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Study identifies key cause of chronic leukemia progression

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Researchers have discovered a key reason why a form of leukemia progresses from its more-treatable chronic phase to a life-threatening phase called blast crisis.

The study, led by cancer researchers at the Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC-James), indicates that chronic myeloid leukemia (CML) progresses when immature white blood cells lose a molecule called miR-328.

Loss of the molecule traps the cells in a rapidly growing, immature state. The cells soon fill the bone marrow and spill into the bloodstream, a tell-tale sign that the disease has advanced to the blast crisis stage.

The research, published in the March 5th issue of the journal *Cell*, should provide a better understanding of the blast-crisis stage of CML, and it suggests a possible new treatment strategy for the disease, the researchers say.

"These findings indicate that the loss of miR-328 is probably essential for progression from the chronic phase of the disease to the blast crisis stage," says principal investigator Danilo Perrotti, associate professor of molecular virology, immunology and medical genetics and a member of the OSUCCC-James.

"Our findings also suggest that maintaining the level of this microRNA

might represent a new therapeutic strategy for CML blast crisis patients who do not benefit from targeted agents such as imatinib (Gleevec) and dasatinib (Sprycel)," Perrotti says

The study also revealed a new function for microRNA. Researchers have known for some time that these molecules help regulate the kinds of proteins that cells make. But this study shows for the first time that microRNA molecules can also attach directly to protein molecules and alter their function.

In this case, miR-328 binds to a protein that prevents immature blood cells from maturing. "We believe that it normally acts as a decoy molecule, tying up the protein and enabling the white blood cells to mature as they should," Perrotti says.

During CML progression, however, the level of miR-328 drops, allowing the protein to be extremely active. This keeps the leukemic white blood cells from maturing and contributes to the transition from the chronic-disease phase to blast crisis phase.

"These findings may help unravel novel pathways responsible for the initiation and progression of leukemia generally," Perrotti says.

Provided by The Ohio State University

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