

Laboratory Tests for B- and T-cell Clonality based on *Immunoglobulin and T cell Receptor Gamma (IGH, TRG) Gene Rearrangement*

Molecular tests of the immunoglobulin heavy chain (*IGH*), kappa light chain (*IGK*), and T cell receptor gamma (*TRG*) genes are used to assess clonality and lineage of lymphoid lesions.

Biology & Clinical Utility of Assays for B- and T- Cell Clonality: *IGH* or *IGK* gene rearrangement is a sign of a cell's commitment to the B cell lineage, while *TRG* gene rearrangement characterizes T cell lineage. Lymphoid leukemia or lymphoma arises from a single transformed lymphocyte harboring a particular set of gene rearrangements encoding antigen receptors, and those rearrangements are inherited by all tumor cell progeny. Every B cell malignancy harbors clonally rearranged IG genes, while every T cell tumor harbors clonally rearranged TR genes. Lymphoid tumors exhibit clonal rearrangements, while benign, reactive lymphoid hyperplasias do not. In patient samples where diagnostic uncertainty remains after morphology and immunophenotyping, gene rearrangement tests help resolve whether a lesion is polyclonal (reactive) or monoclonal (neoplastic). Because clonality is not always synonymous with malignancy, clinicopathologic correlation is required.

Laboratory Tests for *IGH*, *IGK*, or *TRG* gene rearrangement: Tests are performed on **blood** (3mL, EDTA), **bone marrow** (1ml, EDTA), **body fluids**, **paraffin blocks**, or **solid tissue** (frozen or paraffin embedded). DNA is amplified using primers targeting consensus variable and joining regions of the *IGH* and *IGK* genes (Biomed-2 primers from Invivoscribe) or *TRG* genes. Products are visualized by capillary gel electrophoresis to detect variably-sized amplicons characterizing polyclonal lymphocytes, or a dominant product characterizing a clonal lymphoid population. Clones comprising as few as 10% of cells in the sample are detectable. Up to 10% of lymphoid clones are undetectable using the PCR primer sets in this assay. Results are interpreted by a pathologist.

References:

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To consult a pathologist about indications for testing or significance of a result, call the Molecular Genetics Lab at (984) 974-1825 or Dr. Gulley at (919) 843-4595. E-mail margaret_gulley@med.unc.edu

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