

Hormone loss could be involved in colon cancer

October 10 2014

Some cancers, like breast and prostate cancer, are driven by hormones such as estrogen and testosterone, but to date, there are none that are driven by the lack of a hormone. New evidence suggests that human colon cells may become cancerous when they lose the ability to produce a hormone that helps the cells maintain normal biology. If verified by further studies, it suggests that treating patients at high risk for colon cancer by replacing the hormone guanylin could prevent the development of cancer.

The researchers at Thomas Jefferson University examined [colon cancer](#) samples from 281 patients and compared those tissues to nearby colon tissue that wasn't cancerous. They found that guanylin production – measured by number of messenger RNAs for guanylin contained in each cell – decreased 100 to 1,000 times in more than 85 percent of colon cancers tested. They verified their results by also staining for the guanylin hormone production in slices of the tissue samples. They could detect no guanylin hormone in the cancer samples.

In addition, the researchers found that people over 50 years old produced much less of the hormone in their normal colon cells, which could help explain the increase in colon cancer risk in older individuals. The research publishing online October 10th in *Cancer, Epidemiology, Biomarkers & Prevention*, a journal of the American Association for Cancer Research (AACR).

"The fact that the vast majority of cancers stop producing this hormone

leads us to believe that guanylin may be driving the growth of the tumors," says senior author Scott Waldman, M.D., Ph.D., Chair of the Department of Pharmacology & Experimental Therapeutics and the Samuel MV Hamilton Professor at Thomas Jefferson University. If confirmed, "We could prevent colon cancer by giving patients hormone replacement therapy with guanylin." Colon cancer is the second leading cause of death from cancer for men and women and expected to cause 50,000 deaths in 2014, according to the American Cancer Society.

Earlier work has shown that guanylin is a locally-acting hormone, produced by the very cells it acts on. Guanylin activates a receptor called GUCY2C (pronounced "goosy toosy" by researchers). GUCY2C signaling is critical to helping replenish the skin cells lining the gut, and maintaining their overall function. Since the skin of the gut turns over about once every 3 days, the proper control and maintenance of the signals that replenish the skin is essential. Without signals that maintain cell division, aberrant cell division is more likely to occur, which can lead to cancer.

When guanylin is diminished, the cells of the colon produce more GUCY2C receptors in order to try to catch any possible signal from the outside of the cell. As a result, many colon cancers exhibit high numbers of GUCY2C receptors, despite the fact that the receptor no longer receive the hormone signal that help them activate programming that maintains the health and normal function of the cell.

The next steps, says Waldman, are to test whether [hormone](#) replacement can prevent colon cancer development and/or growth in mice, which could then be followed by tests in humans. In addition the team is working on understanding how exactly guanylin functions to maintain the normal health of [colon cells](#).

More information: C. Wilson, et al., "The paracrine hormone for the

GUCY2C tumor suppressor, guanylin, is universally lost in colorectal cancer," *Cancer Epidemiol Biomarkers*, [DOI: 10.1158/1055-9965.EPI-14-0440](https://doi.org/10.1158/1055-9965.EPI-14-0440) , 2014.

Provided by Thomas Jefferson University

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