New genetic mutation identified in melanoma cancer cells

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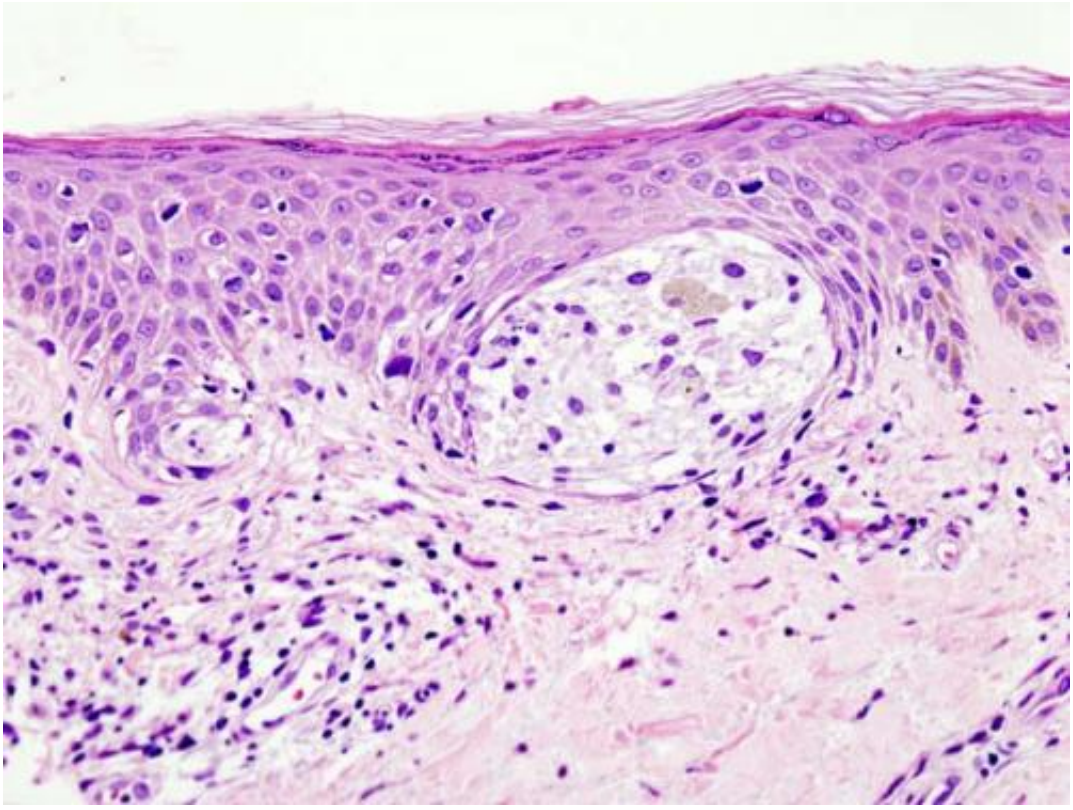

Melanoma in skin biopsy with H&E stain—this case may represent superficial spreading melanoma. Credit: Wikipedia/CC BY-SA 3.0

There is strong evidence that the protein complex APC/C may function as a tumor suppressor in multiple cancers including lymphoma, colorectal and breast cancer, and now melanoma. A new study has revealed that a genetic mutation leading to repression of a specific

protein, Cdh1, which interacts with APC/C, is present in melanoma cancer cells.

The study, led by researchers at Boston University School of Medicine (BUSM), reports sporadic mutations in the APC/C protein complex, specifically in the essential protein component Cdh1, which may predispose humans to developing melanoma from the loss of the APC/C protein complex. This complex is involved in regulating the cell replication cycle, which becomes dysregulated in cancer. The study currently appears in *Science Signaling*.

The researchers used bioinformatics to analyze gene mutations encoding for the APC/C protein complex. They demonstrated that most of the mutations are the result of ultraviolet light and associated with the development of melanoma. Furthermore, they analyzed histological samples and found an inverse relationship between the amount of Cdh1 and another important protein involved in the cell replication cycle, PAX3, which also interacts with APC/C. Their research illustrated the important biochemical interactions between APC/C, Cdh1 and PAX3, among multiple other proteins. In summary, less Cdh1 prevents the normal function of APC/C, which eventually inhibits the degradation of PAX3, potentially leading to unregulated cell proliferation and cancer (melanoma in skin cell models). In addition, they looked at the common chemotherapy drug, doxorubicin, which directly damages DNA and interferes with the cell replication cycle, demonstrating how Cdh1 may be important in doxorubicin's anti-cancer activity.

"These findings have significant implications to the field of cancer by providing important insights into molecular genetics of melanoma and could lead to the identification of novel preventive strategies and therapeutic targets for melanoma," explained corresponding author Rutao Cui, MD, PhD, associate professor of pharmacology and experimental therapeutics at BUSM.

According to the researchers these findings may suggest additional targets for medical therapy to minimize morbidity and mortality from this potentially devastating cancer. "Our ultimate goal is to reduce melanoma mortality through the discovery of effective and targeted small molecules for melanoma treatment. We believe that these results will provide a solid foundation towards successfully achieving our goal," Cui said.

Provided by Boston University Medical Center