Medical Xpress

Study shows different genetic drivers of colorectal cancer in older and younger patients

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Christopher Lieu, MD, and colleagues show that colorectal cancer is genetically different in young patients than it is in older patients. Credit: University of Colorado Cancer Center

A University of Colorado Cancer Center study being presented Saturday at the 2016 Genitourinary Cancers Symposium shows genetic differences between colorectal cancer (CRC) in young and old patients, possibly pointing toward different treatments and strategies in combating the young form of the disease. Comparing 9 tumors from younger patients (median age 31) with 9 tumors from older patients (median age 73), showed "distinct genetic differences between younger and older

patients with colorectal cancer," says Christopher Lieu, MD, investigator at the CU Cancer Center and assistant professor of medical oncology at the University of Colorado School of Medicine.

While the overall rate of colorectal cancer (CRC) is declining, CRC specifically among young patients is increasing. Previous studies have shown that CRC in patients younger than 50 years old tends to be more aggressive than CRC in older patients. The current study seeks to unpack the genetic cause of more aggressive behavior in the young form of the disease.

Toward that end, the group sequenced 45 million "reads" from each of the tested tumors, showing 141 genes that are enriched in samples from younger patients and a largely different cohort of 42 genes enriched in samples from older patients. Many of the enriched genes in samples from younger patients are involved in signaling pathways ERBB2, NOTCH3 and CAV1, which are known to spur cell proliferation commonly associated with cancer. In contrast, pathways enriched in samples from older patients included CDX2, HMGB3 and EPHB2, which are primarily involved not in cell proliferation, but in cell differentiation (the ability or inability of cells to move from stem-like cells to more specialized tissues).

The enrichment of ERBB2 (Her2/neu) in samples from younger patients is an especially interesting target given that there are FDA-approved therapies that target this particular gene.

The group plans to validate the finding of these differences in a larger patient population. Then, if these pathways indeed prove to be important drivers of CRC in young patients, the group hopes to explore trials of drugs targeting these potential tumor drivers. Toward this goal, the group has gathered the important resource of tumor samples grown from the tissues of young CRC patients, allowing further preclinical genetic and

drug testing.

"If I were to shoot for the stars, I would say that our end goal is to be able to offer better treatments for this population of young colorectal cancer patients that seems to be at higher risk from the disease," Lieu says.

More information: ASCO Abstract: meetinglibrary.asco.org/content/159892-173

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