益田　悠貴　先生の論文がJournal of Hepato-Biliary-Pancreatic Sciences（IF 2.8)に受理されました。

本研究では、肝臓内外の接合部に位置するため従来一括して扱われてきた肝門部領域胆管癌に関して、肝内での明瞭な腫瘤形成の有無に基づいて分類し、遺伝子発現解析と病理学的検討を行いました。その結果、両者は異なる分子学的背景を持つ独立した腫瘍群であることが示されました。すでに、胆道癌はその原発部位によって遺伝子異常が異なることがわかっていますので、いままで不明瞭であった肝門部領域の診断枠組みや病態理解の再考を促す知見が得られ、ひいてはゲノム医療にも少なからず影響する内容と思います。なお、本成果は既にUEG Week （United European Gastroenterology Week　欧州消化器病週間）2023で発表され、日本胆道学会で国際交流奨励を受賞しています。（尾島）

オープンアクセス
https://doi.org/10.1002/jhbp.70077

Journal of Hepato-Biliary-Pancreatic Sciences

ORIGINAL ARTICLE OPEN ACCESS

Gross Intrahepatic Mass Formation Predicts the Primary Site of Perihilar Cholangiocarcinoma Based on Molecular Pathologic Studies

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Received: 22 June 2025 | **Revised:** 31 December 2025 | **Accepted:** 20 January 2026

Keywords: alpha 1-antitrypsin | biomarkers | cholangiocarcinoma | claudins | mesothelin

ABSTRACT

Background/Purpose: Intrahepatic cholangiocarcinoma (iCCA) and extrahepatic cholangiocarcinoma (eCCA) are clinically and genetically distinct. However, the classification of perihilar cholangiocarcinoma (phCCA) with an intrahepatic tumor mass remains unclear. This study aimed to position phCCA near the hilar plate (hCCA) within an extrahepatic–intrahepatic framework using pathological and molecular analyses.

Methods: Among 357 resected invasive CCAs, 100 hCCAs were histologically classified as either hCCA with (hCCA-M) or hCCA without (hCCA-NM) a grossly evident intrahepatic mass. Transcriptomic comparison of 9 typical eCCAs and 39 mass-forming iCCAs identified three contextual markers, which were examined by immunohistochemistry in 309 additional cases.

Results: Among 100 hCCAs, 85 were hCCA-NM and 15 hCCA-M. Claudin 18 (CLDN18) and mesothelin (MSLN) were identified as extrahepatic contextual markers, and serpin family A member 1 (SERPINA1) as an intrahepatic contextual marker. SERPINA1 was more highly expressed in hCCA-M than in hCCA-NM, regardless of microscopic liver parenchymal invasion, whereas CLDN18 and MSLN were similarly expressed in both. Cluster analysis revealed that hCCA-NM clustered with eCCA, whereas hCCA-M clustered with iCCA.

Conclusions: Gross intrahepatic mass formation indicates an intrahepatic contextual profile and provides a useful criterion for subclassifying hCCA. This contextual framework shows that hCCA-M and hCCA-NM represent biologically distinct tumor groups.

1 | Introduction

Cholangiocarcinoma (CCA) is one of the most refractory cancers and is on the increase worldwide [1]; moreover, there has been little improvement in prognosis [2]. Surgical resection remains the only radical treatment, but many cases are advanced and unresectable at the time of clinical diagnosis [3]. Furthermore, a high rate of recurrence occurs even after surgical resection [4]. Chemotherapy is indicated for unresectable and postoperative recurrence cases, but current chemotherapy drugs for CCAs, such as gemcitabine and cisplatin, are not sufficiently effective. Recently, molecularly targeted drugs against specific genetic