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DNMT3A, IDH1/2, TET2, General AML

Gene alterations associated with myeloperoxidase positivity in *de novo* AML – a Japanese study

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Myeloperoxidase (MPO), is a microbicidal protein, whose expression is a definite marker for diagnosis of Acute Myeloid Leukemia (AML) and findings from clinical studies conducted by the Japan Adult Leukemia Study Group (JALSG) have shown that MPO is a significant prognostic factor in AML. Rena Kamijo from Nagasaki University Graduate School of Biomedical Science, Nagasaki, Japan, and colleagues, investigated the relationship between MPO positivity and gene alterations. The data from the study were reported in Leukemia Research earlier this month.

In this study, Kamijo *et al.* performed targeted sequencing for 51 genes and 10 chimeric genes on bone marrow samples from 164 adults with newly diagnosed *de novo* AML who were treated in the JALSG AML201 study. Patients were divided into two groups based on the positivity of the MPO enzymatic activity including > 50% MPO-positive blasts (MPO high group, n = 107 [median age = 46 years]) and ≤ 50% MPO-positive blasts (MPO low group, n = 57 [median age = 51 years])

Key findings:

- Mutations in 44 genes and 6 fusion transcripts were identified in all patients
- Mean number of mutated genes in the MPO-high and MPO-low groups were 2.61 ±72 and 2.37 ± 0.19, respectively
- Mutations in CBF-fusion gene, ($P < 0.001$), *KIT* gene ($P < 0.001$), *CEBPA* double mutation ($P < 0.001$) correlated with MPO high group
- Low MPO positivity correlated with mutations in *DNTM3A* ($P = 0.001$), *TP53* ($P = 0.02$) and *FLT3-TKD* ($P = 0.004$)
- Analysis in non-CBF AML patients
    - Mutations in *IDH1/2, TET2* and *WT1* correlated with high MPO positivity; $P = 0.001$

In summary, this is the first study to assess MPO-positivity as a marker for distinct gene alterations. It was demonstrated in this study that MPO-positivity of blasts correlates with distinct gene alterations among *de novo* AML patients. Additionally, high MPO positivity was shown to correlate with distinct DNA methylation profile.

Kamijo *et al.* noted that their study is limited by the fact that the impact of some mutated genes could not be identified due to low frequencies. Moreover, the position and type of each gene affected by MPO positivity was insufficient.

References

1. *Kamijo R. et al.* Distinct gene alterations with a high percentage of myeloperoxidase-positive leukemic blasts in de novo acute myeloid leukemia. Leuk Res. 2018 Jan 2. DOI: 10.1016/j.leukres.2017.12.006. [Epub ahead of print].