B-Cell Gene Rearrangement

Test Code: 4070  Department: Molecular Oncology

Test Synonyms: Immunoglobulin (IgH) Gene Rearrangement
Immunoglobulin (IgH) Clonality
Immunoglobulin light chain clonality
Kappa gene rearrangement
Kappa gene clonality
Gene rearrangements for B-cell lymphoma;
B cell gene rearrangement for clonality

CPT Code(s):
83891
83892
83898 x 3
83909 x 3

Background:
B-cell lymphomas account for greater than 90% of non-Hodgkin lymphomas and may pose a diagnostic challenge on the basis of histopathology alone. During normal B-cell maturation, the immunoglobulin heavy chain gene is rearranged such that each mature B-cell and plasma cell has a unique rearranged heavy chain gene profile. This process is vital to the function of B-cells in normal immune function, but can be exploited to aid in the distinction between reactive (benign; polyclonal) versus neoplastic (clonal) processes of B-cell proliferation. A reactive, benign B-cell proliferation is characterized by a polyclonal expansion of B-cells whereas a malignant process is usually characterized by a clonal expansion of a predominant B-cell population with a clone-specific immunoglobulin heavy (and/or light) chain gene rearrangement. In conjunction with histopathology, flow, and immunohistochemistry, the detection of a clonal immunoglobulin heavy (and/or light) chain gene rearrangements by polymerase chain reaction (PCR) is intended as an aid in the diagnosis of malignant B-cell lymphoma.

Clinical Utility:
PCR-based detection of rearranged immunoglobulin heavy (and/or light) chain genes can be used as an aid to establish a diagnosis of a B-cell lymphoma, plasma cell malignancy, monitor treatment response, and/or measure minimal residual disease (MRD).

Methodology:
Genomic DNA is extracted from blood, lymph node, bone marrow, or other tissue types (formalin-fixed or fresh) and the rearranged immunoglobulin heavy (and/or light) chain genes are amplified by PCR using a multiplex primer method based on the BIOMED-2 strategy (1,2). Precise fragment sizing of the amplicons is accomplished using capillary gel electrophoresis. The presence or absence of a monoclonal B cell population is determined based on the overall analysis of the electrophoretic pattern.

Sensitivity:
> 95% for the detection of clonality in most tissue types. False negative results could be due to:
• Rare clone-specific gene rearrangements that do not bind to any of the primers in BIOMED-2 multiplex mixture.
• Somatic hypermutation
• Clonal B cells present at low abundance in polyclonal background, below the analytical sensitivity of the assay (~1-10%, depending on the loci).
The presence of a clonal immunoglobulin cell gene rearrangement does not always equate to the presence of B cell malignancy.

**Specificity:**
As cross-lineage immunoglobulin heavy chain gene rearrangements have been reported in certain T-cell malignancies, interpretation of this test requires clinical, morphologic, and immunophenotypic correlation. False positive gene rearrangement results are rare but could result from the inadvertent sampling of a predominant B cell clone from within a polyclonal population.

**Specimen Requirements:**
- 5-10 mL of blood or bone marrow — yellow (ACD) or purple (EDTA) tube; or
- Formalin-fixed paraffin-embedded (FFPE) tissue blocks or 10 slides (5 micron)
- Refrigerate or keep at room temperature.

A REQUISITION FORM MUST ACCOMPANY ALL SAMPLES. Please include detailed clinical information.

**Test Performed (Days):**
Monday, Wednesday, Friday

**Turnaround Time:**
5-7 days

**Shipment Sensitivity Requirements:**
Keep specimen cold during transit, but do not ship on dry ice. Please use the cold pack provided in the KDL shipping kit. Ship the specimen overnight express, using the FE priority overnight label provided. The specimen must arrive at the lab no more than 24 hours after collection.

**References:**
