Team uncovers novel epigenetic changes in leukemia

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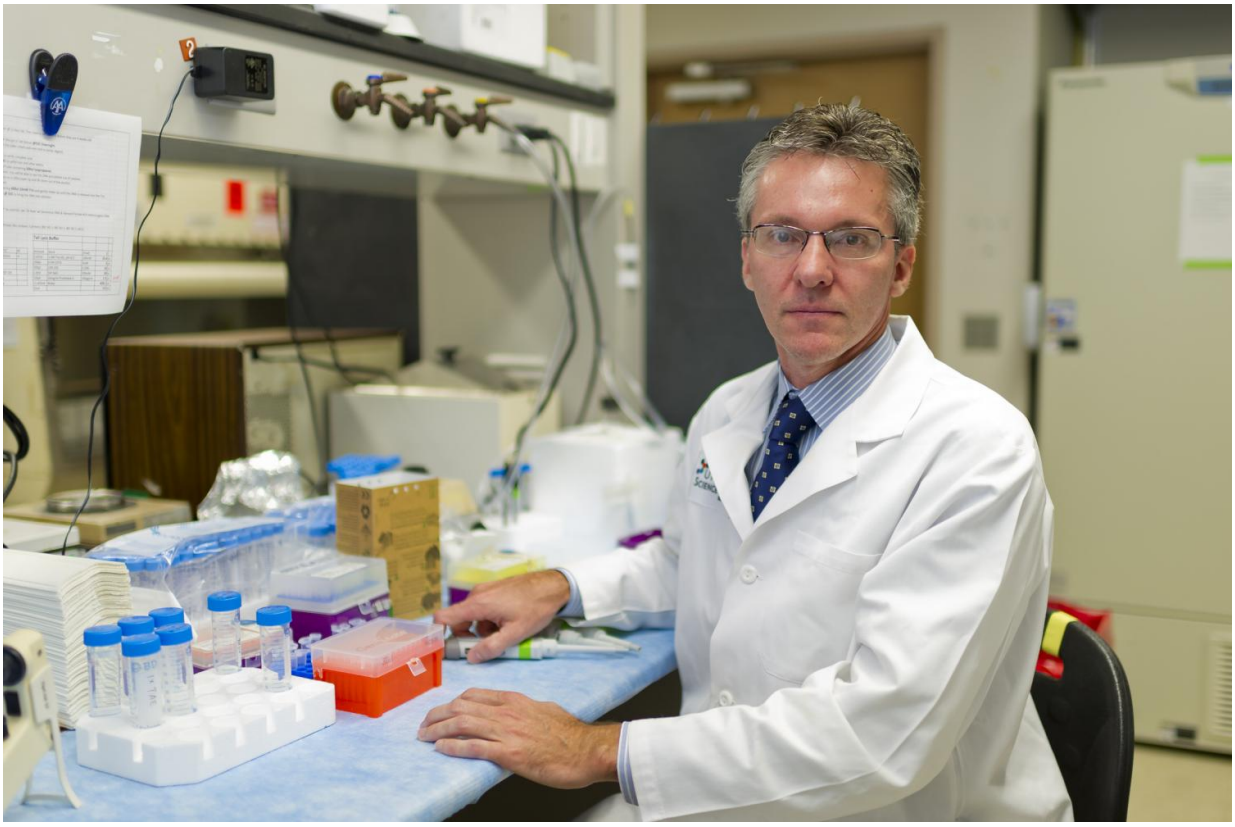

Ricardo Aguiar, M.D., Ph.D., of UT Health San Antonio, led a research team that reports in Cancer Cell on a finding in IDH-mutant cancers. Credit: UT Health San Antonio

UT Health San Antonio researchers discovered epigenetic changes that contribute to one-fifth of cases of acute myeloid leukemia (AML), an

aggressive cancer that arises out of the blood-forming cells in bone marrow.

The mutations also play a role in a large majority of low-grade gliomas, which are among the most-treatable brain tumors.

The UT Health scientists describe the finding in this week's issue of *Cancer Cell.*

"The best way to treat a cancer is to understand it," said Ricardo C.T. Aguiar, M.D., Ph.D., professor of medicine at The University of Texas Health Science Center, now called UT Health San Antonio. "We have added to the understanding of a broad swath of cancers that carry what is called the IDH mutation."

Cancers classified by genetic defect

Dr. Aguiar, a hematology-oncology researcher and member of the UT Health San Antonio Cancer Center, is senior author of the study. He said in the future cancers will be classified not by where they are located but by their genetic defect - such as the IDH mutation. IDH is short for isocitrate dehydrogenase.

The UT Health team found that IDH mutations alter an epigenetic process called RNA methylation, which leads to deregulation of hundreds of other genes and processes inside the tumor cell.

Changes that amplify—or silence—genes

Epigenetic modifications change gene activity but don't structurally change the body's genetic blueprints. Diet, aging, environmental exposure and other factors can prompt epigenetic changes that amplify

or silence certain genes.

A drug that inhibits the IDH mutant enzymes is in non-UT Health-related clinical trials. The UT Health discovery provides evidence for why the drug may help patients with AML and low-grade gliomas.

A difficult-to-treat form of leukemia

"Acute myeloid leukemia remains a very difficult-to-treat tumor and, unfortunately, the majority of patients still die of their disease," Dr. Aguiar said. "In this paper, in addition to sophisticated genetic models created in our lab, we also studied primary AML samples to demonstrate that, in the very IDH-mutant tumors from the patients, we detected this change in RNA methylation. By better understanding how the IDH-dependent cancers work, we may be able to fine-tune future therapies and improve survival."

More information: Sara M. Elkashef et al, IDH Mutation, Competitive Inhibition of FTO, and RNA Methylation, *Cancer Cell* (2017). DOI: 10.1016/j.ccell.2017.04.001

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