Medical Xpress

Researchers identify individuals at risk for developing colon cancer

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A new study identifies a group of individuals at increased risk for developing colon cancer and holds the promise for developing new tailored cancer treatments. The study in this week's issue of the *Proceedings of the National Academy of Sciences* is by Sanford Markowitz, M.D., Ph.D., the Markowitz-Ingalls Professor of Cancer Genetics at Case Western Reserve University School of Medicine and oncologist at the Ireland Cancer Center of University Hospitals Case Medical Center, and colleagues.

"The bottom line is that we have found an uncommon but potentially important group of individuals who are born with certain genetic mutations and are at increased risk for developing colon cancer," says Dr. Markowitz, who is also an investigator in the Howard Hughes Medical Institute. "This is yet another step towards identifying who is at increased risk for this deadly form of cancer and it may potentially allow us a greater ability to detect and treat, as well as develop therapies, for cancer."

Dr. Kishore Guda, a postdoctoral fellow in Dr. Markowitz's laboratory, is lead author on the study. Dr. Markowitz's laboratory along with colleagues at Johns Hopkins Medical Center analyzed DNA from individuals who are born with mutations that cause defects in the pathways that put sugar groups on proteins. The normal process, called glycosylation, is used to synthesize mucus and is involved in many cellular activities. The individuals with this genetic defect appeared to develop colon cancer later in life. Data was from patients at UH Case

Medical Center and Johns Hopkins.

A defect in glycosylation is a hallmark of many cancers, but the reason for this defect has been unknown. This study discovered the presence of mutations in a group of enzymes, called GALNTs, which are required for normal glycoslylation. These mutations contribute to alterations in the glycosylation process, and in turn, to the development of colon cancer.

"Our findings support the idea that defects in glycosylation, the process for making mucus, can contribute to tumor development," said Dr. Markowitz. "Knowing how these glycosylation enzymes malfunction and contribute to tumor formation may give us another target that can be potentially used to prevent the development of colon and other cancers. Certainly, individuals who have these mutations should be getting screening for colon cancer, so that the disease can be caught during the early stages when it is highly curable."

Colon cancer, the second leading cause of cancer deaths in the U.S., accounts for 50,000 deaths annually.

Source: University Hospitals Case Medical Center

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