

## **Researchers Discover Drug can Prevent Colon Cancer Development in Mice**

February 12 2009

Researchers at the Mayo Clinic campus in Florida have found that a drug now being tested to treat a range of human cancers significantly inhibited colon cancer development in mice. Because the agent appears to have minimal side effects, it may represent an effective chemopreventive treatment in people at high risk for colon cancer, the investigators say.

Their study, published in the Feb. 15 issue of *Cancer Research*, found that use of the agent, enzastaurin, significantly reduced development of cancerous colon tumors in treated animals. Furthermore, the tumors that did develop in the mice were of a lower grade, which meant they were less advanced and aggressive than the tumors seen in animals not given the drug.

"There is need for an agent that has a proven ability to reduce colon cancer risk, and this study suggests that enzastaurin could be uniquely effective," says the study's senior investigator, Nicole Murray, Ph.D., of the Department of Cancer Biology.

Individuals at high risk for colon cancer often develop numerous precancerous colon polyps, which must be periodically removed during a colonoscopy, Dr. Murray says.

The laboratories of Dr. Murray, and her collaborator and co-author, Alan Fields, Ph.D., chair of the Department of Cancer Biology, focus on characterizing the genes involved in different stages of colon



carcinogenesis. They have zeroed in on the protein kinase C (PKC) family of enzymes as major players in cancer development and progression, but it has taken them years to understand the different roles of each type of PKC molecule or "isozyme."

"All PKC isozymes act in essentially the same way. They add phosphate groups to proteins to change the function of the protein, but within cells we find that each PKC isozyme plays a different role," Dr. Murray says.

Using transgenic mice in which different PKC genes have been selectively deleted or silenced, the researchers have determined pivotal roles for two of the major isozymes. In the Jan. 15 issue of *Cancer Research*, they reported that PKCß (PKC-beta) is necessary for initiation of colon cancer in mice exposed to a carcinogen. "These mice develop colon tumors similar to tumors found in humans, but mice without a PKCß gene do not," Dr. Murray says.

In that study, they also demonstrated that a different PKC isozyme known as PKCi/l (PKC iota-lambda) is involved in progression of colon cancer. If the PKCi/l gene is deleted in mice models that mimic the type of cancer seen in people with an inherited form of colon cancer, the cancer doesn't progress at such a rapid rate, Dr. Murray says. "But in those same mice, if we knock out the PKCß gene, there is no effect," she says.

"This tells us that over-expression of PKCß and PKCi/l serve distinct, nonoverlapping roles in colon carcinogenesis, conspiring to drive initiation and progression of colon carcinogenesis, respectively," Dr. Murray says.

Those findings suggested that targeting these different PKC isozymes could have distinct cancer treatment benefits. Targeting PKCß in colon cells could help prevent initial cancer development, and inhibiting



PKCi/l might help stop progression of cancer that has already developed, she says.

In the current study, the research team tested enzastaurin, an oral drug specifically designed to suppress signaling through the PKCß pathway. The drug is now in clinical trials to treat B-cell lymphoma and high-grade brain gliomas, among other cancers.

Researchers gave the agent daily to one group of mice, and then exposed this group, as well as a control group of mice, to a carcinogen that produces colon tumors. After 22 weeks, 80 percent of mice in the control group developed colon tumors, but only 50 percent of the treated mice developed tumors, and the cancers that developed were not as advanced, Dr. Murray says.

The agent could be tested for colon cancer chemoprevention in a fairly simple manner, Dr. Murray says. Because precancerous colon polyps can be observed during a colonoscopy, it would be possible to see if a drug that targeted PKCß reduced polyp formation over time in people who are using the agent, she says.

Source: Mayo Clinic

Citation: Researchers Discover Drug can Prevent Colon Cancer Development in Mice (2009, February 12) retrieved 27 April 2024 from <u>https://medicalxpress.com/news/2009-02-drug-colon-cancer-mice.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.