Reliable Clonality Detection with *IGH* FR1/2/3

IdentiClone® Dx
IGH Assay

A Data-Driven Approach to Streamlined *IGH* Clonality Testing

In B-cell clonality assessment, *not all IGH targets are created equal.*

Comprehensive evidence supports that routine testing for incomplete ***IGH*** **D_H–J_H** rearrangements offer little diagnostic value while increasing interpretive complexity. By relying on well-characterized ***IGH*** **FR1, FR2, and FR3 (V_H–D_H–J_H)** assays as the first-line approach laboratories can:

- Maintain diagnostic accuracy and specificity
- Reduce false-positive risk from physiologic intermediates
- Streamline workflows and reporting consistency

FR1/2/3 Capture the Vast Majority of Clonal *IGH* Rearrangements

The **BIOMED-2 Consortium** designed and validated *IGH* FR1/2/3 assays as the primary tools for identifying clonal B-cell populations because **complete V_H–D_H–J_H rearrangements represent 80-90% of clinically relevant *IGH* targets**.[1] Because incomplete rearrangements are both infrequent and often less stable, targeting FR1,2 and 3 regions maximizes sensitivity and specificity for detecting clinically meaningful B-cell clonality.[2]

Incomplete D_H–J_H Rearrangements Are Rare and Often Non-Specific

Incomplete rearrangements occur infrequently in mature B-cell populations and are frequently seen as physiologic byproducts of normal B-cell development. Their amplification can **produce pseudo-clonal results**, especially when testing samples with low tumor burden, resulting in **false-positive or ambiguous peaks**.[3,4]

D_H–J_H Testing Adds Complexity Without Diagnostic Benefit

Including D_H–J_H assays in first-line testing can **increase the need for sequencing confirmation** and complicate interpretation without substantially improving sensitivity. Diagnostic experience and published data consistently show that the added workload outweighs any marginal gain in detection.[5,6]

Summary Recommendation:

First-line clonality testing will use *IGH* FR1/2/3 assays only. Incomplete *IGH* (D–J) testing is omitted from routine analysis because the vast majority of clonal rearrangements are complete V_H–D_H–J_H events.

References

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