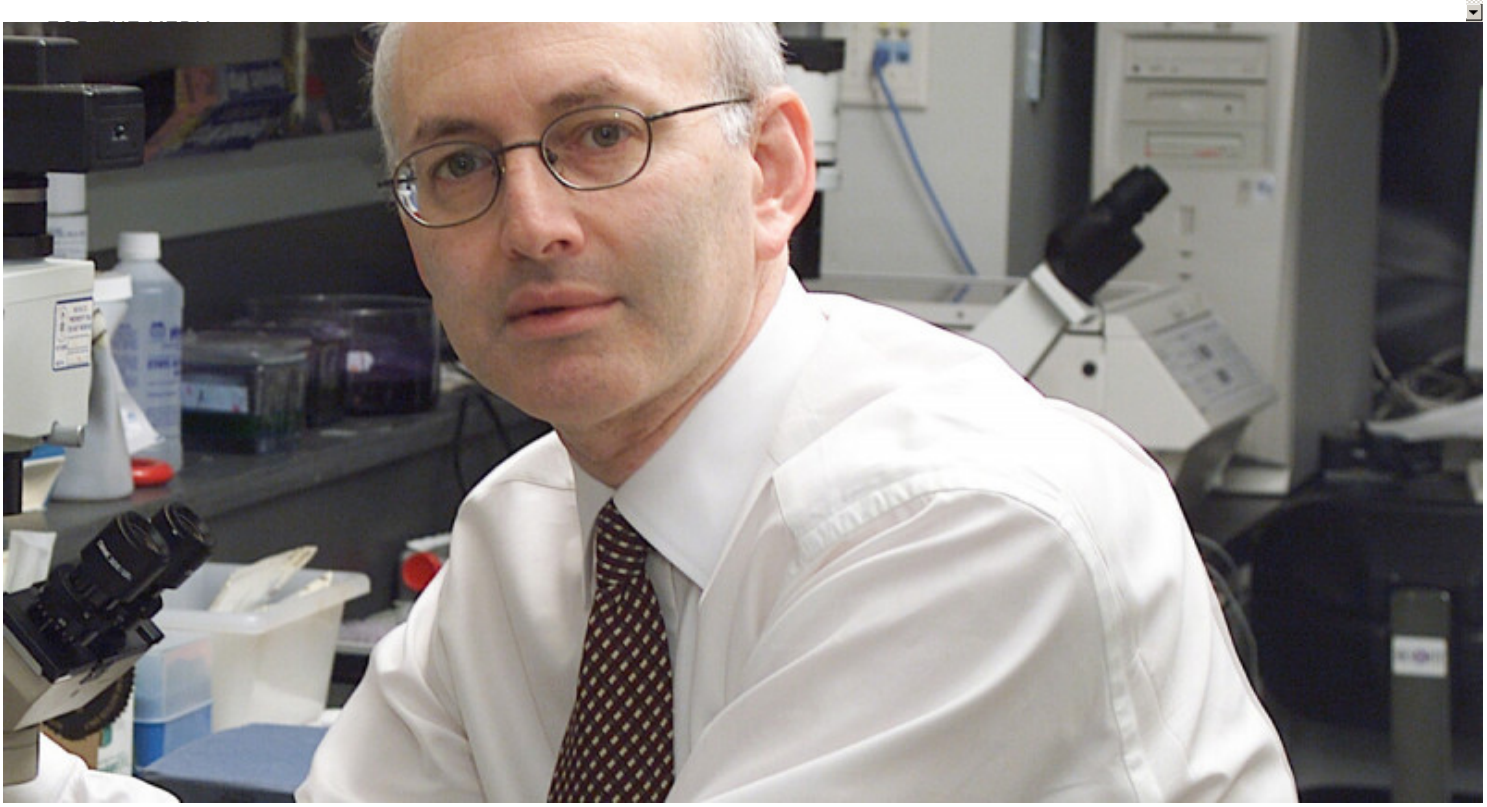

A new study led by researchers at Memorial Sloan Kettering Cancer Center (MSKCC) reports on a novel mechanism that can enhance the function of a protein that is frequently impaired in patients with acute forms of leukemia. The protein, called AML1, plays a critical role in the development of the blood system and in the production of platelets and immune cells. The findings are published in the March 1, 2008, issue of *Genes & Development*. [PubMed Abstract]

> We hope to utilize these new findings to help develop and ultimately test new treatment strategies for patients with either myeloid or lymphoid types of acute leukemia.

Xinyang Zhao, study's first author and a member of Dr. Nimer's laboratory

According to the study, investigators identified the methyltransferase enzyme that controls the activity of the normal AML1 protein - also called RUNX1 - demonstrating its ability to regulate the function of transcription factors, proteins that control cell fate by turning genes on or off. The researchers found that the cellular pathways that regulate the activity of the normal AML1 protein through a process called arginine methylation cannot similarly regulate the activity of AML1-ETO, a protein associated with causing acute leukemia.

Methylation is the process by which methyltransferases catalyze the attachment of a methyl group to DNA or protein in order to regulate gene expression or protein function. Demethylase enzymes that remove methyl groups from proteins have only recently been discovered.

“By manipulating the activity of these enzymes, it may be possible to promote the activity of the normal protein, and thereby lessen the impact of the protein that promotes leukemia,” said the study’s senior author Stephen D. Nimer, MD, Chief of the Hematology Service at MSKCC. “We are just beginning to explore whether we can tilt the balance toward a normally functioning AML1 protein in leukemic cells and either trigger their death or their reversion to normal behavior.”

There are currently no available drugs that target protein methylation, although two drugs that target DNA methylation are FDA approved for treating patients with myelodysplastic syndromes.

“We hope to utilize these new findings to help develop and ultimately test new treatment strategies for patients with either myeloid or lymphoid types of acute leukemia,” said the study’s first author, Xinyang Zhao, a member of Dr. Nimer’s laboratory.

Dr. Nimer has been researching the AML1-ETO protein at MSKCC since 1993. He and his colleagues first demonstrated in 1995 that AML1-ETO functions as a transcriptional repressor and dominantly inhibits AML1 function.

Researchers from The Rockefeller University also contributed to this research, which was supported by a Leukemia & Lymphoma Society Specialized Center of Research (SCOR) grant; the Herbert and Lee Friedman Memorial Fellowship; an NCI Cancer Center Support Grant; and the Mayo Foundation Scholars Program.