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Original contribution

# IMP3 expression in lesions of the biliary tract: a marker for high-grade dysplasia and an independent prognostic factor in bile duct carcinomas

**Marc-Oliver Riener MD[a], Florian R. Fritzsche MD[a], Pierre-Alain Clavien MD, PhD[b], Bernhard C. Pestalozzi MD[c], Nicole Probst-Hensch MD[a,d], Wolfram Jochum MD[e], Glen Kristiansen MD[a,*]**

[a]*Department of Pathology, University Hosptial Zurich, CH-8091 Zurich, Switzerland*
[b]*Department of Visceral & Transplantation Surgery, University Hosptial Zurich, CH-8091 Zurich, Switzerland*
[c]*Department of Oncology, University Hosptial Zurich, CH-8091 Zurich, Switzerland*
[d]*Institutes of Social and Preventive Medicine/Surgical Pathology, University Hospital Zurich, CH-8091 Zurich, Switzerland*
[e]*Institute of Pathology, Kantonsspital St. Gallen, CH-9007 St. Gallen, Switzerland*

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**Summary** The oncofetal protein IMP3 (insulin-like growth factor II mRNA binding protein 3) is expressed during embryogenesis and carcinogenesis. Various tumor types have been analyzed for IMP3 expression, which was exclusively found in tumor cells and correlated with increased tumor aggressiveness and reduced overall survival. To our knowledge, IMP3 expression has not been investigated in bile duct carcinomas. Using large tissue sections from resection specimens of the extrahepatic biliary tract, we analyzed IMP3 in normal bile ducts (n = 36), bile ducts with acute inflammation and reactive epithelial changes (n = 26), low-grade dysplasia (n = 9), and high-grade dysplasia (n = 11). Furthermore, IMP3 expression was assessed in bile duct carcinoma (n = 115) using clinically well-characterized tissue microarrays. The findings were correlated with clinical-pathologic parameters including survival. High-grade dysplasia was strongly positive for IMP3 in all cases studied compared with no or weak expression in normal, inflamed, and low-grade dysplastic bile ducts. Of the bile duct carcinomas 58.3% (67/115) were strongly positive for IMP3, which was associated with a higher proliferation rate ($P$ = .004) and p53 positivity ($P$ = .022). Patients with strong IMP3 expression had significantly reduced overall survival ($P$ = .037) similarly to the subgroup of pT3 carcinomas ($P$ = .007). In multivariate analysis, IMP3 expression was an independent prognostic factor for overall survival ($P$ = .040, RR = 1.809). This comprehensive study shows that IMP3 is an independent prognostic biomarker in bile duct carcinoma. In addition, it may be a marker for high-grade dysplasia in the extrahepatic biliary tract.


## 1. Introduction

Carcinomas of the biliary tract including intrahepatic cholangiocarcinoma (ICC), extrahepatic cholangiocarcinoma (ECC), and gallbladder carcinoma (GBC) have a poor

* Corresponding author.
*E-mail address:* glen.kristiansen@usz.ch (G. Kristiansen).

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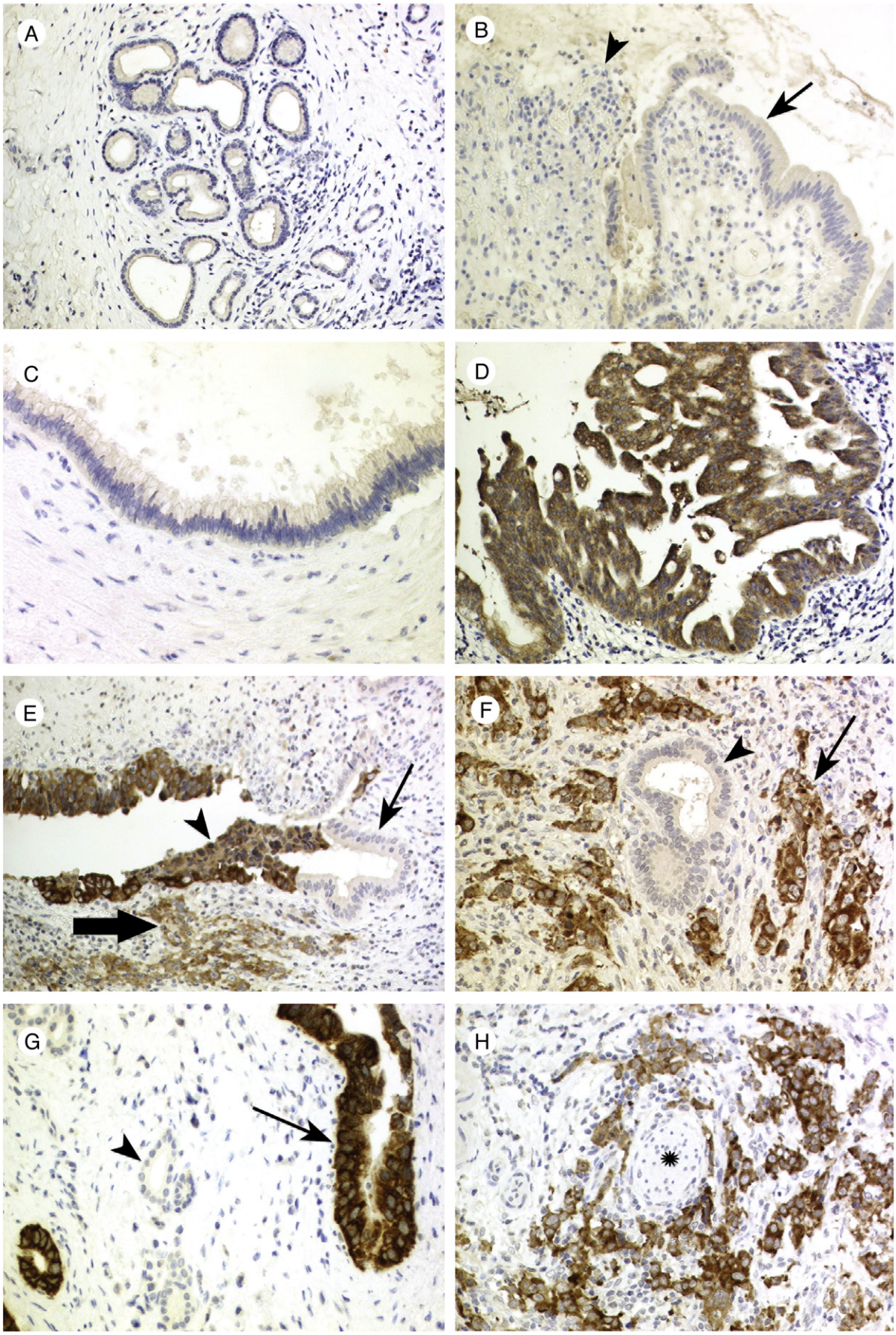
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