

CEBPA Mutation Detection

DETECTS CEBPA MUTATIONS IN ACUTE MYELOID LEUKEMIA

Clinical Background

- CCAAT/enhancer-binding protein alpha (CEBPA) is a transcription factor important for myeloid differentiation and suppression of proliferation.^{1,2}
- Mutations in *CEBPA* confer an improved prognosis in cytogenetically normal acute myeloid leukemia (AML). However, only those cases with two mutations (one in each allele) show improved prognosis.³⁻⁵ The significance of a single mutation is unclear.
- In affected cases, one allele typically demonstrates a frameshift mutation in the N-terminal transcriptional activation domain (TAD), and the other allele demonstrates a mutation in the C-terminal basic-leucine zipper (bZIP) domain. Other types and locations of mutations have also been observed.

Indications for Use

The principal use for this test is to determine the prognosis of newly diagnosed cases of AML with normal cytogenetics.

Interpretation

- Not detected: No mutations were detected.
- Positive—double mutation: Two mutations were detected.
- Positive—single mutation: One mutation was detected.

Limitations

- Results of this test must always be interpreted in the context of morphologic and other relevant data, and should not be used alone for a diagnosis of malignancy.

- Samples that do not show a *CEBPA* mutation by this test may still harbor mutations, but in quantities below the detection limit of this test.
- This test may not accurately detect mutations if present in fewer than 40 percent of white blood cells.

Methodology

Genomic DNA is extracted, and two overlapping fragments covering the entire *CEBPA* coding sequence are PCR-amplified. The fragments are sequenced, and the results are compared to the published unmutated sequence.

References

1. Zhang P, et al. Enhancement of hematopoietic stem cell repopulating capacity and self-renewal in the absence of the transcription factor C/EBP alpha. *Immunity* 2004;21(6):853–63.
2. Fukuchi Y, et al. Activation of CCAAT/enhancer-binding protein alpha or PU.1 in hematopoietic stem cells leads to their reduced self-renewal and proliferation. *Stem Cells* 2008;26(12):3172–81.
3. Dufour A, 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(4):570–7.
4. Wouters BJ, 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(13):3088–91.
5. Pabst T, et al. Heterogeneity within AML with *CEBPA* mutations; only *CEBPA* double mutations, but not single *CEBPA* mutations are associated with favourable prognosis. *Br J Cancer* 2009;100(8):1343–6.

Test Information

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For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult[®] at www.arupconsult.com.