

# Long noncoding RNAs: A novel prognostic marker in older patients with acute leukemia

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A new study led by researchers at The Ohio State University Comprehensive Cancer Center - Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James) describes a novel marker that might help doctors choose the least toxic, most effective treatment for many older patients with acute myeloid leukemia (AML). AML occurs mainly in older patients and has a three-year survival rate of 5 to 15 percent.

The researchers investigated patterns of molecules called long noncoding RNAs (lncRNAs), a class of RNA molecules more than 200 nucleotide units long that are involved in regulating genes. The researchers examined the abundance, or expression, of lncRNAs in [patients](#) who were 60 years and older and who had cytogenetically normal (CN) AML.

The study is published online in the *Proceedings of the National Academy of Sciences*.

"We have identified a pattern of 48 lncRNAs that predicted both response to standard chemotherapy and overall survival in older CN-AML patients," says first author Ramiro Garzon, MD, associate professor of internal medicine at Ohio State.

"Patients in the favorable group had a high probability of responding to standard chemotherapy, while those in the unfavorable group generally responded poorly to the treatment and had worse overall survival," he says.

These findings are important for several reasons, says principal investigator Clara D. Bloomfield, MD, Distinguished University Professor, Ohio State University Cancer Scholar and holder of the William Greenville Pace III Endowed Chair in Cancer Research.

"First, they strongly suggest that lncRNA expression profiles can predict which patients will respond to standard therapy. That's important

because it would spare these patients from the toxic side effects of experimental therapies.

"Patients who are classified in the unfavorable group would receive different therapy, stem cell transplant or a clinical trial using new therapeutic approaches. Thus, this research will help to tailor leukemia therapy to each individual."

In addition, she says, this study identified many novel targets for the development of new therapies.

Garzon, Bloomfield and their colleagues developed the prognostic scoring system using bone-marrow samples from 148 [older patients](#) with CN-AML treated on Cancer and Leukemia Group B clinical trials. All had received similar chemotherapy regimens.

The researchers first identified 48 lncRNAs that were most associated with survival. Using these 48 lncRNAs, the researchers divided patients into two groups, those with a favorable outcome score and those with an unfavorable outcome score. The researchers then validated the outcome scores in an independent matched set of 71 similarly treated CN-AML patients.

Comparing patients with an unfavorable score to those with a favorable score revealed the following:

- Patients with an unfavorable score had a lower complete response (CR) rate (54 percent vs 89 percent respectively);
- Three years after CR, only 7 percent of patients with an unfavorable score were disease free compared with 39 percent of patients with a favorable score.
- Overall survival at three years for those with an unfavorable score was 10 percent versus 43 percent for patients with a favorable score.
- Distinct lncRNA profiles were associated with six clinically important CN-AML

mutations.

In summary, the [researchers](#) showed that lncRNA [expression profiles](#) were associated with recurrent mutations, clinical features, and outcome in AML. A fraction of these lncRNAs may have a functional role in leukemogenesis. Furthermore, lncRNAs could be used as biomarkers for outcome in AML.

**More information:** Expression and prognostic impact of lncRNAs in acute myeloid leukemia, *PNAS*, DOI: [10.1073/pnas.1422050112](https://doi.org/10.1073/pnas.1422050112)

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