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学 位 記 番 号	千大院医薬博甲第医 2053 号
学位記授与の日付	令和５年３月３１日
学位記授与の要件	学位規則第４条第１項該当
学 位 論 文 題 目	Bile proteome analysis by high-precision mass spectrometry to explore novel biomarkers of primary sclerosing cholangitis (高精度質量分析を用いた胆汁プロテオーム解析による原発性硬化性胆管炎の新規バイオマーカー探索)
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論　文　内　容　の　要　旨

【Purpose】

Primary sclerosing cholangitis (PSC) is a chronic inflammatory disease of unknown etiology that affects the intra- and extrahepatic bile ducts. The present study examined the utility of a bile proteome analysis using a high- sensitivity mass spectrometer to comprehensively screen for novel PSC biomarkers.

【Methods】

Bile endoscopically collected from patients with PSC, common bile duct stones, and biliary tract cancer were subjected to high-precision liquid chromatography/mass spectrometry. Some of the proteins specifically up- regulated in the bile of the PSC group were re-examined by an enzyme- linked immunosorbent assay.

【Results・Discussion】

A total of 8,094 proteins were successfully identified and 332 were specifically up-regulated in the PSC group. The bioinformatics analysis showed that proteins involved in the proliferation and activation of diverse inflammatory cells were up-regulated in the PSC group. A receiver operating characteristic curve analysis showed good area under the curve values for interleukin-8 and annexin A1 (ANXA1) (0.836 and 0.914, respectively). Immunostaining for ANXA1 revealed its strong expression in inflammatory cells infiltrating the peripheral biliary tract in PSC livers.

【Conclusion】

A bile proteome analysis is a useful tool for elucidating the pathogenesis of PSC and developing new diagnostic approaches. Therefore, ANXA1 has potential as a bile biomarker for PSC.