Could regulating intestinal inflammation prevent colon cancer?

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Every day, our gut comes in contact with bacteria, inducing an inflammatory response that is tolerated and controlled. Sometimes the control of inflammation is lost and this can lead to inflammatory bowel disease that may predispose to colon cancer. Caspase-1, an important protein involved in the mechanism of inflammation, has long been believed to be one of the culprits behind excessive inflammation in the colon. Dr. Saleh's team suggests the opposite in a new study.

The MUHC/McGill researchers have demonstrated that Caspase-1 plays a crucial role in inflammation regulation and intestinal tissue repair. But too much of any good thing can sometimes be bad. They also demonstrated that if Caspase-12--the protein that blocks Caspase-1--is absent, the inflammation mechanism caused by Caspase-1 goes out of control. Their findings, which were published in the journal *Immunity*, open the door to a greater understanding of and more targeted treatment strategy for preventing diseases linked to inflammation of the intestine as well as certain cancers.

This discovery is of major interest from the therapeutic point of view because many pharmaceutical companies have developed Caspase-1 inhibitors since the late 1990s with the goal of relieving the symptoms of colitis. However, Dr. Saleh's team observed that inhibition or deletion of Caspase-1 was not protective and actually caused an intense inflammatory reaction that led to severe colitis.

"Caspase-1 is needed to maintain the intestinal barrier and to repair it if

injured. It works by stimulating the cells that line the intestinal barrier to proliferate and fill the site of damage or ulcer. This barrier shields us from the bacteria that colonize our gut," explains Dr. Saleh. "Without it, these bacteria invade to deeper tissues and trigger a persistent inflammation."

According to Dr. Saleh, the absence of Caspase-12 leads to uncontrolled cell proliferation and higher risk of colorectal cancer. "If Caspase-1 is not eventually blocked, it could lead to appearance of tumours," she says.

"Our challenge at present is to further our research on the action of Caspases in the immune response and also to see whether they play a role in other types of cancer."

More information: Immunity journal: www.cell.com/immunity/newarticles

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