

FEATURES

- Highly sensitive and specific detection of albumin mRNA in hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC)¹
- Powerful evaluation tool for distinguishing ICC from extrahepatic cholangiocarcinoma (ECC), metastatic adenocarcinoma to the liver, and carcinoma of unknown origin²
- Strong hybridization signal and low background allow for definitive visualization of albumin expression vs. IHC
- Automated, easy-to-perform assay allows for clear and reliable chromogenic detection of albumin in histologic sections

THE CHALLENGE OF LIVER CANCER ASSESSMENT

With almost one million new cases yearly, liver cancer is one of the most common cancers in the world and the 3rd most common cause of cancer related mortality.³ Determining whether a malignant liver mass is a primary hepatocellular carcinoma (HCC), an intrahepatic cholangiocarcinoma (ICC), or a metastatic carcinoma is of major clinical significance.² However, the evaluation of HCC vs. ICC vs. metastatic carcinoma can be highly challenging with routine histopathology and currently available immunohistochemistry (IHC) antibodies, highlighting the need for better markers. In the case of HCC, particularly of poorly differentiated and undifferentiated forms, assessment is difficult due to the lack of a reliable IHC marker of hepatocellular differentiation. Similarly, distinguishing ICC from metastatic adenocarcinomas based on histopathologic or IHC analysis is problematic and requires an extensive workup due to similar morphologic features and overlapping keratin profiles.

ALBUMIN MESSENGER RNA (mRNA)

Albumin, a protein synthesized by hepatocytes, was first proposed as a marker of hepatocellular differentiation in 1980s.⁴ However, detection of albumin using IHC proved challenging primarily due to its ubiquitous presence as a serum protein,

leading to high background staining. The application of RNA ISH technology for the detection of albumin mRNA rather than protein successfully addressed this issue. In this regard, albumin mRNA has recently been identified as a marker of hepatocellular differentiation that is highly useful in the evaluation of hepatocellular neoplasms.^{1,2,5}

HIGHLY SENSITIVE AND SPECIFIC DETECTION OF ALBUMIN MESSENGER RNA (mRNA)

Albumin mRNA, as detected by RNA *in situ* hybridization (ISH) technologies such as Advanced Cell Diagnostics' RNAscope, has demonstrated high sensitivity and specificity as a marker for the evaluation of HCC and ICC.^{2,5} For HCC, albumin mRNA has a very high sensitivity ranging from 97%-100%, significantly exceeding the sensitivity of IHC markers such as Hep Par1 and Arginase-1. For ICC, albumin mRNA also has a high sensitivity, up to 99% in some studies.^{2,5,6} In contrast, extrahepatic cholangiocarcinoma, including perihilar and distal bile duct carcinomas, as well as metastatic carcinomas to the liver are consistently negative for albumin mRNA (FIGURE 1).¹ The combined high sensitivity and specificity of albumin mRNA make it an ideal evaluation tool for identification of HCC and ICC (FIGURE 2), as well as distinguishing ICC from ECC, metastatic adenocarcinoma to the liver, and carcinoma of unknown origin.¹ In practice, albumin RNA ISH represents the solution for patients with a liver mass (FIGURE 3), including cases in which no primary malignancy has been identified to avoid extensive and costly pathological workups.¹

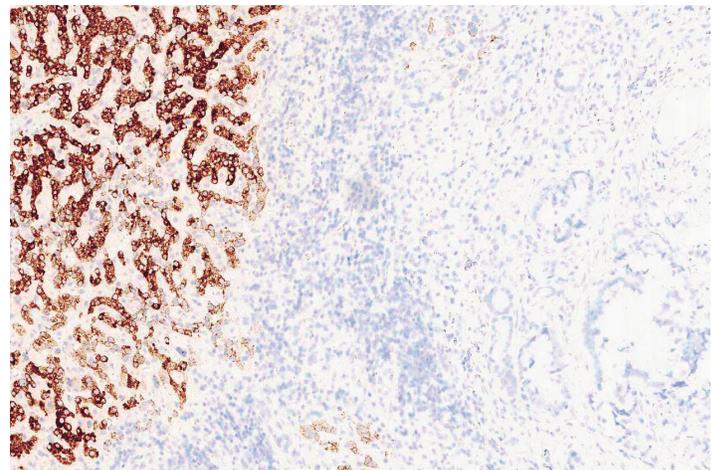


FIGURE 1. Liver tumor (metastatic adenocarcinoma) with positive albumin staining of normal hepatocytes and negative staining of nonhepatic adenocarcinoma.

CONSISTENT, EASY-TO-INTERPRET RESULTS ENABLED BY AUTOMATION

The RNAscope ISH Platform, including chromogenic detection reagents and target-specific probes like albumin, is a robust technology that allows for the identification of mRNA expression and localization at the single cell level with morphologic context in histologic sections. RNAscope is highly sensitive and specific due to its unique double Z probe design, resulting in an extremely high signal-to-noise ratio relative to traditional RNA ISH. The technology allows pathologists to visualize, localize, and quantify expression of a variety of biomarkers with an easy-to-interpret chromogenic format. RNAscope is readily available on automated staining platforms, including the Leica BOND III, for ease of use, high reproducibility, and seamless fit into the anatomic pathology laboratory workflow. Furthermore, RNAscope provides labs with the opportunity to add new ISH markers to their menus and provide better options for problematic IHC tests.

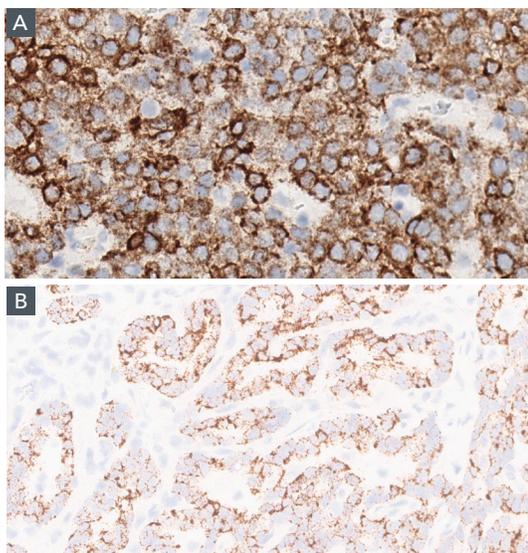


FIGURE 2. Positive albumin staining of A. hepatocellular carcinoma (HCC) and B. intrahepatic cholangiocarcinoma (ICC).

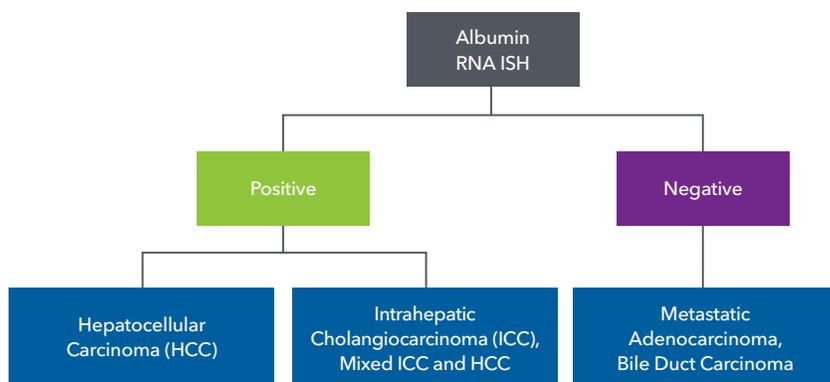


FIGURE 3. Algorithm for use of Albumin RNA ISH for the evaluation of liver tumors.¹

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