Letrozole could be repurposed for the treatment of liver fibrosis, study finds

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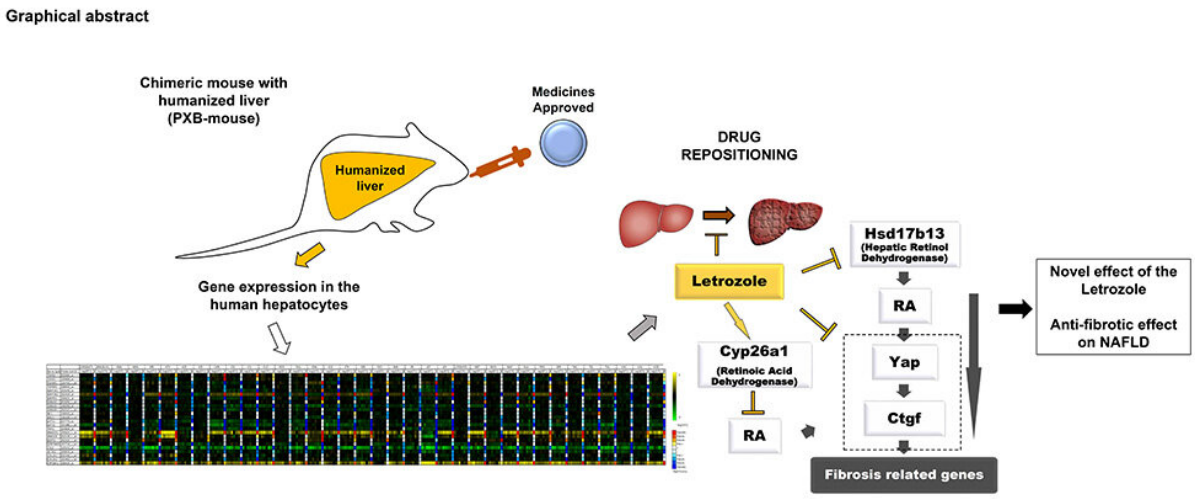

Letrozole ameliorates liver fibrosis through the inhibition of the CTGF pathway and 17β-hydroxysteroid dehydrogenase 13 expression. Credit: Niigata University

A gene expression-based screening assay using chimeric mice with humanized hepatocytes revealed that letrozole has a modifying effect on fibrosis-related gene expression in the hepatocytes, including YAP, CTGF, TGF-β, and CYP26A1. Because of its off-target effect, letrozole could be repurposed for the treatment of liver fibrosis.

The research group of Professor Kamimura in Niigata University have reported the usefulness of a drug repositioning method based on the gene

expression alteration in the chimeric mice with humanized hepatocytes and revealed that letrozole, which is used to treat breast cancer, is effective in suppressing the progression of liver fibrosis.

Their research is published in the *Journal of Gastroenterology*.

"Letrozole ameliorated MCD- and CCl4-induced liver fibrosis by suppressing the Yap-Ctgf pathway by partially modifying the expressions of Hsd17b13 and Cyp26a1, which reduced retinoic acid level in the hepatocytes," says Prof. Kamimura.

He concluded that letrozole might be repurposed for the treatment of liver fibrosis as its off-target effect, and that gene expression-based screening using a PXB-mouse is effective to identify the drug specific efficacy and off-target effect of the repurposing drugs for the hepatocytes in the human liver.

More information: Norihiro Sakai et al, Letrozole ameliorates liver fibrosis through the inhibition of the CTGF pathway and 17β-hydroxysteroid dehydrogenase 13 expression, *Journal of Gastroenterology* (2022). DOI: 10.1007/s00535-022-01929-w

Provided by Niigata University

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