

Researchers discover genetic differences between lethal and treatable forms of leukemia

January 7 2010

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

In recent years it has been appreciated that there are additional chemical codes in addition to DNA sequence that control the behavior of normal and malignant cells. These additional codes are called "epi"genetic 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. These results are expected to lead to tailored cancer therapies for patients who fall within the different epigenetically defined cancer subtypes.

The promising findings are published today in the journal *Cancer Cell*.

To make their conclusions, Dr. Ari Melnick, the study's senior author and associate professor of medicine from the Raymond and Beverly Sackler Center for Biomedical and Physical Sciences at Weill Cornell

Medical College, 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, Dr. Melnick and his team were able to separate patients into 16 different groups. Five of these groups defined completely new AML subtypes that shared no other known feature, besides the newly discovered methylation similarities.

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

Traditionally, AML patients are treated with first-line chemotherapy drugs. If they fail, patients are classified as having a more severe and difficult-to-treat disease, and are then given a more aggressive therapy, like a bone marrow transplant. Being able to tell which patients are most likely to fail standard treatments could lead to the administration of more precise therapies at the outset of treatment.

They also concluded that a set of 15-gene [DNA methylation](#) biomarker 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," explains Dr. Melnick. "This saves time trying therapies that will eventually prove to have no effect."

In addition, the investigators 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 more effectively therapeutically target AML

in the future.

"Investigators from the Sackler Center at Weill Cornell are leaders in the field of decoding epigenetic information from human tumors and ascertaining their clinical impact," says Dr. Andrew I. Schafer, chairman of the Department of Medicine at NewYork-Presbyterian Hospital/Weill Cornell Medical College. "Such findings will lead to the development of new therapies that give hope to cancer patients who are now without effective treatment."

Provided by New York- Presbyterian Hospital

Citation: Researchers discover genetic differences between lethal and treatable forms of leukemia (2010, January 7) retrieved 18 April 2024 from <https://medicalxpress.com/news/2010-01-genetic-differences-lethal-treatable-leukemia.html>

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