Researchers find triggers in cells' transition from colitis to cancer

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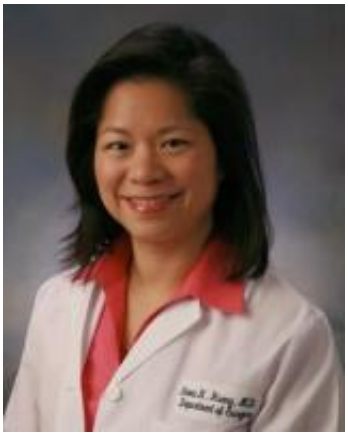

Emina Huang, M.D., a UF colorectal surgeon

(PhysOrg.com) -- University of Florida researchers have grown tumors in mice using cells from inflamed but noncancerous colon tissue taken from human patients, a finding that sheds new light on colon cancer and how it might be prevented.

Scientists observed that cancer stem cells taken from the gastrointestinal system in patients with a chronic digestive disease called ulcerative colitis will transform into cancerous tumors in mice.

The finding, now online and to be featured on the cover of the Thursday (Oct. 15) issue of *Cancer Research*, may help explain why patients with colitis have up to a 30-fold risk of developing colon cancer compared

with people without the disease.

New understanding of the link between colitis and cancer could lead to diagnostic tests that would evaluate tissue taken from patients with colitis for signs of cancer stem cell development, thereby identifying patients who may be at greater risk for cancer.

“Ultimately it would be great if we could prevent colitis or treat colitis so it never gets to the cancerous stage,” said UF colorectal surgeon Dr. Emina Huang, who is a member of the Program in Stem Cell Biology and Regenerative Medicine at UF’s McKnight Brain Institute and the UF College of Medicine.
Although colonoscopy is very effective in screening and preventing colon cancer for most people, for patients with colitis no diagnostic tests work well because the inflamed tissue makes identification of precancerous changes difficult.

According to the Crohn’s and Colitis Foundation of America, approximately 700,000 people have colitis in the United States. The National Cancer Institute estimates that cancer of the colon and rectum will claim the lives of about 50,000 people this year.

UF scientists gathered colitic tissue from humans and chemically screened it for colon cancer stem cells, also called tumor initiating cells. These cells were then isolated and monitored in mice to see if tumors would grow.

Huang said these findings shed light on that fact that it may not be just the cancer “seed” cell, but the “soil” — in this case inflamed colon tissue — that plays a role in the development of cancer.

“Is it the seed, is it the soil or is it their interaction?” she said. “We think probably both, but now we have a new way to look at it and a new

method of attack."

Dr. B. Mark Evers, a professor and vice chair of surgery at the University of Kentucky College of Medicine, said the study emphasizes the emerging role of the surrounding inflammatory tumor microenvironment on tumor growth and subsequent metastasis.

"Dr. Huang and her group have identified a potentially important mechanism to explain why long-standing inflammation of the colon predisposes patients to the development of cancer," said Evers, who is director of the Lucille P. Markey Cancer Center in Lexington, Ky.

To further understand the role of the "seed" and "soil" interaction, UF researchers paired colon cancer stem cells with normal, colitic and cancerous human cells taken from the scaffolding layer of the large intestine. The cells were implanted into mice to analyze growth rates. The combination of tumor cells and normal scaffolding tissue cells grew at the slowest rate. Tumor cells paired with cancerous tissue grew at an intermediate rate, and tumor cells paired with the colitic tissue grew at the fastest rate.

Huang said they found heightened levels of two immune system hormones called interleukin-6 and interleukin-8 in the cells from the colitic and cancerous tissues, which had the faster growth rates.

When UF researchers decreased the expression of these hormones within the cells, the tumor growth drastically decreased. When the hormones returned, the tumors began to grow again.

"We don't understand the transition at the molecular level so we are trying to figure out what we can target to interfere, intervene or inhibit that transformation of the benign colitic cells," she said. "The thought is if we can create a therapy to decrease function of these hormones, we

may be able to prevent or inhibit cancer growth."

Clinical trials looking at the role of one of these hormones in humans are under way in England, Huang said.

Provided by University of Florida (news : web)