

UCLA DIAGNOSTIC MOLECULAR PATHOLOGY LABORATORY
Department of Pathology and Laboratory Medicine
David Geffen School of Medicine at UCLA
Phone: (310) 794-2781, Fax: (310) 794-2765

BCR-ABL Gene Rearrangement

↑CPT

83891; 84311; 83902; 83898 (x2); 83896 (x4); 83912

↑Synonyms

bcr/abl; Gene Rearrangement *bcr*; Philadelphia Chromosome; t(9:22) Translocation

↑Applies to

Acute Myelogenous Leukemia (ALL); Chronic Myelogenous Leukemia (CML)

↑Test Includes

Relative quantitation of *bcr/abl* fusion transcripts in CML and some ALL patients

↑Laboratory

Molecular Pathology

↑Availability

Monday-Friday, 0700-1700

↑Turnaround Time

3-14 days

↑Specimen

Blood, bone marrow

↑Minimum Volume

10 mL whole blood, 4 mL bone marrow

↑ Container

Lavender top (EDTA) tube

↑ Storage Instructions

All specimens should be sent to the Laboratory immediately after collection, preferably by overnight delivery (within 48 hours). Specimens should be refrigerated but not frozen.

↑ Causes for Rejection

Specimen received after 48 hours; inadequately identified specimen

↑ Reference Range

No rearrangement observed

↑ Use

The *bcr/abl* rearrangement assay is clinically useful for:

- confirmation of Philadelphia chromosome-positive CML
- diagnosis of Philadelphia-negative CML
- diagnosis and monitoring of CML during and after chemotherapy or bone marrow transplantation
- confirmation of remission or early detection of relapse

↑ Limitations

The amount of RNA extracted may not be sufficient to perform the assay when the white blood count of patient is very low. RNA is very labile, and significant degradation during collection or transport may result in assay failure.

↑ Methodology

Real-Time Polymerase Chain Reaction (RT-PCR) to detect t(9;22): b2a2, b3a2, b3a3, and e1a2 fusion transcripts. RNA is reverse transcribed and the generated cDNA is amplified with specific primers. The amplicons are detected by a specific pair of probes. In two separate PCR reactions, *bcr/abl* and G6PDH are amplified from the same cDNA. The G6PDH reaction product serves as both a control for RT-PCR performance and as a reference for relative quantification.

↑ Additional Information

Chronic myelogenous leukemia (CML) is characterized by a reciprocal translocation between chromosomes 9 and 22 producing the Philadelphia chromosome. The translocation involves a fusion of the breakpoint cluster region (*bcr*) gene located on chromosome 22 with the *c-abl* oncogene on chromosome 9. The hybrid *bcr/abl* gene is transcribed into an abnormal messenger RNA which is translated into an abnormal tyrosine kinase of 210,000 molecular weight instead of the normal 160,000 molecular weight protein. More than 90% of patients with CML have the Philadelphia chromosome by cytogenetic analysis, and almost 100% will show rearrangement of *bcr/abl* by molecular methods. Most patients with clinically documented CML that lack the Philadelphia chromosome still have the *bcr/abl* rearrangement. A small number of patients do not have the Philadelphia chromosome as detected by the *bcr/abl* rearrangement. During reassessment many of these patients prove to have a myelodysplastic syndrome, usually chronic myelomonocytic leukemia. A very small number of patients with clinical CML remain both Philadelphia chromosome negative and *bcr/abl* negative. Cytogenetically the Philadelphia chromosome has been found in 20% to 25% of patients with acute lymphoblastic leukemia (ALL) and 2% of patients with acute myelogenous leukemia (AML). The Philadelphia chromosome from ALL cases appears similar to CML Philadelphia chromosomes in cytogenetic analysis. However, the two chromosomes result from distinct molecular rearrangements that can be analyzed and detected at the molecular level. Some ALL Philadelphia chromosomes have been found to be identical to the CML Philadelphia chromosome even at the molecular level. These ALL cases are generally regarded as the blast crisis of CML.
