

## Colon cancer treatment shows promise

Anti-inflammatory drugs such as aspirin and ibuprofen seem to prevent some cases of colon cancer by suppressing two enzymes that promote the manufacture of prostaglandins, hormonelike fatty acids, in the body. Too much prostaglandin promotes runaway cell growth by disrupting programmed cell death. An aspirin-a-day regimen that reins in prostaglandins can cut colon cancer risk in half.

The two suppressed enzymes, COX-1 and COX-2, appear in colon tumors in rodents as well as humans. COX-2 seems to be the culprit behind excessive prostaglandin production, whereas COX-1 apparently doesn't promote cancer. In fact, subduing COX-1 can cause side effects, including ulcers, intestinal bleeding, and, less often, kidney damage.

Now, a study in rats shows that a recently developed anti-inflammatory drug, celecoxib, thwarts COX-2 but not COX-1, say scientists at the American Health Foundation, a nonprofit cancer research center in Valhalla, N.Y.

The researchers added celecoxib to the food of 36 rats, starting at age 5 weeks. Two weeks later, the rats received an injection of the cancer-causing compound azoxymethane. After 50 weeks, only two of the rats had tumors. An additional 36 rats received azoxymethane but no celecoxib; 29 of these developed cancer.

Nutritionist Bandaru S. Reddy, a coauthor of the report in the Feb. 1 *Cancer Research*, says celecoxib looks promising. "I've been working for 26 years on colon cancer, and I have yet to see a compound or drug so potent against it," he says. "It is amazing, really."

Several COX-2 inhibitors are now being tested. By using the COX-2 inhibitor from which celecoxib was derived, cancer biologist Raymond N. DuBois of Vanderbilt University Medical Center in Nashville has also limited colon cancer in rodents. "Evidence is mounting that COX-2 inhibitors have some effect on tumor genesis," he says.

DuBois and his colleagues are trying to figure out how too much COX-2 and prostaglandin cause cancer and how the drugs inhibit this process. Prostaglandins are instrumental in platelet formation.

The COX-2 research is auspicious, and any gains in colon cancer treatment will probably apply to rectal cancer as well, DuBois says.

Because COX-2 inhibitors are relatively new, however, "nobody knows what the whole profile of side effects [from them] is; that's the downside," says Heinz-Josef Lenz of the University of Southern California in Los Angeles. Lenz plans to test COX-2 inhibitors in people who are genetically predisposed to colon cancer and in colon cancer survivors.

In the first test of such drugs in people, researchers at St. Mark's Hospital in London are studying whether COX-2 inhibitors prevent the formation of sometimes precancerous growths called polyps. U.S. researchers are about to begin giving the drugs to people who have colon polyps.

—N. Seppa