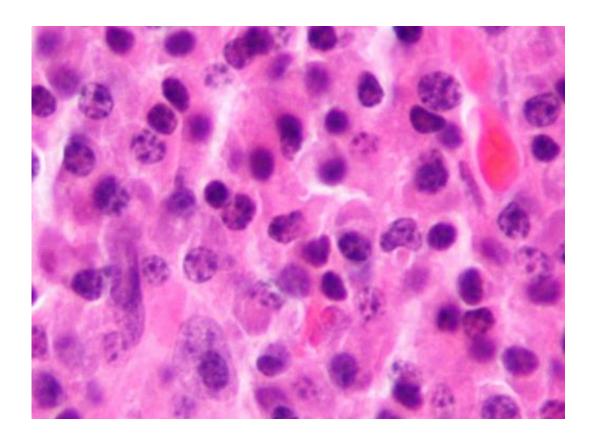


Researchers discover genes that predict good response to blood cancer therapy

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Micrograph of a plasmacytoma, the histologic correlate of multiple myeloma. H&E stain. Credit: Wikipedia/CC BY-SA 3.0

Mount Sinai researchers have, for the first time, identified genes that predict a good response to a vital new therapy for a blood cancer that can have serious side effects for some patients.



The therapy, selinexor, is part of many groundbreaking therapies for the blood cancer multiple myeloma, but the ability to target its use to patients who would benefit the most remained elusive until now, according to a study published in *JCO Precision Oncology* in June.

The Mount Sinai scientists sequenced RNA of multiple myeloma tumors from patients treated with selinexor and identified a signature of three genes that were activated in patients who had positive responses. They validated the signature in an independent group of patients who participated in an international clinical trial that led to Food and Drug Administration (FDA) approval of the drug.

"This signature has important clinical significance, as it could identify patients who are most likely to benefit from treatment with selinexorbased therapy, especially in earlier lines of therapy," said one of the senior authors, Alessandro Lagana, Ph.D., Assistant Professor of Oncological Sciences at The Tisch Cancer Institute at Mount Sinai and Assistant Professor of Genetics and Genomic Sciences at the Icahn School of Medicine at Mount Sinai.

Samir Parekh, MD, Director of Translational Research in Myeloma at The Tisch Cancer Institute at Mount Sinai, the other senior author of the study, added, "Our findings provide the basis for improving patient selection for targeted agents using a small panel of genes to guide precise application of these drugs in real world scenarios, including relapse following CAR-T, an increasingly important clinical challenge in myeloma."

Selinexor has proven helpful for patients who failed other FDAapproved therapies for multiple myeloma. However, the majority of patients who take the drug experience side effects, sometimes severe, so it is important to identify patients who will respond positively and potentially expand the use of the drug into patients who haven't failed



other therapies.

Mount Sinai researchers identified the three genes, WNT10A, DUSP1, and ETV7, by sequencing the tumors of about 100 multiple myeloma patients who received the drug. They also found the three-gene signature in patients with the brain cancer glioblastoma who responded well to selinexor.

As a result of this study, Mount Sinai has begun to further study tests for this signature to identify patients who may benefit from selinexor in patients who qualify to use the drug as well as patients who participate in a precision medicine clinical trial launching soon.

More information: Paula Restrepo et al, A Three-Gene Signature Predicts Response to Selinexor in Multiple Myeloma, *JCO Precision Oncology* (2022). DOI: 10.1200/PO.22.00147

Provided by The Mount Sinai Hospital

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