

Study shows potential new way to detect colorectal and other cancers

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A unique new study led by University of Kentucky Markey Cancer Center researchers Guo-Min Li and Libya Gu, in collaboration with Dr. Wei Yang at National Institutes of Health, reveals a novel mechanism explaining the previously unknown root cause of some forms of colorectal cancers.

The study, published in *Cell*, discovers that an abnormal histone protein modification impairs a DNA repair machinery that controls cancer development, yielding a potential new way of detecting these types of [colorectal cancers](#). It represents the first time that epigenetic histone marks regulate the genome maintenance system.

DNA errors created during DNA replication can lead to many forms of cancer, including colorectal cancer. Cells possess [DNA mismatch repair](#) (MMR) machinery that aids in correcting these errors, thus preventing disease development. Defects in MMR genes lead to development of colorectal cancers characterized by frequent alterations in simple [repetitive DNA sequences](#), a phenomenon referred to as microsatellite instability (MSI). Some cancers develop in individuals who possess MSI without MMR gene defects, and until now, the reason for this has been unknown.

Dr. Li's study shows that defects in SETD2 – an enzyme that is not involved in MMR but chemically or epigenetically modifies [histone proteins](#) associated with DNA that control the [regulation of gene expression](#) and DNA replication – prevent the association of MMR

proteins with damaged DNA, thus preventing DNA mismatch repair.

"This study provides new clues to cancer etiology, that is, from the classical genetic defects to abnormal epigenetic modifications in the future," Li said. "Since SETD2 mutations have been shown in many types of cancers, including clear cell [renal cell carcinoma](#), lung cancer, gastric cancer and hematological malignancies, our next goal is to determine association of MMR defects with these cancers, as well as SETD2 mutations in MSI-positive MMR-competent colorectal cancers."

Although most colorectal cancers are preventable or treatable with proper screening, colorectal cancer remains the second-leading cause of cancer death in the United States. Kentucky is ranked in the highest tiers for both colorectal and lung cancer incidence and death.

Provided by University of Kentucky

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