Revista Brasileira de Hematologia e Hemoterapia
Brazilian Journal of Hematology and Hemotherapy
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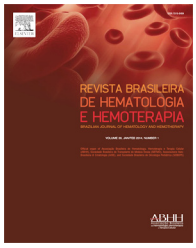

Scientific Comment

Metaphase cytogenetics and single nucleotide polymorphism arrays in myeloid malignancies☆

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ARTICLE INFO

Article history:
Available online 30 January 2015

Chromosomal abnormalities provide useful diagnostic and prognostic information, and may also guide therapy in myeloid malignancies, especially in myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). The revised international prognostic score system for MDS highlights the implication of chromosomal abnormalities on the prognosis of MDS patients.[1] The successes of acute promyelocytic leukemia patients harboring t(15;17) and treated with all-trans retinoic acid (ATRA) indicates the value of chromosomal abnormalities on the diagnosis, prognosis and therapy of AML.[2] Metaphase cytogenetics is a routine test in the management of myeloid malignancies that allows the detection of multiple clones, unbalanced chromosomal defects (deletions and gains) and balanced translocations. However, metaphase cytogenetics is time consuming, it needs cellular proliferation, its sensitivity depends on the proportion of clonal cells in the sample, and its resolution depends on the size of the lesion. At least 50% of MDS and AML patients have normal metaphase cytogenetic results, and the great clinical diversity among these patients has indicated the need for new techniques able to detect additional molecular alterations that can help in the diagnosis, prognosis and treatment. Whole genome scanning technologies have opened up a new road of investigation for chromosomal abnormalities in myeloid malignancies and also other neoplasms.[3] Array-based technologies include comparative genomic hybridization arrays (CGH-A) and single nucleotide polymorphism arrays (SNP-A).[4] More recently, next generation sequencing (NGS) technology has also provided valuable information on chromosomal abnormalities.[5]

In the last issue of the Revista Brasileira de Hematologia e Hemoterapia, Noronha et al.[6] reported the comparative results of metaphase cytogenetics and SNP-A in 25 Brazilian patients with diagnoses of AML or MDS; chromosomal abnormalities were detected in 40% and 68% of patients by metaphase cytogenetics and SNP-A technology, respectively. As demonstrated by Noronha et al.,[6] SNP-A technology does not depend on the presence of dividing cells, has the ability to detect copy number variations (deletions and gains) with a higher resolution than conventional cytogenetics, and to detect copy number neutral loss of heterozygosity (CN-LOH), also named somatic uniparental disomy (UPD). However, SNP-A does not detect balanced translocations, does not distinguish individual clones; and does not detect small clones.[4] As such, SNP-A does not replace metaphase cytogenetics, and combined methods will probably be necessary to improve the clinical care of patients with myeloid malignancies. Another interesting issue illustrated by Noronha et al.[6] was the comparison of SNP-A results obtained from the germ-line DNA sample (buccal cells) and the tumor sample (bone marrow mononuclear cells). This approach is recommended to exclude

☆ See paper by Noronha et al. in Rev Bras Hematol Hemoter. 2015;37(1):48–54.

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http://dx.doi.org/10.1016/j.bjhh.2015.01.007

normal copy number variations from somatic/acquired gains, deletions or UPD. Normal copy number variations, in general, are smaller than 1 Mb and may have characteristic locations,[7] as indicated in public databases.

Two other important contributions of SNP-A technology to myeloid malignancies need to be highlighted. SNP-A was first used as an investigative tool, which allowed the identification of various common deleted regions and the discovery of several important gene mutations exemplified by *CBL*, *TET2*, and *EZH2* mutations.[8] New lesions detected by SNP-A may have prognostic implications in MDS[9] and AML[10]; however, the validation of this finding in different cohorts of patients is necessary. The high cost of SNP-A limits its use in the routine clinical setting. The work by Noronha et al.[6] represents an important step in establishing the use of SNP-A in Brazilian patients with myeloid malignancies in a research scenario, which may be important to better define the somatic chromosomal abnormalities in our population and may be a valuable tool to investigate molecular mechanisms involved in Brazilian cases of familial myeloid malignancies.

Conflicts of interest

The authors declare no conflicts of interest.

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