Researchers discover epigenetic reason for drug resistance in a deadly melanoma

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Mount Sinai researchers have discovered a previously unknown reason for drug resistance in a common subtype of melanoma, one of the deadliest forms of cancer, and in turn, have found a new therapy that could prevent or reverse drug resistance for melanoma patients with a particular gene mutation, according to a study published in *Nature Communications* in August.

The researchers identified a novel epigenetic mechanism that causes resistance to the standard treatment in melanoma patients with mutations in the BRAF genes, which are found in about half of all melanomas. Researchers also found a biomarker, or a biological signature that accompanies this drug resistance: a gene called IGFBP2, which is also associated with poor prognosis in melanoma patients.

Patients with high levels of IGFBP2 could benefit from combination therapies, which could be created in response to these findings, that inhibit BRAF mutations and IGFBP2-driven biological pathways as a multi-pronged approach to preventing drug resistance or reversing it once it has occurred, the study shows. Other studies show the potential to find IGFBP2 via urine samples so the implications for detection and later treatment are large.

"The incidence of cutaneous malignant melanoma is rising and its therapeutic management remains challenging," said lead researcher Emily Bernstein, Ph.D., Associate Professor of Oncological Sciences and Dermatology at the Icahn School of Medicine at Mount Sinai. "In recent years, there has been extensive therapeutic development to inhibit key biological targets. Although a large proportion of patients with advanced metastatic melanoma harboring BRAF mutations respond to the standard therapy, known as MAPK inhibitors, subsequent resistance remains a major clinical challenge."

Provided by The Mount Sinai Hospital