



Division of Human Genetics

Quantitative BCR-ABL (BCR-ABL QUANT)

Molecular Genetics Laboratory

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Additional information and test requisitions are available at:

www.cincinnatichildrens.org/molecular-genetics



Shipping Instructions

Please enclose an oncology test requisition with sample. All information must be completed before sample can be processed.

Place samples in Styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday

Ship to:

Cytogenetics and Molecular Genetics
Laboratories

3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229

The Philadelphia chromosome, a translocation of chromosomes 9:22 that results in the BCR-ABL fusion gene, is present in approximately 95% of chronic myeloid leukemia and 25-30% of adult acute lymphoblastic leukemia cases. If present, the ratio of fusion gene to a reference gene can be used to monitor disease progress.

Monitoring the level of BCR-ABL is helpful for both prognosis and management of therapy in patients with disease. Cincinnati Children's Molecular Genetics Laboratory will use a methodology that measures the number of copies of the BCR-ABL fusion gene (p210) present relative to the number of BCR gene transcripts in the same sample. Comparing the ratio of disease fusion gene copies to normal gene copies allows physicians to have a numerical measure of response to therapy and allows for a more sensitive monitoring for possible disease relapse.

A major molecular response is considered to be a 3-log reduction in the ratio from baseline of diagnosis (50% BCR-ABL/BCR ratio must reduce to 0.05% BCR-ABL/BCR ratio or 5 copies of fusion gene compared to 10000 copies of the BCR gene).

INDICATION

Quantitative BCR-ABL testing is indicated for any patient known to have BCR-ABL fusion gene present by FISH for monitoring of disease. An initial sample should be sent once FISH testing is positive for a baseline measurement. Disease can then be monitored by FISH testing until that result does not indicate presence of fusion gene, and then a quantitative sample should be sent for continued monitoring of disease. This is because the quantitative testing is much more sensitive at measuring small levels of fusion gene products as compared to FISH cytogenetic testing.

TESTING METHODOLOGY:

A RQ-PCR reaction is completed on isolated RNA sample using the Ipsogen FusionQuant® Kit. Ipsogen proprietary FusionQuant® technology precisely quantitates the amount of control and fusion gene transcripts in patient samples by generating standard curves based on the known concentration of plasmid dilutions of both genes. Importantly, the calculation of the ratio of specific fusion gene transcript concentration to endogenous BCR transcript concentration provides a normalized quantification of the specific fusion gene in each assayed sample. Ipsogen's standardized FusionQuant® technology has been shown to be highly reproducible in multi-centric studies, and offers ideal calibrators for inter- and intra-laboratory normalization of RQ-PCR analysis.

ACCURACY:

Results are reported as the log reduction of the ratio of amount of BCR-ABL fusion transcripts to BCR transcripts. Sensitivity studies within the laboratory have shown that a ratio as low as 10^{-5} can be detected. This means that 1 cell with the translocation present within 100,000 normal cells can be detected with our assay. Because of variability of the RNA quantity within a specimen and assay variability, only changes of 0.5 log or greater should be considered significant. Therefore results of 1% BCR-ABL/BCR would be considered equivalent to any results between 3% and 0.3%.

SPECIMEN:

PLEASE NOTE SAMPLE SHOULD BE RECEIVED SAME DAY OR SHIPPED OVERNIGHT ON ICE (DO NOT FREEZE)

5-10mls peripheral blood OR 3-5mls bone marrow in EDTA tube

TURN-AROUND TIME:

7-10 days

COST:

Please contact laboratory for pricing

CPT CODES:

83891, 83896, 83898, 83902, 83907, 83912

REFERENCES:

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Beillard E, et al. (2003). Evaluation of candidate control genes for diagnosis and residual disease detection in leukemic patients using 'real-time' quantitative reverse-transcriptase polymerase chain reaction (RQ-PCR)- a European Against Cancer program. *Leukemia* 17:2474.

Gabert J, et al. (2003). Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia- A Europe Against Cancer Program. *Leukemia* 17:2318.

Hughes TP, et al. (2003). Frequency of major molecular responses to imatinib or interferon a plus cytarabine in newly diagnosed chronic myeloid leukemia. *Blood* 103:2873.

Kantarjian H, et al. (2008). Monitoring the response and course of chronic myeloid leukemia in the modern era of BCR-ABL tyrosine kinase inhibitors: practical advice on the use and interpretation of monitoring methods. *Blood* 111:1774.

Muller MC, et al. (2008). Harmonization of BCR-ABL mRNA quantification using a uniform multifunctional control plasmid in 37 international laboratories. *Leukemia* 22:96.

Press et al., (2007). A half-log increase in BCR-ABL RNA predicts a higher risk of relapse in patients with chronic myeloid leukemia with an imatinib-induced complete cytogenetic response (CCR). *Clin Cancer Research* 13:6136.