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Scientists discover experimental therapy for chronic inflammatory bowel disease, colon cancer

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UCLA scientists have discovered a groundbreaking experimental therapy that has the ability to suppress the development of ulcerative colitis (UC), a disease which causes inflammation in the digestive tract and colon cancer. The treatment utilizes a chemical inhibitor able to block an RNA molecule (microRNA-214) involved in the transmission of genetic information.

High levels of microRNA-214 are typically seen in UC patients, who have an increased risk of developing colon cancer. It is still unclear why colitis patients also develop colon cancer.

Thirty percent of all patients who complain of gastrointestinal pain are typically diagnosed with "indeterminate inflammatory bowel disease" by their gastroenterologist. Even if the patient has all available biomarkers and underwent a colonoscopy, many clinicians are still unable to determine if the patient has UC or Crohn's disease.

In the two-year study, UCLA Jonsson Comprehensive Cancer Center member Dr. Dimitrios Iliopoulos and his colleague Dr. Christos Polytarchou, UCLA assistant professor of digestive diseases, examined 401 colon tissue samples from patients in the United States and Europe with UC, Crohn's disease, irritable bowel syndrome, sporadic colorectal cancer and colitis-associated colon cancer, and compared them to specimens from people without these disorders or diseases.

The team hoped the research would assist physicians in diagnosing this disease correctly and provide the appropriate treatment, said Dr. Iliopoulos. They developed a systems approach that could expedite the drug discovery process by utilizing sophisticated computer programs and high-tech robotics that combines molecular and clinical information to identify the most important genes to create new drugs. The integration of this complex data is what led them to discover a new microRNA-214 chemical inhibitor to treat UC and colon cancer.

"The first steps of the drug discovery process usually take five to six years and by using our novel approach we expedited the drug discovery process only in two years," said Iliopoulos, an associate professor of digestive diseases.

Previous studies have mentioned findings related to inflammatory responses in both sporadic and colitis-associated colon cancers, but it was unclear until now whether the inflammatory signals regulated the same signaling pathways.

"We evaluated this drug in mice with ulcerative colitis and colon tumors and found that in both cases it was highly effective to suppress these diseases," Iliopoulos said.

Colorectal cancer, or colon cancer, is the third leading cause of cancer-related deaths in the United States (when men and women are considered separately), and the second leading cause when both sexes are combined. The American Cancer Society estimates 93,090 new cases of colon cancer and 39,610 new cases of rectal cancer will be diagnosed in the United States in 2015. Additionally, 49,700 people are expected to die from the disease this year.

Iliopoulos will continue testing the microRNA-214 inhibitor and will apply for an investigational new drug application with the U.S. Food &

Drug Administration. He hopes to eventually begin phase I clinical trials for patients with UC next year.

The study is now available online, and the print edition will be released Oct. 1, 2015 in *Gastroenterology*.

More information: "MicroRNA214 is Associated with Progression of Ulcerative Colitis, and Inhibition Reduces Development of Colitis and Colitis-associated Cancer in Mice," *Gastroenterology*, Available online 6 June 2015, ISSN 0016-5085, dx.doi.org/10.1053/j.gastro.2015.05.057

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