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Scientists discover new role for miRNA in leukemia

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Scientists here have found that mini-molecules called micro-RNA may play a critical role in the progression of chronic myeloid leukemia (CML) from its more treatable chronic phase to a life-threatening phase, called blast crisis.

Furthermore, they discovered an entirely new function for these molecules. The researchers show that microRNAs can sometimes directly control a protein's function – not just whether or not the protein is made by the cell, as has been believed.

The study, using cells from CML patients in blast crisis, suggests that certain progenitor white blood cells are kept from maturing when levels of one microRNA, called miR-328, fall abnormally low. Immature white cells then build up in the blood and bone marrow, a telltale sign that the patient has entered the therapy-resistant blast-crisis phase.

The findings are being presented at the 2007 annual meeting of the American Society of Hematology (ASH), Dec. 8-11 in Atlanta.

"If verified, our study suggests that altering microRNA levels might represent a potentially new therapeutic strategy for CML patients who do not benefit from effective targeted agents such as imatinib (Gleevec) and dasatinib (Sprycel)," says principal investigator Danilo Perrotti, assistant professor of molecular virology, immunology and medical genetics and a researcher with the Ohio State University Comprehensive Cancer Center.

“The findings also reveal a new function for microRNAs, which should further our understanding of their role in cancer development and progression, and in normal cells.”

Researchers have known for some time that microRNAs bind to molecules called messenger RNA, which are part of the cell’s protein-making machinery, and in this way help regulate the types and amount of proteins made by cells.

But this study shows for the first time that the microRNA molecules sometimes bind directly with proteins themselves and affect their function.

In this case, a microRNA called miR-328 binds with a protein that, in blast phase CML, prevents immature blood cells from maturing. “We believe that miR-328 acts as a decoy molecule that normally ties up the protein, which enables the white blood cells to mature as they should,” Perrotti says.

During progression from chronic-phase to blast-crisis CML, however, the level of miR-328 falls, allowing the protein to be extremely active. This keeps the progenitor white blood cells from maturing, thus favoring blast-crisis conditions.

“These findings are important because they help us understand the biology of blast-crisis CML, and they may help unravel novel pathways responsible for the initiation and progression of leukemia generally,” Perrotti says.

Source: Ohio State University