soho2023
ELEVENTH ANNUAL MEETING

Genomic Landscape of Acute Myeloid Leukemia with t(8;21) and inv(16)

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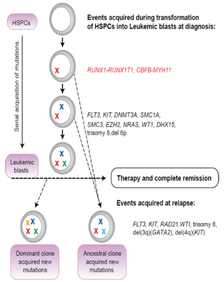
ФГБУ РосНИИГТ ФМБА России

ЦЕНТР КЛЕТОЧНОЙ И МОЛЕКУЛЯРНОЙ ПАТОЛОГИИ ФГБУРНИИГТ

INTRODUCTION

In clinical trials, the subgroups of t(8;21) and inv(16) acute myeloid leukemia (AML) are often combined because of their high survival rate and the involvement of core binding factors (CBF) transcription factors in the pathogenesis.

However, these groups have their own biological and clinical features.

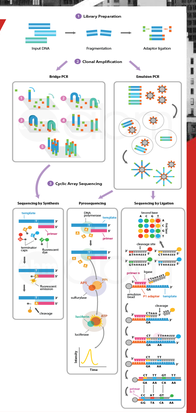


AIM

To compare the mutational landscape of patients with t(8;21) and inv(16) AML and evaluate its impact on the prognosis.

METHOD

46 CBF-AML patients were studied. 24 patients with t(8;21) and 22 patients with inv(16), all patients with de novo AML, median age was 40 years (18-60 years).
Samples were analyzed by high-throughput sequencing on MiSeq using TruSight Myeloid Sequencing Panel kit (Illumina, USA) to create amplicon libraries. A targeting panel consisting of 118 genes was developed. The clinical significance of mutations was established using COSMIC, ClinVar, and Varsome databases.



RESULTS

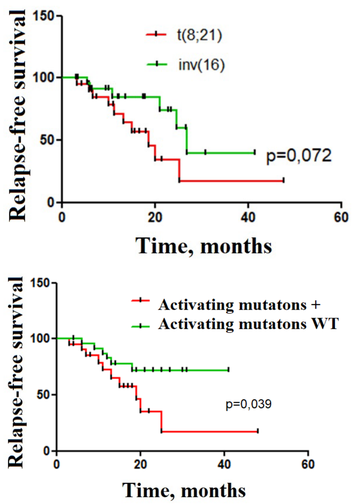
Most patients with t(8;21) (74%) had additional chromosomal aberrations (mainly -X/-Y) and only 33% of patients with inv(16) had additional chromosomal aberrations (p=0.01). Complex karyotype was rare in both groups and didn't affect prognosis. Morphologically AML with t(8;21) was associated with M2 variant (79%) and inv(16) with M4 (84%).

In 96% of CBF-AML patients, at least 1 mutation was detected. The highest frequency of occurrence in both groups had mutations in *NRAS+KRAS* (t(8;21): 16%; inv(16): 38%), *KIT* (t(8;21): 24%; inv(16): 24%). Patients with t(8;21) had significantly more mutations than with inv(16): 2.8 versus 1.7 mutations, respectively (*P*=0.03).

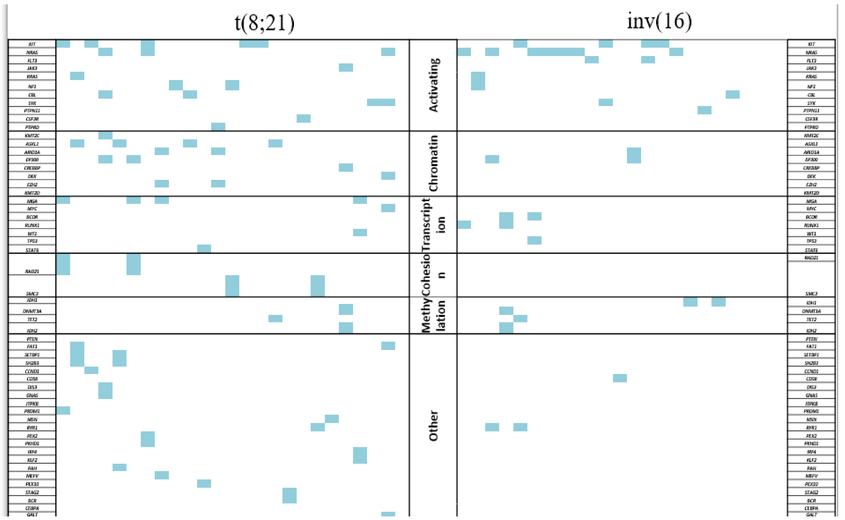
Multiple mutations in the same signaling pathway were detected in both groups of CBF-AML, indicating clonal interference, that may be associated with worse event-free survival.
Prognostically unfavorable mutations were detected in chromatin modifiers *ASXL1* (20%) and *EZH2* (7%); cohesin genes, *RAD21* (13%) and *SMC3* (7%), were detected only in t(8;21) AML.

There was a trend toward worse relapse-free survival in patients with t(8;21) compared with those with inv(16) (*P*=0.072). Mutations in *KIT* gene as well as other mutations in genes involved in the activation of signaling pathways were found to negatively affect the relapse-free survival of patients with CBF-AML (*P*=0.04).

Prognostic significance of mutations



Molecular-genetic profile of patients with AML with t(8;21) and with inv(16)



CONCLUSIONS

Patients with CBF-AML have a highly heterogeneous molecular genetic profile.

AML with t(8;21) and AML with inv(16) have significant differences in morphological, cytogenetic, and molecular-genetic characteristics, which makes it reasonable to analyze them separately.

The peculiarities of molecular genetic characteristics of individual AML variants can be used for individualization of target therapy.

REFERENCES

Paschka P, Döhner K. Core-binding factor acute myeloid leukemia: can we improve on HiDAC consolidation? Hematology Am Soc Hematol Educ Program. 2013;2013:209-19.

CONTACT INFORMATION

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