Discovery may lead to targeted melanoma therapies

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Melanoma patients with high levels of a protein that controls the expression of pro-growth genes are less likely to survive, according to a study led by researchers at Icahn School of Medicine at Mount Sinai and published online in the journal *Molecular Cell*.

The research team found that the protein, called H2A.Z.2, promotes the abnormal growth seen in melanoma cells as they develop into difficult-to-treat tumors. H2A.Z.2 is part of the chromosome structure that packages genes, and has the ability to switch them on off. Having high levels of this protein aberrantly activates growth-promoting genes in melanoma cells.

An emerging theory in cancer research is that abnormal growth may result not only from unfortunate, mutations in patients' genes, but also from epigenetic mechanisms that turn genes on and off. In the current study, authors found that blocking the functions of H2A.Z.2, either alone or in combination with cancer therapies, effectively blocked tumor growth and killed melanoma cells.

"Cancer is a disease consisting of both genetic and epigenetic changes," said Emily Bernstein, PhD, Associate Professor of Oncological Sciences and Dermatology, the Icahn School of Medicine at Mount Sinai, and lead study author. "I believe that the study of epigenetic mechanisms may lead to the development of new approaches for molecular diagnosis and targeted treatments."

"Here we show that the histone variant H2A.Z.2 drives melanoma progression by affecting chromatin structure," said Bernstein. "This is the first study to identify a specific role for the histone variant H2A.Z.2 in any tumor type. Next, we need to better understand how to prevent H2A.Z.2 function in chromatin."

Research has only "scratched the surface" of the epigenetic mechanisms involved in cancer, Bernstein said. Gaining insights will pave the way for the design of innovative therapeutic regimens in melanoma as well as in other cancer types, she said.

Provided by The Mount Sinai Hospital