

JENS KOOPMAN
GI Pathology

Mac-2 binding protein is a diagnostic marker for biliary tract cancer

Jens Koopmann¹, Paul J. Thuluvath², Marianna L. Zahurak³, Troels Z. Kristiansen⁴, Akhilesh Pandey⁴, Richard Schulick^{3,5}, Pedram Argani¹, Manuel Hidalgo³, Stefano Iacobelli⁶, Michael Goggins^{1,2}, Anirban Maitra^{1,3,*}

¹ Department of Pathology, Johns Hopkins Medical Institutions, Baltimore, MD, 21205, USA

² Department of Medicine, Division of Gastroenterology, Johns Hopkins Medical Institutions, Baltimore, MD, 21205, USA

³ Department of Oncology, Johns Hopkins Medical Institutions, Baltimore, MD, 21205, USA

⁴ McKusick-Nathans Institute of Genetic Medicine and Department of Biological Chemistry, Johns Hopkins University, Baltimore, MD 21287, USA

⁵ Department of Surgery, Johns Hopkins Medical Institutions, Baltimore, MD, 21205, USA

⁶ Department of Oncology, University G. D'Annunzio, Chieti, 66100, Italy

Purpose:

Biliary tract cancer is a lethal disease, accounting for nearly 4,500 cancer related deaths each year in the United States. Early detection has the potential to improve the survival of patients with biliary tract malignancies, enabling curative surgical resection. Early detection approaches would benefit from an accurate, minimally-invasive diagnostic test. In order to identify new diagnostic markers, we recently completed a comprehensive proteomic study of bile from biliary cancer patients. One of the proteins identified by tandem mass spectrometry was Mac-2 binding protein (Mac-2BP). We evaluated the performance of Mac-2BP and its ligand, galectin-3, as diagnostic markers for biliary cancer.

Experimental design:

We measured Mac-2BP, galectin-3 and CA19-9 levels by ELISA in bile samples from patients with biliary tract cancer, benign biliary diseases and primary sclerosing cholangitis. Serum levels of Mac-2BP and galectin-3 were also determined by ELISA. Mac-2BP tissue expression was investigated by immunohistochemistry on a biliary cancer tissue microarray.

Results:

Bile Mac-2BP levels were elevated ~3-fold in the cancer group compared to patients with PSC and other non-neoplastic biliary diseases. In contrast, Mac-2BP levels were not elevated in the serum of patients with biliary cancer. Mac-2BP was expressed in 34/36 (94.4%) of biliary tract cancers by immunohistochemistry. As a diagnostic marker of biliary cancer, Mac-2BP was as accurate as biliary CA19-9 levels, with an area under the curve on receiver-operator characteristics analysis of 0.70. Combining both bile

markers however led to a significantly better diagnostic accuracy than CA19-9 alone (AUC 0.75, $p < 0.001$). Serum and biliary galectin-3 levels did not differ in the cancer and control groups.

Conclusion:

Biliary Mac-2BP levels in bile show promise as a new diagnostic marker for biliary tract cancer, especially when combined with bile CA19-9 levels.