

# Bile acids link high-fat diet to colon cancer

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Carol and Harris Bernstein in the UA's department of cell biology and anatomy and scientists elsewhere have accumulated evidence that bile acids could cause colon cancer, but until now, it wasn't clear how. (Photo by Patrick McArdle/UANews)

(PhysOrg.com) -- Bile acids could be the missing link between a high-fat, Western-style diet and colon cancer, UA researchers Carol and Harris Bernstein and their collaborators have discovered.

Bile acids could be the missing link between a high-fat, Western-style diet and colon cancer, University of Arizona researchers and their collaborators have discovered.

Seventeen out of 18 mice fed a standard diet topped off with bile acid developed colon tumors after eight or 10 months, the scientists report in the journal *Archives of Toxicology*.

"It has been known for a while that a diet rich in fat poses a risk for colon cancer," said Carol Bernstein, a research associate professor in the UA College of Medicine's department of cell biology and anatomy and lead author of the study.

"But until now, it wasn't known exactly why."

Her husband and co-author, Harris Bernstein, added: "Since the 1970s, people in the field have suspected that bile acids play a role, but they were thought to act merely as promoters, enhancing the cancer-causing effect of some other substance. Our findings show that bile acids themselves cause colon cancer."

Harris Bernstein is a professor of cell biology and anatomy.

Over the past 25 years, the Bernsteins have collected evidence suggesting that bile acids cause changes in the cells lining the walls of the colon, sending them down a path toward becoming cancerous.

"The bile acids cause damage to the cells' DNA, leading to mutations," explained Carol Bernstein. "Those mutations then cause changes in the activity of cancer-related genes."

Encouraged by their findings in mice, the Bernsteins are submitting a grant proposal to investigate the bile acids' role in [cancer formation](#) in more detail and how it compares to the situation in humans.

Bile acids are the body's own "dishwashing detergent." Produced by the liver and stored in the gall bladder, they are released into the [intestinal tract](#) to emulsify fat in food once it is passed on from the stomach to the intestine.

"Because it has been known for a while that bile acids such as

deoxycholic acid, or DOC, play a key role in the formation of colon cancer, we wanted to know whether DOC alone is enough to trigger tumor formation," said Carol Bernstein.

To test their hypothesis, the scientists divided wild-type mice into four groups and fed them a standard diet for eight to 10 months, either with or without DOC added. DOC levels were assessed in the study animals' excrements. To make the experiments relevant to the human condition, the Bernsteins added DOC to the point where it showed up at the level found in previous studies in humans who were eating a high-fat diet.

"Obviously, there is still a difference in that mice are much smaller than humans," Carol Bernstein said, "and the exposure is much longer in humans. We get colon cancer mostly after the age of 50."

Of the 18 mice that received DOC in addition to the standard diet, all but one (94 percent) developed colon tumors, including 10 animals whose tumors had progressed to full-blown cancers. In contrast, no tumors were found in mice eating a standard diet without DOC.

Previous work done by the Bernsteins and other scientists showed that bile acids lead to the formation of additional reactive oxygen species, molecules that can damage cells. Also called free radicals, these molecules are normal by-products of metabolism. They are highly reactive, and if they encounter another molecule such as a protein or DNA, a chemical reaction occurs in which the target molecule is damaged.

The Bernsteins believe that DOC could increase reactive oxygen species to a level beyond the ability of a cell to repair all the damages they cause, ultimately leading to cancer.

"Even the average human cell that is not exposed to excess bile acids

accrues about 10,000 damages over the course of a day through normal metabolism," Harris Bernstein said. The cells in our bodies depend on specialized enzymes to repair these average levels of damage."

Could bile acid cause [colon cancer](#) by ramping up the levels of the destructive free radicals? To address this question, the researchers fed mice with a standard diet containing bile acid, but also chlorogenic acid, an antioxidant found at high levels in blueberries, coffee and eggplant. Antioxidants are known to protect cells from damage by oxygen radicals.

Only 64 percent of mice in this category developed tumors, suggesting that chlorogenic acid offsets some of the cell damage inflicted by the bile acid.

Again, no colon tumors were found in any of the mice belonging to the control group fed with a standard diet plus antioxidant.

The Bernsteins are now beginning to measure the levels of excess DNA damage caused by increased DOC in the colons of mice. They are also starting to find reductions in DNA repair enzymes caused by addition of DOC to the diet.

Their new work could further explain the mechanism of how bile acids cause progression to cancer in the colon.

Provided by University of Arizona

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