

the signaling of collagen catabolic process, extracellular matrix structural constituent and negative-regulation of JAK-STAT cascade etc. **Conclusion:** Improvement of liver fibrosis post DAA treatment could be affected by the change of miRNAs expression profile in the liver and serum.

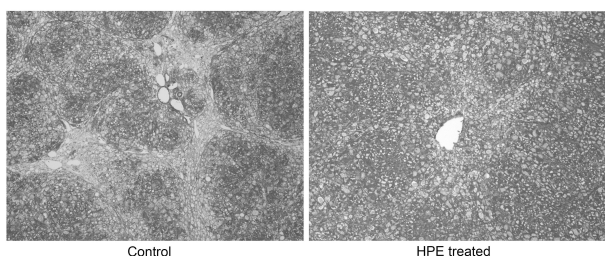
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1426 | HUMAN PLACENTAL EXTRACT ATTENUATES HEPATIC FIBROSIS AND CIRRHOSIS IN RATS WITH NONALCOHOLIC STEATOHEPATITIS

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Background: Nonalcoholic steatohepatitis (NASH) is always accompanied with hepatic fibrosis that could potentially progress to liver cirrhosis and hepatocellular carcinoma (HCC). Employing a rat model, we evaluated the role of human placental extract (HPE) to arrest the progression of hepatic fibrosis to cirrhosis and HCC in patients with NASH. **Methods:** SHRSP5/Dmcr rats were fed with a high-fat and cholesterol diet for 4 weeks and evaluated the development of steatosis. The animals were divided into control and treated groups and received either saline or HPE (3.6 mg/kg body weight) subcutaneously thrice a week. A set of control and HPE treated animals were sacrificed at



Control HPE treated
Azan staining for collagen in the liver sections of SHRSP5/Dmcr rats fed with a high-fat and cholesterol diet for 12 weeks and after the treatment with human placental extract (HPE) at a dose of 3.6 mg/kg body weight for 8 weeks. Azan staining demonstrated well developed fibrosis and early cirrhosis in untreated control animals at 12 weeks. Treatment with HPE for 8 weeks prevented formation fibrous septa, depicted marked reduction in the deposition of collagen fibers, and significant decrease of hepatic fibrosis.

the end of 6th, 8th, and 12th weeks from the beginning of the experiment. Blood and liver samples were collected for biochemical studies and histopathological evaluations. Immunohistochemical staining was performed for α -SMA, TNF- α , 4-hydroxy-2-nonenal (4-HNE), collagen type I, and type III. **Results:** Control rats depicted progression of liver fibrosis at 6 weeks, advanced fibrosis and bridging at 8 weeks, and cirrhosis at 12 weeks, which were significantly decreased in HPE treated animals. Immunohistochemical staining demonstrated marked decrease in the staining intensity of α -SMA, TNF- α , 4-HNE, and both collagen type I and type III in HPE treated rats compared to control animals. **Conclusion:** The results of the present study indicated that HPE treatment mediates immunotropic, anti-inflammatory, and antioxidant responses and attenuates hepatic fibrosis and cirrhosis. Therefore, HPE may be used as a therapeutic agent to prevent progression of liver fibrosis to cirrhosis in patients with NASH. *Presenting author Email: georgej@kanazawa-med.ac.jp

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1427 | ACTIVATION OF LXR/RXR REVERSES HEPATIC FIBROSIS IN ATP7B-/- (WILSON DISEASE) MICE VIA NON-CANONICAL TGF β SIGNALING PATHWAY

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Background: Wilson disease (WD) is caused by inactivation of the copper-transporter ATP7B, associated elevation of hepatic copper (Cu) and reduction in nuclear receptor (NR) function. Activation of the liver X receptor/retinoid X receptor (LXR/RXR) pathway in *Atp7b*^{-/-} mice prior to the development of hepatitis improves liver function and delays the development of fibrosis without Cu chelation. Here, we tested whether activation of LXR/RXR after the onset of disease will reverse fibrosis and characterized the associated signaling mechanisms. **Methods:** *Atp7b*^{-/-} (knockout) and *Atp7b*^{+/-} (heterozygous) mice of C57BL/6x129S6/SvEv background were fed with a LXR agonist, T0901317 for 8 weeks starting at 12 weeks (advanced disease stage) after birth. Total RNA-sequencing in male livers was performed to identify the affected metabolic and signaling pathways. Indicators of fibrosis were evaluated by qRT-PCR, Western blotting (WB), immunofluorescence