

NSAIDs prevent colon cancer by inducing death of intestinal stem cells that have mutation

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Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) protect against the development of colorectal cancer by inducing cell suicide pathways in intestinal stem cells that carry a certain mutated and dysfunctional gene, according to a new study led by researchers at the University of Pittsburgh Cancer Institute (UPCI) and the School of Medicine. The findings were published online today in the *Proceedings of the National Academy of Sciences*.

Scientists have long known from animal studies and clinical trials that use of NSAIDs, such as aspirin and ibuprofen, lowers the risk of developing [intestinal polyps](#), which can transform into colon cancer. But they have not known why, said senior investigator Lin Zhang, Ph.D., associate professor, Department of Pharmacology and Chemical Biology, Pitt School of Medicine, and UPCI, a partner with UPMC CancerCenter.

"Our study identifies a biochemical mechanism that could explain how this preventive effect occurs," he said. "These findings could help us design new drugs to prevent [colorectal cancer](#), which is the third leading cause of cancer-related deaths in the country."

The research team performed experiments in animal models and examined tumor samples from patients who had taken NSAIDs and those who hadn't. They found that NSAIDs activate the so-called death

receptor pathway, which selectively triggers a suicide program in [intestinal stem cells](#) that have a mutation in the APC gene that renders the cells dysfunctional. Healthy cells lack the mutation, so NSAIDs cause them no harm. In that manner, the drugs instigate the early auto-destruction of cells that could lead to precancerous polyps and tumors.

"We want to use our new understanding of this mechanism as a starting point to design better drugs and effective cancer prevention strategies for those at high risk of [colon cancer](#)," Dr. Zhang said. "Ideally, we could harness the tumor-killing traits of NSAIDs and avoid possible side effects that can occur with their chronic use, such as gastrointestinal bleeding and ulcers."

More information: BID mediates selective killing of APC-deficient cells in intestinal tumor suppression by nonsteroidal antiinflammatory drugs, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1415178111

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