

Findings bolster fiber's role in colon health

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This shows Dr. Vadivel Ganapathy, Chairman of the Department of Biochemistry and Molecular Biology at the Medical College of Georgia at Georgia Regents University; Dr. Nagendra Singh, MCG immunologist, member of the Cancer Immunology, Inflammation and Tolerance Program at the GRU Cancer Center, both corresponding study authors. Credit: Phil Jones

Scientists have more reasons for you to eat fiber and not abuse antibiotics.

They've shown that a receptor doctors already activate with mega-doses of niacin to protect patients' cardiovascular systems also plays a key role in preventing colon inflammation and cancer, according to a study



featured on the cover of the journal Immunity.

The finding helps explain why a high-fiber diet reduces the risk of colon problems and indicates that when fiber is lacking, niacin, or vitamin B3, just may help keep the colon healthy as well, said Dr. Vadivel Ganapathy, Chairman of the Department of Biochemistry and Molecular Biology at the Medical College of Georgia at Georgia Regents University and a corresponding study author.

The study found that mice lacking the receptor, Gpr109a, were prone to inflammation and cancer of the colon, said Dr. Nagendra Singh, MCG immunologist, member of the Cancer Immunology, Inflammation and Tolerance Program at the GRU Cancer Center, and a corresponding study author.

And, when they gave niacin to mice whose healthy colonic bacteria had been wiped out by antibiotics – a frequent occurrence in chronic antibiotic use – it helped steer <u>immune cells</u> in the colon into a safe, anti-inflammatory mode.

Good bacteria in the colon thrive on fiber and its digestion produces butyrate, a short-chain fatty acid, which Ganapathy discovered years before naturally activates Gpr109a. However this relationship appears limited to the colon, where butyrate levels can soar in the face of a high-fiber diet.

Research teams at GlaxoSmithKline and the University of Heidelberg, Germany showed in 2003 that Gpr109a receptors on the surface of fat cells mediate the protective cardiovascular effect of niacin, including increasing good cholesterol, or HDL, while decreasing levels of disease-producing LDL. Their search for other activators identified butyrate, which led Ganapathy to find that not only is the Gpr109a receptor expressed on the surface of colon cells, but that with sufficient fiber



intake, butyrate levels in the colon can activate it.

Now, he and Singh have shown activation of Gpr109a in the colon by butyrate prompts immune cells, which are in ample supply in that region, to suppress rather than promote inflammation, a factor in a number of painful conditions such as ulcerative colitis, Crohn's disease, and colorectal cancer.

Once butyrate activates the Gpr109a receptor on dendritic cells and macrophages in the colon, these immune cells start producing anti-inflammatory molecules and sending messages to the T cells, key orchestrators of immunity, to do the same, Singh said. Butyrate also prompts epithelial cells that line the colon to produce cytokines, which aid wound-healing, a critical step for resolving the intestinal inflammation that occurs in ulcerative colitis and Crohn's.

"To protect your colon, you need this receptor, as well as the fiber and butyrate which activate it," Ganapathy said. For people who won't or can't eat high-fiber diets, mega-doses of niacin, may help protect the colon, the way it's already protecting hearts, the scientists suggest.

"We think mega-doses of niacin may be useful in the treatment and/or prevention of <u>ulcerative colitis</u>, Crohn's disease, and <u>colorectal cancer</u> as well as familial adenomatous polyposis, or FAP, a genetic condition that causes polyps to develop throughout the gastrointestinal tract," Singh said. In fact, they've already shown that fiber depletion increases and mega-niacin doses decrease development of polyps in mice with FAP.

The colon and intestines are constantly exposed to foreign bacteria that enter the body primarily through the mouth. The good bacteria, which are essential to digestion and colon health, regularly communicate to immune cells that they are not the enemy and butyrate appears to be a key signal there as well, said Ganapathy, who also leads the Signaling



and Angiogenesis Program at the GRU Cancer Center.

Next steps include pursuing clinical trials of niacin supplements in colon health and, potentially, epidemiological studies that examine <u>intestinal</u> <u>inflammation</u> and colon cancer rates in patients already taking <u>niacin</u> for cardiovascular health. The research was funded by the National Institutes of Health.

Provided by Medical College of Georgia

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