

*BloodCenter of Wisconsin
Diagnostic Laboratories offers CEBPA mutation analysis.*

BACKGROUND:

CEBPA mutations define the provisional category of “acute myeloid leukemia with mutated *CEBPA*” in the 2008 WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues¹. Mutations in *CEBPA* are found in 15 -18% of cases of cytogenetically normal AML and are associated with a favorable prognosis².

Germline mutations in *CEBPA* are a cause of nonsyndromic, familial AML³. Inheritance appears to be autosomal dominant with high to complete penetrance. Pabst et al. detected germline *CEBPA* mutations in 2 of 18 (11%) *CEBPA*-positive AML patients⁴.

CEBPA MUTATION ANALYSIS:

This analysis can also be ordered separately or as a reflex test with our *NPM1* Analysis. The reflex algorithm adds *CEBPA* Mutation Analysis to *NPM1*-negative specimens.

REASONS FOR REFERRAL:

- Risk stratification in patients with cytogenetically normal AML.
- Evaluation for familial AML.

METHOD:

CEBPA mutations in leukemic cells are detected and characterized by a combination of PCR amplification, fragment analysis, and direct sequencing of the coding and junctional regions of the *CEBPA* gene. Germline mutations are detected by PCR amplification and direct sequencing of the *CEBPA* coding and junctional regions.

LIMITATIONS:

The lower limit of detection of the assay is approximately 20%. The assay is expected to detect >99% of germline variants within the *CEBPA* coding and junctional regions, and >99% of somatic variants within the coding and junctional regions if the mutation is present at a level of 20% or greater.

REFERENCE INTERVAL:

No mutation detected.

Sequence variations are reported using standard nomenclature.

SPECIMEN REQUIREMENTS:

3-5 ml EDTA (lavender top) whole blood or 2-5 ml EDTA bone marrow.

SHIPPING REQUIREMENTS:

Place the room temperature specimen and requisition in plastic bags, seal and insert in a Styrofoam container. Seal the Styrofoam container, place in a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines. Address package to:

Client Services/Molecular Diagnostics Laboratory
BloodCenter of Wisconsin
638 N. 18th Street
Milwaukee, WI 53233
800-245-3117, ext. 6250

TURNAROUND TIME: 10-14 days

CPT CODES:

CEBPA Mutation Analysis

83891, 83892 x 4, 83898 x 4, 83900, 83901, 83904 x 4, 83909, 83912

NPM1 Mutation Analysis with Reflex to CEBPA Analysis

83891, 83900, 83909, 83912

If CEBPA reflex performed add:

83900, 83901, 83909, 83898 x 4, 83892 x 4, 83904 x 4

AML Familial Evaluation (CEBPA)

83891, 83898 x 4, 83892 x 4, 83904 x 4, 83912

ORDER CODE:

4629

CITED REFERENCES:

1. Arber DA, Brunning RD, Le Beau MM, et al. 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, 2008:110-23.
2. Leroy H, Roumier C, Huyghe P, et al. *CEBPA* point mutations in hematological malignancies. *Leukemia* 2005;19:329-34.
3. Smith ML, Cavenagh JD, Lister, A, et al. Mutation of *CEBPA* in Familial Acute Myeloid Leukemia. *N Engl J Med* 2004;351:2403-7.
4. Pabst T, Eyholzer M, Haefliger S, et al. Somatic *CEBPA* Mutations Are a Frequent Second Event in Families With Germline *CEBPA* Mutations and Familial Acute Myeloid Leukemia. *J Clin Oncol* 2008;26:5088-93.

ADDITIONAL REFERENCES:

- Benthous T, Schneider F, Mellert G, et al. Rapid and sensitive screening for *CEBPA* mutations in acute myeloid leukaemia. *Br J Haematol* 2008; 143:230-39.
- Lin L, Lin T, Chou W, et al. A novel fluorescence-based multiplex PCR assay for rapid simultaneous detection of *CEBPA* mutations and *NPM* mutations in patients with acute myeloid leukemias. *Leukemia* 2006;20:1899-1903.
- Marcucci G, Maharry K, Radmacher MD, et al. Prognostic Significance of, and Gene and MicroRNA Expression Signatures Associated With, *CEBPA* Mutations in Cytogenetically Normal Acute Myeloid Leukemia With High-Risk Molecular Features: A Cancer and Leukemia Group B Study. *J Clin Oncol* 2008;26:5078-87.
- Renneville A, Roumier C, Biggio V, et al. Cooperating gene mutations in acute myeloid leukemia: a review of the literature. *Leukemia* 2008;22:915-31.
- Schlenk RF, Dohner K, Krauter J, et al. Mutations and Treatment Outcome in Cytogenetically Normal Acute Myeloid Leukemia. *N Engl J Med* 2008;358:1909-18.

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