

# Study identifies possible new acute leukemia marker, treatment target

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A study has identified microRNA-155 as a new independent prognostic marker and treatment target in patients with acute myeloid leukemia that has normal-looking chromosomes under the microscope (that is, cytogenetically normal acute myeloid leukemia, or CN-AML).

The study was led by researchers at the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James). The researchers found that when microRNA-155 (miR-155) is present at abnormally high levels in CN-AML cells, patients are less likely to have a complete remission, and they experience a shorter disease-free period and shorter overall survival. The effect is independent of other known prognostic gene mutations present in the cells.

Published in the *Journal of Clinical Oncology* with an accompanying editorial and an "Understanding the Pathway" article, the findings suggest that miR-155 plays a [pivotal role](#) in CN-AML development, and that it could be a valuable target for the emerging class of drugs designed to inhibit microRNAs, says first author Dr. Guido Marcucci, professor of [hematology](#), a leukemia specialist and associate director for Translational Research at the OSUCCC – James. "MiR-155 would be relatively easy to measure at the time of diagnosis," Marcucci says. "We believe it will prove to be a good marker for stratifying patients according to [recurrence risk](#) and a good target for emerging compounds designed to inhibit microRNAs."

Principal investigator Dr. Clara D. Bloomfield, Distinguished University Professor and Ohio State University Cancer Scholar and Senior Advisor and William Greenville Pace III Endowed Chair in [Cancer Research](#) notes that, "Overall, our findings indicate that miR-155 expression is a strong and independent [prognostic marker](#) in CN-AML, and they provide [clinical validation](#) of data from preclinical models that support a crucial role of miR-155 in leukemia."

The researchers also note that because a molecule called NF-kB is believed to regulate miR-155, treatments that inhibit that molecule might also help patients with high miR-155 levels.

Cells use microRNA molecules to help regulate the kinds and amount of proteins they make. Abnormal levels of certain microRNAs are likely to play a key role in cancer development. Abnormally high expression of miR-155 is associated with lymphoma, aggressive chronic leukemias and certain solid tumors, and microRNA levels have been associated with patient survival.

For this study, Marcucci, Bloomfield and their colleagues analyzed bone-marrow or blood specimens from 363 CN-AML patients, 153 of whom were under age 60 and 210 were age 60 and over. All were treated on Cancer and Leukemia Group B (CALGB) clinical trials.

The researchers evaluated the association of abnormal miR-155 expression levels with clinical and molecular characteristics and with disease-free survival and overall survival.

The study's key technical findings include:

- Overall, patients with high miR-155 expression were about 50 percent less likely to achieve complete remission, and to have a

60 percent increase in the risk of death compared to patients with low miR-155 expression.

- High miR-155 expression was associated with pro-survival, proliferation and inflammatory gene activity, suggesting a pivotal role in leukemia development.
- In patients under age 60, higher miR-155 expression was associated with a lower complete response rate, and shorter disease-free survival and overall survival; in older patients, higher miR-155 expression was associated only with a lower complete response rate and shorter overall survival.
- The difference between older and younger patients may be related to differences in the intensity of consolidation therapy administered to younger versus older patients, as well as to biological differences.

Provided by Ohio State University Medical Center

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