MedicalXpress

Molecules might identify high-risk acute-leukemia patients

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New research suggests that certain small molecules used by cells to control the proteins they make might also help doctors identify adult acute-leukemia patients who are likely to respond poorly to therapy.

Researchers say the findings should improve the understanding of acute myeloid leukemia (AML) and could lead to new therapies for patients with few treatment options.

The study examined the levels of molecules called microRNAs in leukemia cells from 122 patients with high- and intermediate-risk AML and in normal blood stem cells from 10 healthy donors.

The findings showed that both the leukemia cells and their normal counterparts had similar kinds of microRNA, but that the two groups differed in the levels of miRNAs present.

The research also identified two microRNAs present at abnormally high levels that were clearly associated with patient survival.

The investigators verified their findings in an additional group of 60 patients using a different technology.

The study, published online Jan. 10 in the journal *Blood*, was led by researchers with The Ohio State University Comprehensive Cancer Center and the M.D. Anderson Cancer Center.

“If our results are validated by other groups, these two elevated microRNAs can be used to determine which patients require more aggressive treatment,” says first author Dr. Ramiro Garzon, assistant professor of internal medicine and a researcher with The Ohio State University Comprehensive Cancer Center.

“In addition, they may provide new targets for future therapies – knocking out these two microRNAs might benefit patients who have a poor prognosis.”

This possibility is particularly intriguing, he says, because the two microRNAs – called miR-191 and miR-199a – are also associated with cancers of the lung, prostate, colon, stomach and breast. This suggests that they may be part of a common cancer pathway.

Garzon noted that the study also found an association between high levels of a microRNA called miR-155 in AML patients and a gene mutation called FLT3-ITD. High levels of this microRNA have been reported in other cancers and to cause leukemia in mice.

“Clearly, our findings suggest that the quantity of microRNAs present is important in cancer, suggesting that modulating their levels might offer an effective way to treat the disease in these patients,” he says.

For this study, Garzon and his colleagues used blood samples from newly diagnosed AML patients who had either normal-looking chromosomes, a feature that indicates intermediate risk of recurrence, or other chromosome alterations. These included isolated trisomy 8, the t(11q23) translocation and multiple chromosomal abnormalities that signal a high risk of recurrence.

Together, these groups make up the majority of the 13,400 people expected to be diagnosed with AML in 2007. About 9,000 people that

year were expected to die of the disease.

“Our efforts now should concentrate on characterizing how these altered microRNAs might promote leukemia and on developing drugs designed to inhibit their action,” Garzon says.

Source: Ohio State University