

# Weill researchers find new approach to leukemia

Cornell University

By [George Lowery](#) [1]



Melnick

A tumor's genetic profile is often useful to diagnose and decide on treatment for certain cancers, but genetically similar leukemias in different patients do not always respond well to the same therapy. Weill Cornell Medical College (WCMC) researchers believe they may have discovered what distinguishes these patients by evaluating the certain differences between patients with acute myeloid leukemia (AML).

Chemical codes in addition to DNA sequence control the behavior of normal and malignant cells. These additional codes are called epigenetic since they are contained outside of the DNA sequence.

The investigators have concluded that much of the inter-patient difference in leukemia cell behavior is dependent on a patient's specific epigenetic alterations. This knowledge is expected to lead to cancer therapies tailored for patients who fall within the different epigenetically defined cancer subtypes. The findings are published in the recent issue of the journal *Cancer Cell*.

Dr. Ari Melnick, the study's senior author and associate professor of medicine at WCMC, and colleagues studied a specific epigenetic marker called DNA methylation, which plays a critical role in controlling gene expression.

They examined the DNA methylation patterning of 14,000 genes in 344 patients diagnosed with AML. By grouping these patients according to their DNA methylation profile, the team was able to separate patients into 16 different groups. Five of these groups defined completely new AML subtypes that shared no known feature other than DNA methylation similarities.

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"The epigenetic difference between the AML subtypes may play a critical role in determining the responsiveness of the disease to therapy," said Melnick.

Traditionally, AML patients are treated with first-line chemotherapy drugs. If the drugs fail, patients are given more aggressive therapy like a bone marrow transplant. Being able to tell which patients will most likely not benefit from standard treatments could lead to more precise therapies at the outset of treatment.

The investigators conclude that a set of 15-gene DNA methylation biomarkers was highly predictive of overall patient survival.

"The findings have the potential to tell physicians whether or not a patient has a relatively easy or difficult disease to treat, and tailor a patient's therapy accordingly," said Melnick. "This saves time trying therapies that will eventually prove to have no effect."

The team also discovered a set of 45 genes that are almost universally methylated in AML patients. Methylation of these genes was far more common than any genetic mutation associated with AML and could provide new ways to therapeutically target AML more effectively in the future.

"Such findings will lead to the development of new therapies that give hope to cancer patients who are now without effective treatment," said Dr. Andrew I. Schafer, chairman of the Department of Medicine at NewYork-Presbyterian Hospital/WCMC.

Cornell collaborators on the study include Maria E. Figueroa, Yushan Li, Xutao Deng, Paul J. Christos, Lucy Skrabanek, Fabien Campagne and Madhu Mazumda, all from WCMC; and Elizabeth Schifano and James Booth from Cornell, Ithaca.

The study was supported by the Leukemia and Lymphoma Society.

[SOURCE](#) [2]

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