology Biomarkers & Prevention* (2018). [DOI: 10.1158/1055-9965.EPI-18-0121](https://doi.org/10.1158/1055-9965.EPI-18-0121)

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