

Researchers show that nitric oxide-donating naproxen can boost colorectal cancer prevention

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Past randomized clinical trials have shown that non-steroidal anti-inflammatory drugs (NSAIDs), including naproxen, can reduce the risk of colon cancer and precancerous polyps in humans. Now, researchers at Fox Chase Cancer Center have found that an investigational form of naproxen, called nitric oxide-donating naproxen (NO-naproxen), can block one of the earliest molecular changes that lead to colorectal cancer development while also reducing gastrointestinal toxicity, a relatively common side effect associated with NSAIDs.

"It appears that the investigational form of naproxen we studied may be more effective than standard naproxen in inhibiting colorectal [tumor development](#)," says Margie Clapper, Ph.D., Co-Leader of the Cancer Prevention and Control Program at Fox Chase Cancer Center. "An added benefit would be the reduced gastrointestinal toxicity of this novel type of naproxen." Clapper's group will present the new data at the 2010 annual meeting of the American Association for Cancer Research.

"This new form of naproxen is probably more protective because it blocks one of the first steps in the colorectal cancer-causing pathway," she says.

Previous work from Clapper and others has shown that increased activity of the WNT/ β -catenin pathway is one of the earliest events in [colorectal cancer](#) formation. To test whether NO-naproxen could reduce activation

of the pathway, the team used [colon cancer](#) cells that become bioluminescent when the WNT/ β -catenin pathway is active. They found that cells treated with NO-naproxen had about 50% less bioluminescence than cells treated with naproxen.

"The major and novel finding from the study is that the NO-naproxen can alter a particular signaling pathway that is one of the earliest events in colon cancer formation," Clapper says. "Based on the in vitro data, we think that NO-naproxen is much better than naproxen in nipping this whole process in the bud."

To confirm the in vitro results, the team has treated mice that are genetically predisposed to develop colorectal adenomas with NO-naproxen and [naproxen](#) and are awaiting the results of this study.

NSAIDs have been shown to reduce the risk of colon cancer and precancerous polyps in people. However, some of the agents have been taken off the market due to cardiovascular toxicity. With that in mind, Clapper says, "If we can find something in the same arena that is effective and nontoxic, it will be extremely valuable."

NO-naproxen and other NO-donating NSAID derivatives are a new class of agents being developed with the aim of reducing gastrointestinal toxicity, a relatively common side effect associated with NSAIDs.

Provided by Fox Chase Cancer Center

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