Acetaldehyde dehydrogenases in liver zonation and liver cancer

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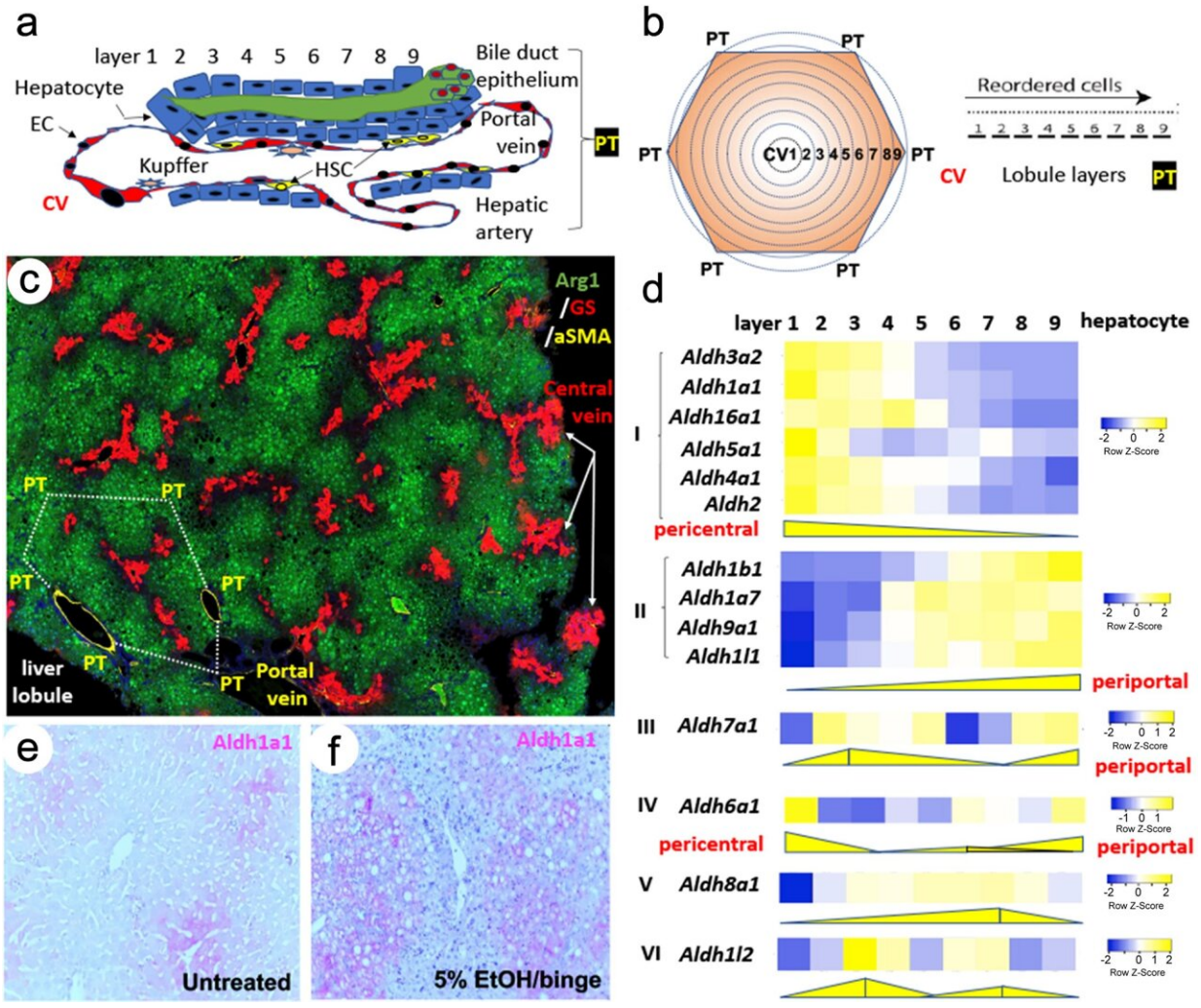

(a) A cartoon showing the hepatic architecture with layers of hepatic cords, central veins (CV), and portal triads (PT) that contain portal veins, hepatic arteries, and bile ducts. EC: vascular endothelial cells; HSC: hepatic stellate cells. (b) Overview of a liver lobule related to nine layers of hepatocytes in analyses of

spatial transcriptomics according to Halpern et al.36 (c) The immunofluorescent staining detects periportal hepatocytes by the Arg1 antibody (green signal), pericentral hepatocytes by the glutamine synthetase (Gs) antibody (red signal), and large hepatic vasculatures by an alpha-smooth muscle actin antibody (yellow signal). The white dashed lines show areas of a liver lobule consisting of 6 PT in the periphery and one CV in the middle. Scar bar: 100 mm. (d) Six types of zonation patterns are found in Aldhs. (e) and (f) Immunohistochemistry showed pericentral patterns of Aldh1a1 protein in normal and damaged livers that were exposed to 5% ethanol/binge in chronic and acute liver injury. Magnification: 200×. ALDH, acetaldehyde dehydrogenase. Credit: by Brady Jin-Smith and Liya Pi

A study, published in the journal *Gene Expression* and led by Brady Jin-Smith from the Department of Pathology at Tulane University, focuses on ALDHs, a group of key enzymes that catalyze the irreversible oxidation of various aliphatic and aromatic aldehydes to the corresponding carboxylic acids. Understanding their distribution and function within the liver is key to addressing liver diseases, including cancer.

The team utilized data from public databases like the Human Protein Atlas to analyze the expression patterns of ALDHs in normal adult livers, liver zonation, hepatocellular carcinoma (HCC), and cholangiocarcinoma (CCA). They examined how these enzymes are distributed across different liver zones, which is crucial for understanding their role in liver homeostasis and disease.

ALDH2 is a potential therapeutic target for liver disease. This enzyme can alleviate alcoholic liver disease by preventing acetaldehyde exposure in the reduction of signal transducer and activator of transcription one methylation.

The study revealed that ALDHs exhibit distinct expression patterns in different liver zones. For instance, some ALDHs are primarily found in the pericentral zones, while others dominate the periportal zones. These patterns shift significantly in liver cancers. In HCC, for example, certain ALDHs are upregulated, suggesting a potential role in cancer progression. In contrast, other ALDHs are downregulated, hinting at a loss of protective function.

The researchers concluded that the diverse spatial and temporal expression of ALDHs in the liver plays a critical role in maintaining liver health. Alterations in their expression and function are closely linked to the development of liver diseases, including HCC and CCA.

This study underscores the importance of ALDHs in liver health and disease. By mapping their zonal distribution and understanding their altered expression in liver cancers, new strategies for diagnosis, prognosis, and treatment can be developed. Further understanding of ALDH genes in the liver, in particular their relation to liver zonation, may help us to develop more accurate and personalized strategies for the treatment of liver diseases such as HCC and CCA.

More information: Brady Jin-Smith et al, Acetaldehyde Dehydrogenases in Liver Zonation and Liver Cancer, *Gene Expression* (2023). DOI: 10.14218/GE.2022.00022

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