



Molecular Diagnostic Laboratory  
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## IGH Gene Rearrangement

Proliferation of B lymphoid cells characterized by clonal rearrangements of the *IGH* gene

### Indications for Molecular Testing

- Suspected clonal B lymphoid proliferation or neoplasm

### Testing Methodology

Identification of rearrangement(s) of the *IGH* gene by multiplexed Polymerase Chain Reaction (PCR).  
(PCR is utilized pursuant to a license agreement with Roche Molecular Systems, Inc.)

### Interpretation of DNA analysis

Leukemia and lymphoma of B lymphoid lineages have clonal DNA rearrangements from the original tumor cell. This is in contrast to normal, functional cells of B lineage which demonstrate patterns of extreme diversity of antigen specificity and DNA rearrangement. Clonal *IGH* gene rearrangements are diagnostic for leukemias and lymphomas derived from B lymphoid hematopoietic cell precursors. Specific DNA rearrangements identified at diagnosis constitute a tumor-specific marker which may be used to identify minimal residual disease post-treatment. *IGH* rearrangement occurs early in B cell development with light chain genes for kappa and lambda chains rearranging after heavy chain gene rearrangement has occurred. Thus *IGH* gene rearrangement is an earlier marker of clonal B lymphoid cell populations.

Clonally rearranged *IGH* V-D-J segments are typical of B lymphoid neoplasias and may be amplified by PCR using consensus V and consensus J region primers. The DNA fragments detection efficiency depends on the extent of sequence homology for PCR primers used and the proportion of tumor cells in the specimen (>5% required). Normal B cell populations will have a broad variety of *IGH* rearranged DNA fragment sizes described as a polyclonal population, representing the continuum of *IGH* antigenic variation in the CDR (complementarily determining region). Non-rearranged *IGH* genes, characteristic of non-B lymphoid populations, will have no clonal rearrangements detected. Although the presence of a clonal population is suggestive of malignancy, these findings should be interpreted in the context of other clinical and laboratory results. PCR-based testing does not identify 100% of clonal cell populations due to limited sequence complementation with the consensus primer sequences used. Southern blot may be advisable as an additional approach to detect clonality when sufficient cellular material is available.

### Specimen Requirements

**Frozen Tissue**--10 mm<sup>3</sup> of fresh frozen tissue in sterile, plastic container. Forward frozen tissue on dry ice.

**Separated Cell Pellets**--1 x 10<sup>6</sup> nucleated cells. Freeze cells in a sterile plastic container. Forward promptly on dry ice. **Peripheral Blood**--1 lavender-top (EDTA) tube. Invert several times to mix blood. **Bone Marrow**--Place 1-2 mL of anticoagulated bone marrow in a lavender-top (EDTA) tube. Invert several times to mix bone marrow.

**Formalin-Fixed, Paraffin-Embedded (FFPE) Tissue**--Twenty 10 micron sections of FFPE tissue in a sterile, microcentrifuge tube. Do not freeze blood, bone marrow, or FFPE, forward promptly at ambient temperature to the following address:

**Molecular Diagnostic Laboratory**  
**Barnes-Jewish Hospital North, Room 2320**  
**Mail Stop 90-35-709**  
**216 South Kingshighway**  
**St. Louis, MO 63110**

Clinical information must be provided with specimen referral to correctly interpret test results.

### Current Pricing

Contact Lab Customer Service for current pricing 314 362-1470.  
CPT codes: PCR - 83907, 83890, 83900, 83898, 83894, 83912.

vanDongen J JL, Langerak AW, Bruggemann M, Evans PAS, Hummel M, et al. Design and standardization of PCR primers and protocols for detection of clonal immunoglobulin and t-cell receptor gene recombinations in suspect Lymphoproliferations: Report of the BIOMED-2 concerted Action BMH4-CT98-3936. *Leukemia* 2003; 17:2257-2317.