

Dietary Vitamin D Prevents Inflammation-driven Colon Cancer

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Diet and lifestyle choices influence the risk for and, possibly, the prognosis of colon cancer. Colon cancer often arises from colonic inflammation; the risk of colon cancer is particularly increased in patients with inflammatory bowel disease (IBD). Epidemiological studies have revealed a link between adequate serum vitamin D levels and a decreased risk of colon cancer as well as a decreased risk of IBD. A new study published in *Cancer Research* provides insight into the nature of this association and reveals a potential mechanism for this protection. The results of this study indicate that vitamin D reduces inflammation and subsequent colon cancer in a mouse model of IBD-associated colon cancer. The study was led by graduate student Dr. Stacy Meeker in conjunction with Dr. William Grady in the Clinical Research Division and Dr. Lillian Maggio-Price in the Department of Comparative Medicine at the University of Washington.

The researchers used a mouse model they developed that recapitulates human inflammation-associated colon cancer more closely than other such mouse models, which use chemicals or other carcinogens to induce extensive damage to the colon (Maggio-Price *et al.*, 2006). In this study, the mice are genetically engineered to lack *SMAD3*, which is involved in a cell signaling pathway often disrupted in human colon cancer. After infection with the gut bacteria *Helicobacter bilis*, the mice develop inflammation and colitis and subsequent colon cancer within months. This model thus better mimics the disease in humans, since IBD is partly driven through the inflammatory response to gut bacteria.

Using this mouse model, the researchers assessed the influence of vitamin D on colon cancer formation by feeding mice an identical diet except for either low or high vitamin D levels (1 IU or 5 IU). The researchers found that high vitamin D intake boosted vitamin D levels in the blood roughly double that of control mice (mean: 38.4 vs. 14.4 ng/ml, $p < 0.0001$). Furthermore, the high vitamin D diet decreased the incidence of invasive colon cancer 11% vs 41% ($p = 0.0121$).

To determine the mechanism of this decrease in colon cancer formation, the researchers examined the mice at the inflammatory stage 3-7 days after bacterial infection. Mice fed the high vitamin D diet had decreased evidence of IBD versus the control mice as detected by a fecal-based assay (0.2 vs 1.0 fecal score, $p = 0.0003$), although there was no difference in bacterial colonization in the colon.

The mice fed high vitamin D at this stage had decreased immune cell infiltrates in their colons and reduced colitis compared to control animals (mean 2.7 vs. 15.5, $p < 0.0001$). The researchers examined the presence of inflammatory cytokines in the mice, and found lower IL1 β , MIP1 α , IL6, TNF α , and IFN γ levels one week post infection in the mice fed high dietary vitamin D versus control mice. These inflammatory cytokines influence cell growth, survival, differentiation and angiogenesis to contribute to carcinogenesis. The researchers found that mice fed the high vitamin D diet also had a decrease in the activity of the pro-inflammatory MAPK and NFkappaB signaling pathways in the acute phase of disease.

"Our next step is to find out how vitamin D is working to prevent inflammation and whether there is a window of opportunity when vitamin D is effective in colon cancer prevention in inflammation-associated colon cancer," according to Dr. Meeker. "We believe that further studies are needed to evaluate the potential use of vitamin D supplementation as an adjunct treatment in human patients with IBD. Our studies suggest that vitamin D could potentially aid in preventing colitis associated colon cancer by limiting inflammation which drives tumor formation in these patients."

[Meeker, S., Seamons, A., Paik, J., Treuting, P.M., Brabb, T., Grady, W.M., Maggio-Price, L.](#) 2014. Increased dietary vitamin D suppresses MAPK signaling, colitis and colon cancer. *Cancer Research*. Epub ahead of print, doi: 10.1158/0008-5472.CAN-13-2820.

See also: [Maggio-Price L, Treuting P, Zeng W, Tsang M, Bielefeldt-Ohmann H, Iritani BM.](#) 2006. Helicobacter infection is required for inflammation and colon cancer in SMAD3-deficient mice. *Cancer Research* 66:828-838

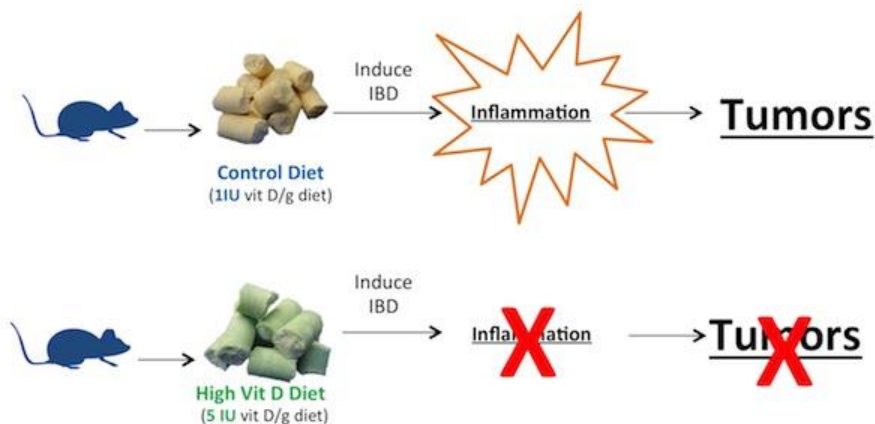


Image provided by Dr. Stacey Meeker

Increased dietary vitamin D blocks inflammation and subsequent tumor formation in a mouse model of inflammatory bowel disease-associated colon cancer.