# 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 Tissues[1]. Mutations in *CEBPA* are found in 15 -18% of cases of cytogenetically normal AML and are associated with a favorable prognosis[2].

Germline mutations in *CEBPA* are a cause of nonsyndromic, familial AML[3]. 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 patients[4].

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 or DNA, high quality, ≥ 500ng at 25ng/ul.

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 Oncology Laboratory
BloodCenter of Wisconsin
638 N. 18th Street
Milwaukee, WI 53233
800-245-3117, ext. 6250

PO Box 2178
Milwaukee, WI 53201-2178
Location/Sample Deliveries:
638 N. 18th St. Milwaukee, WI 53233-2121
p800-245-3117 | f414-937-6202 | www.bcw.edu

TURNAROUND TIME: 5-10 days

CPT CODES: 81218

PANEL ORDERING:

| | | |
|---|---|---|
| AML post-FLT3 Comprehensive Mutation Panel | Turnaround Time: 7-10 days | |
| NPM1 Mutation Analysis | CPT Codes: 81310 | |
| CEBPA Mutation Analysis | CPT Codes: 81218 | |
| DNMT3A Exon 23 Sequence Analysis | CPT Codes: 81403 | |
| IDH1 Exon 4 Mutation Detection | CPT Codes: 81403 | |
| IDH2 Exon 4 Mutation Detection | CPT Codes: 81403 | |
| AML Mutation Panel | Turnaround Time: 7-10 days | |
| FLT3 Mutation Analysis | CPT Codes: 81245, 81246 | |
| NPM1 Mutation Analysis | CPT Codes: 81310 | |
| CEBPA Mutation Analysis | CPT Codes: 81218 | |

REFLEX ORDERING:

| | | |
|---|---|---|
| AML Mutation Panel - Reflex | | |
| FLT3 Mutation Analysis | CPT Codes: 81245, 81246 | Turnaround Time: 7-10 days |
| NPM1 Mutation Analysis (if indicated) | CPT Codes: 81310 | Turnaround Time: add 3-6 days |
| CEBPA Mutation Analysis (if indicated) | CPT Codes: 81218 | Turnaround Time: add 5-10 days |
| NPM1 Mutation Analysis with Reflex to CEBPA | | |
| NPM1 Mutation Analysis | CPT Codes: 81310 | Turnaround Time: 3-6 days |
| CEBPA Mutation Analysis (if indicated) | CPT Codes: 81218 | Turnaround Time: add 5-10 days |

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:


- Benthaus 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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