CEBPA Mutation Analysis

Background

Mutations in the *CEBPA* gene are identified in 15-18% of acute myeloid leukemia (AML) with normal cytogenetics, and AML with mutated *CEBPA* represents a provisional diagnostic entity in the 2008 WHO classification.[1]

AML with mutated *CEBPA* displays distinct clinicopathologic features including a favorable clinical course, and the identification of *CEBPA* mutations may assist in treatment selection.[2-6] *CEBPA* mutation analysis is recommended for cases of AML with normal cytogenetics in current National Comprehensive Cancer Network (NCCN) and European LeukemiaNet guidelines.

Clinical Indications

Cleveland Clinic Laboratories offers *CEBPA* mutation analysis for classification and prognostic assessment of new acute myeloid leukemias, especially those with normal cytogenetics. Concurrent *NPM1* and *FLT3* studies are also recommended (see Acute Myeloid Leukemia Mutation Profile technical brief).

Interpretation

Mutations in *CEBPA* include single and dual (usually biallelic) mutations. Initial studies reported that the presence of any *CEBPA* mutation was associated with a favorable clinical course, while more recent studies have suggested that the favorable clinical course and distinctive clinicopathologic features are limited to AML with dual CEBPA mutations.[2-6] All identified mutations are reported, and cases are classified as wild type (no mutations detected), single mutated or dual mutated.

Limitations of the Assay

Sanger sequencing is expected to identify >99% of mutations, provided that mutations represent at least 15-20% of total *CEBPA* alleles. This test is not intended for detection of minimal residual disease.

Methodology

DNA is extracted from peripheral blood or bone marrow. The entire *CEBPA* coding region is amplified by PCR and analyzed by Sanger sequencing.

References

1. Arber DA *et al*. (2008). Acute myeloid leukaemia with recurrent genetic abnormalities. In: Swerdlow SH, Campo E, Harris NL *et al*., eds. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon, France: WHO Press. 110-23.
2. Taskesen E, Bullinger L, Corbacioglu A, *et al*. Prognostic impact, concurrent genetic mutations and gene expression features of AML with CEBPA mutations in a cohort of 1182 cytogenetically normal AML patients: further evidence for CEBPA double mutant AML as a distinctive disease entity. *Blood.* 2011;117:2469-2475.
3. Green CL, Koo KK, Hills RK, *et al*. Prognostic significance of CEBPA mutations in a large cohort of younger adult patients with acute myeloid leukemia: impact of double CEBPA mutations and the interaction with FLT3 and NPM1 mutations. *J Clin Oncol.* 2010;28:2739-47.
4. Dufour A, Schneider F, Metzeler KH, *et al*. Acute myeloid leukemia with biallelic CEBPA gene mutations and normal karyotype represents a distinct genetic entity associated with a favorable clinical outcome. *J Clin Oncol*. 2010;28:570-7.
5. Pabst T, Eyholzer M, Fos J, *et al*. Heterogeneity within AML with CEBPA mutations: only CEBPA double mutations, but not single CEBPA mutations are associated with favorable prognosis. *Br J Cancer*. 2009;100:1343-6.
6. Wouters BJ, Lowenberg B, Erpelinck-Verschueren CA, *et al*. Double CEBPA mutations, but not single CEBPA mutations, define a subgroup of acute myeloid leukemia with a distinctive gene expression profile that is uniquely associated with a favorable outcome. *Blood*. 2009;113:3088-91.

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Test Overview

Test Name	*CEBPA* Mutation Analysis
Ordering Mnemonic	CEBPA
Specimen Requirements	Volume/Size: 5 mL; Type, blood; Container, EDT (Lavender); Transport temperature, ambient.
Minimum Specimen Requirements	Volume/Size: 3mL
Alternate Specimen Requirements	Volume/Size, 2ug; Type, blood; Container, EDTA (lavender); Transport temperature, ambient.
Reference Range	*CEBPA* mutations are not detected.
CPT Code	81218

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