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Correspondence

Both liver parenchymal and non-parenchymal cells express JCAD protein under various circumstances

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Keywords: Junctional protein associated with coronary artery disease (JCAD); Hepatocytes; Hepatic stellate cells; Bile epithelial cells; Liver sinusoidal endothelial cells

Dear Editor,

In Volume 30, Issue 2 of Clin Mol Hepatol, Dr. Byoung Kuk Jang from the Department of Internal Medicine, Keimyung University School of Medicine, Daegu, Korea, provides an editorial[1] to summarize the major findings of our publication in the same issue.[2] All authors appreciate the positive comments to this original article. Regarding junctional protein associated with coronary artery disease (JCAD) expression in other cell types involved in cholestatic insults, the authors would provide additional evidence to clarify this concern.

As demonstrated in the publication, JCAD is expressed in hepatic stellate cells (HSCs), which are the critical effector cell type for cholestatic fibrosis through the Hippo-YAP signaling pathway. Bile epithelial cells (BECs) are often damaged, and the remaining cells may proliferate to respond to cholangiocyte injury and develop bile duct reactions. This repair process is essential for the maintenance of bile duct integrity. Proliferative bile duct cells may release cytokines and other intermediates to portal fibroblasts and HSCs to coordinate the repair process. Therefore, it is of great interest to investigate whether JCAD participates in the proliferation of BECs. In serial sections of primary biliary cholangitis (PBC), immunohistochemical staining shows that bile duct epithelial cells are CK-19-positive, and JCAD is also positive in the structure of newly formed bile ducts in the same location. Moreover, transcription factor YAP is positive in some bile duct structures. In contrast, very faint staining in the portal triads was visualized in the control sections (Fig. 1). This piece of preliminary evidence demonstrates that JCAD is highly expressed in reactive bile duct epithelial cells and presumably may contribute to their proliferative response through the same underlying mechanism. In fact, the author's team has acquired other preliminary data to support that CK-19-positive cells are overlapped with JCAD-positive cells in mouse models of cholestatic insults in an on-going project. In addition, JCAD

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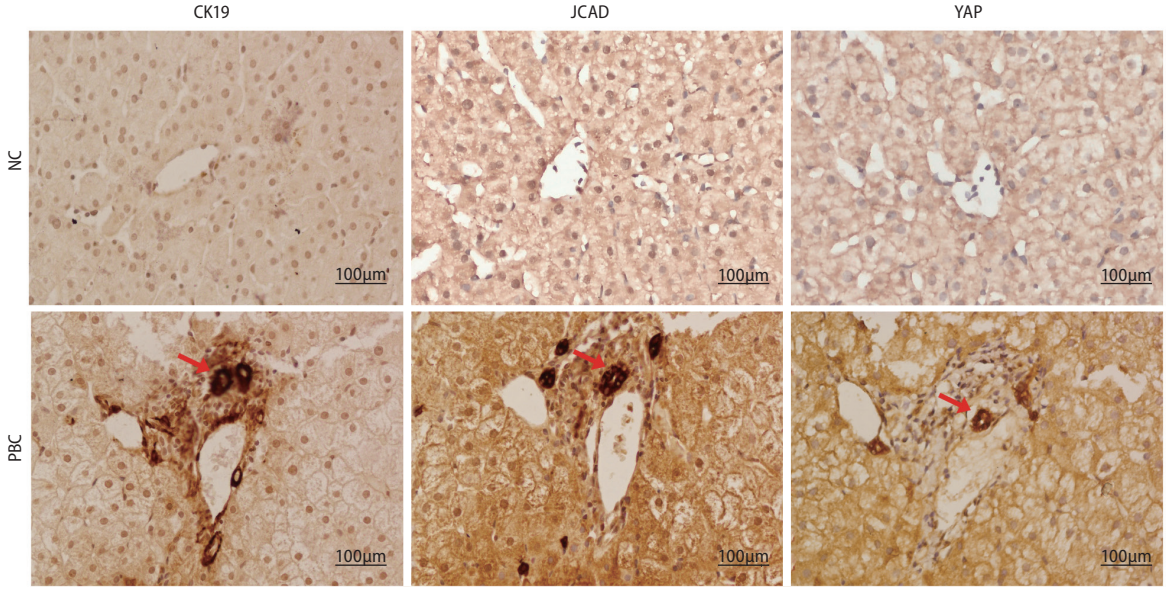

Figure 1. JCAD was highly expressed in primary biliary cholangitis (PBC) specimens. Representative immunohistochemical staining in series sections of biopsied specimens from patients with PBC. Immunohistochemical staining was positive for CK19, JCAD, and YAP in the portal triads from PBC patients compared to the normal control (NC). The use of patient samples was approved by the Ethic Committee of Fudan University School of Basic Medical Sciences. The image was taken at original magnification (200×). Scale bars=100 μm. Red arrows: bile ducts. JCAD, junctional protein associated with coronary artery disease; YAP, Yes-associated protein.

was co-localized with F-actin in bile canaliculi in regenerative mouse liver, which implies that JCAD functions as a conjunction protein critical for the formulation of tight conjunction between hepatocytes. As a conjunction protein, it is unsurprising to demonstrate that JCAD is positive for liver sinusoidal endothelial cells (LSEC) in an on-going project. Whether inflammatory cells, such as Kupffer cells, macrophages or lymphocytes, express JCAD needs further investigation. In summary, so far, the author's team has demonstrated that JCAD is expressed in parenchymal hepatocytes, non-parenchymal bile epithelial cells and hepatic stellate cells under different conditions and will further investigate its role in various modes of chronic injury and repair processes. Hopefully, in-depth investigation of this novel protein would facilitate the development of new molecular therapeutics for chronic injury, which may advance to hepatic fibrosis, end-stage liver disease, and malignancies.

Authors' contribution

Li Xie, Li Zhang, Hui Chen and Yong-Yu Yang are responsible for data acquirement, and manuscript preparation. Jian Wu is for concept synthesis, manuscript preparation and finalization.

Conflicts of Interest

All authors declare that no conflict of interest is involved in participation or contribution to the present work.

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Abbreviations:

JCAD, junctional protein associated with coronary artery disease; HSCs, hepatic stellate cells; BECs, bile epithelial cells; LSEC, liver sinusoidal endothelial cells; PBC, primary biliary cholangitis; YAP, Yes-associated protein

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