Background:

- Bile duct adenomas may be difficult to distinguish from metastatic well-differentiated pancreatic adenocarcinomas. However, this distinction is critical for proper management of patients with pancreatic malignancy.
- In challenging cases, immunohistochemistry for SMAD4 may help in distinguishing pancreatic ductal adenocarcinoma from a bile duct adenoma; however, SMAD4 expression is lost in only about half of these neoplasms.
- In a prior study, we showed that >95% of intrahepatic cholangiocarcinomas stain positively for albumin.
- Herein, we investigated the utility of albumin in making the distinction between metastatic pancreatic adenocarcinoma and bile duct adenoma.

Methods:

- We studied 13 bile duct adenomas, 3 bile duct hamartomas, and 95 pancreatic ductal adenocarcinomas.
- Chromogenic in situ hybridization (CISH) was performed on formalin-fixed, paraffin-embedded tissue using the QuantiGene® ViewRNA technology (Affymetrix, Santa Clara, CA). QuantiGene® ViewRNA ISH is based on the branched DNA technology wherein signal amplification is achieved via a series of sequential steps (figure 1).
- Hepatocytes adjacent to bile duct adenomas served as an internal positive control.
- Nonspecific reactivity was considered with detection of a single dot per 100 epithelial cells.

Figure 1. QuantiGene® ViewRNA in situ hybridization assay protocol. After the formalin-fixed, paraffin-embedded tissue is prepared, target-specific probes (in this case, albumin-specific probes) are applied and hybridize to the target RNA as pairs. Signal amplification occurs via a series of sequential hybridization steps and can be detected with light microscopy.

Figure 2. Bile duct adenomas (panel A and C) showed diffuse dot-like positivity for albumin (panel B and D). Adjacent hepatocytes (panel C) showed more dots per cell with albumin staining, as compared to bile duct adenomas (panels D).

Figure 3. Intrahepatic cholangiocarcinomas (panel A) showed more dots per cell with albumin staining (panel B), as compared to bile duct adenomas. Pancreatic ductal adenocarcinomas (panel C) were negative for albumin (panels D).

Results:

- Seven (53.8%) bile duct adenomas were biopsied during surgical resection of a primary malignancy; the remainder were biopsied during surgery for benign conditions or were incidental findings in a liver biopsy.
- Eleven (84.6%) bile duct adenomas were diffusely positive for albumin. Albumin reactivity was also identified in the background hepatocytes. The reactivity within the nonneoplastic liver and bile duct adenomas had a dot-like pattern. The number of dots per cell was significantly less within bile duct adenomas as compared to within adjacent hepatocytes and within intrahepatic cholangiocarcinomas (figures 2-3).
- All pancreatic ductal adenocarcinomas and all bile duct hamartomas were negative for albumin.
- The sensitivity and specificity of albumin, as detected by branched-chain CISH, for distinguishing bile duct adenomas from metastatic pancreatic adenocarcinomas was 84.6% and 100%, respectively.

Conclusions:

- Branched-chain chromogenic in situ hybridization for albumin represents a useful marker of bile duct adenomas.
- Using this platform, diagnostically challenging examples of bile duct adenomas may be distinguished from metastatic pancreatic adenocarcinoma.

Table 1. Branched-chain in situ hybridization properties of bile duct adenomas and pancreatic ductal adenocarcinomas. The sensitivity and specificity of this assay in distinguishing bile duct adenomas from pancreatic ductal adenocarcinomas is 84.6% and 100%, respectively.

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tr>
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References: