Assessment of Immunoglobulin Light Chain Restriction with **RNAscope™ ISH** Probes Kappa and Lambda

RNAscope ISH Probes Kappa and Lambda are designed for the detection of Kappa and Lambda light chain mRNA expression in B- lymphocytes.

Detection of B-lymphocyte Clonality

Lymphoma is one of the most common cancers. Clonal expansion of B-lymphocytes harboring specific immunoglobulin gene rearrangements is a hallmark of B-cell lymphomas, resulting in expression of either immunoglobulin kappa (IgK) or lambda (IgL) light chains in combination with a specific immunoglobulin heavy chain.[1] This selective expression of immunoglobulin kappa or lambda is known as "light chain restriction". Evaluation of a population of lymphocytes for light chain restriction is an important component in the pathologic work-up. Currently, flow cytometric analysis serves as the gold standard for evaluation of kappa and lambda light chain expression.[2] However, some B-cell lymphomas lack sufficient surface immunoglobulin expression for detection by flow cytometry. In addition, fresh tissue is not always available for flow-cytometry. In these cases, evaluation of light chain expression in formalin-fixed, paraffin-embedded (FFPE) tissues are required. Several methods including Immunohistochemistry (IHC) and conventional bright field *in situ* hybridization are available for FFPE tissue evaluation but are often insufficiently sensitive to detect the much lower abundance of light chains present in B-cells relative to plasma cells.

The RNAscope RNA ISH Platform, including chromogenic detection reagents and target specific probes for kappa and lambda light chain mRNA, provides assessment of light chain restriction in FFPE tissue (**Figure 1**).

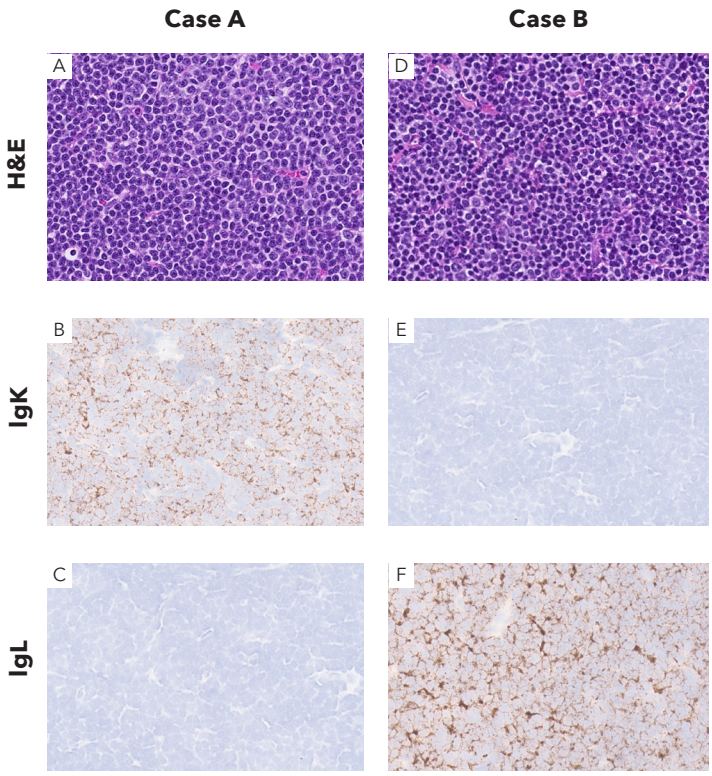

Figure 1. RNAScope RNA ISH evaluation of IgK and IgL expression. *Case A.* Neoplastic B-cell population (A) demonstrates kappa light chain restriction with clear IgK ISH expression (B) and negative IgL ISH expression (C). *Case B.* Sheets of neoplastic B-cells (D) demonstrate absence of kappa light chain expression (E) and clear lambda light chain restriction (F).

In some cases, positivity is seen with both Kappa and Lambda RNAscope ISH probes. This "polyclonal" pattern can be reflective of a non-clonal B-cell proliferation. However, this pattern can also be seen in approximately 10-20% of B-cell lymphomas. A third RNAscope ISH probe for immunoglobulin lambda like peptide 5 (IGLL5) can be employed to resolve the assessment. IGLL5 is expressed during B-cell development and in a subset of B-cell lymphomas, regardless of clonality. IGLL5 shares some but not all sequences with the IgL constant region gene segments.[2,3] The RNAscope ISH probe IGLL5 targets those sequences unique to the IGLL5 gene, leading to no cross-hybridization with IgL mRNA. Combining Kappa and Lambda target probes with a third probe for IGLL5 clarifies IGLL5 expression – something that is unavailable in IHC and traditional ISH. The use of RNAscope ISH Probe Kappa, Lambda, and IGLL5 can help detect B-cell clonality in multiple subtypes of B-cell lymphoma.

Product Information

Cat. No.	Product Name	Regulatory Status
201428	RNAscope ISH Probe Kappa	ASR
201438	RNAscope ISH Probe Lambda	ASR
201448	RNAscope ISH Probe IGLL5	ASR

Analyte Specific Reagents (ASRs) are critical building blocks for Laboratory Developed Tests (LDTs) and play a key role in ensuring the accuracy and reliability of test results. By using ASRs, Clinical Laboratory Improvement Amendments (CLIA) certified labs can develop customized tests that are tailored to the specific needs of their patient population, while maintaining high standards of analytical and clinical performance.

References

1. Tubbs, R. R., H. Wang, *et al.* (2013). "Ultrasensitive RNA *in situ* hybridization for detection of restricted clonal expression of low-abundance immunoglobulin light chain mRNA in B-cell lymphoproliferative disorders." Am J Clin Pathol **140**(5): 736-46.

2. Guo, L., Z. Wang, *et al.* (2018). "Ultrasensitive automated RNA *in situ* hybridization for kappa and lambda light chain mRNA detects B-cell clonality in tissue biopsies with performance comparable or superior to flow cytometry." Mod Pathol **31**(3): 385-394.

3. Warford, A., M. Rahman, *et al.* (2019). "Pushing the boundaries of *in situ* hybridisation for mRNA demonstration: demonstration of kappa and lambda light chain restriction in follicular lymphoma." Br J Biomed Sci **76**(3): 143-146.

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