

## Supplementary Information

### Supplementary Tables

**Supplementary Table 1.** Overview of cohorts

Entity	Sample size	Alb-ISH*	CRP IHC*
Intrahepatic cholangiocarcinoma (iCCA)	153	151	151
Perihilar cholangiocarcinoma (pCCA)	153	153	148
Distal cholangiocarcinoma (dCCA)	126	126	126
Adenocarcinoma of the gallbladder	131	112	119
Colorectal liver metastasis	98	88	86
Pancreatic adenocarcinoma	92	87	80
Pulmonary adenocarcinoma	73	72	70
Invasive breast carcinoma	212	206	212
<b>Total</b>	<b>1038</b>	<b>995</b>	<b>992</b>
<b>Total (other than iCCA)</b>	<b>885</b>	<b>844</b>	<b>841</b>

\* Presented are the analysis-dependent numbers of evaluable cases per entity. Differences to original sample size numbers are due to tissue core detachment, rolling and floating.

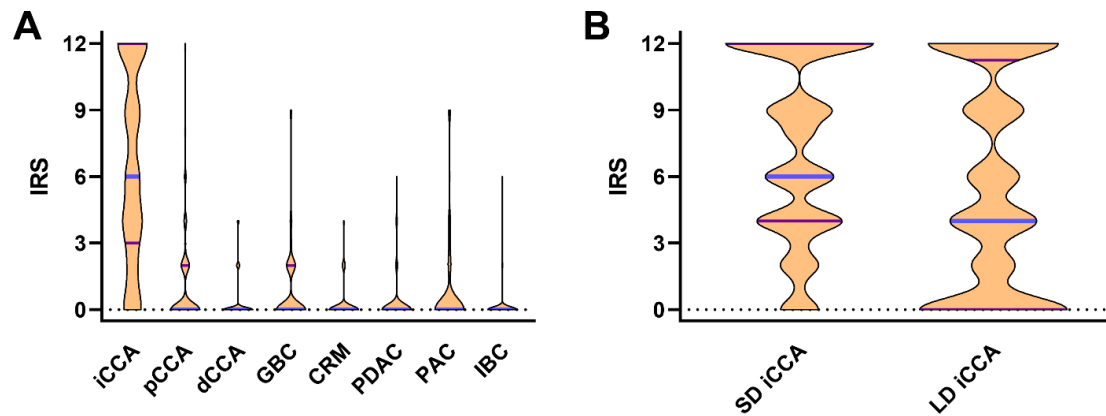
Abbreviations: Alb-ISH, Albumin in situ hybridization; CRP IHC, C-reactive protein immunohistochemistry.

**Supplementary Table 2.** Metrics using a CRP threshold of IRS=2.

	Sensitivity	Specificity
<b>CRP IHC</b>	83.4%	86.7%
<b>Alb-ISH &amp; CRP*</b>	88.0%	86.4%

\*For combined assessment of Alb-ISH and CRP, positivity of a single marker was considered sufficient for a diagnosis of iCCA (i.e., diagnosis rejection required co-negativity). Abbreviations: Alb-ISH, albumin in situ hybridization; CRP, C-reactive protein; IHC, immunohistochemistry.

## Supplementary Figures



**Supplementary Figure 1. Distribution of CRP expression.** Violin plots of CRP expression for the comparison iCCA vs. other adenocarcinomas (A), and small duct vs. large duct iCCA (B). The median is highlighted in blue, and the interquartile range is highlighted in purple. CRM, colorectal metastasis; dCCA, distal cholangiocarcinoma; GBC, gallbladder cancer; IBC, invasive breast cancer; iCCA, intrahepatic cholangiocarcinoma; IRS, immunoreactive score; LD, large duct; PAC, pulmonary adenocarcinoma; pCCA, perihilar cholangiocarcinoma; PDAC, pancreatic adenocarcinoma; SD, small duct.