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Low micro-RNA level linked to high gene activity in AML

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A new study suggests that a type of acute leukemia may occur in part because abnormally low levels of one small molecule result in the over-activity of genes important to the disease.

The research involved patients with acute myeloid leukemia (AML) and a gene mutation called NPM1, an alteration seen in about one-third of adult AML cases.

The findings suggest new therapeutic targets for treating the disease and should improve the understanding of AML, researchers say.

The study showed that a type of microRNA – molecules important in controlling cell development and proliferation – regulates two genes whose elevated activity has been linked to leukemia in humans and proven to cause leukemia in mice.

The two genes belong to the Hox family of genes, known to play a critical role in embryonic development and blood-cell development.

The study, led by researchers at the Ohio State University Comprehensive Cancer Center, was published online Feb. 28 in the *Proceedings of the National Academy of Sciences*.

“We’ve shown that low levels of a microRNA called miR-204 are at least partly responsible for the high activity of these Hox genes,” says first author Dr. Ramiro Garzon, an Ohio State cancer researcher.

“If this is verified, and if we can develop a drug to modulate this microRNA, it may provide a new therapeutic intervention for these patients.”

For this study, the investigators examined microRNAs levels in leukemia cells from 85 patients. They also looked for mutations in two genes in the leukemic cells: NPM1 and FLT3 (pronounced “Flit-3”).

The pattern of microRNA molecules present in the cells enabled the researchers to distinguish the 55 patients with mutated NPM1 genes from those with a normal gene.

Furthermore, 26 of the 85 patients had FLT3 mutations. These cases also had high levels of a microRNA called miR-155. Further experiments showed that while the high levels of miR-155 were closely associated with FLT3 mutations, they were independent of the mutation (i.e., it did not cause the high levels).

“This is significant,” says Garzon, an assistant professor of internal medicine. “We already have drugs that target FLT3, but they are not effective by themselves. This finding suggests that if we develop a drug that targets miR-155, and combine it with a FLT3 inhibitor, we might achieve a more complete response in these patients.”

Garzon and his colleagues are studying that possibility now.

Source: Ohio State University Medical Center