

7th World Congress on

Molecular Pathology

July 25-26, 2016 Melbourne, Australia

Connective tissue growth factor and a disintegrin and metalloprotease with thrombospondin motifs-7: A pair of substrate and protease critical for hepatic progenitor cell activation and alcohol induced liver injury

Liya Pi

University of Florida, USA

Hepatic progenitor cells (HPC) are activated in chronic liver disease when hepatocyte replication is impaired. Expansion of the progenitor cell compartment in the setting of liver fibrosis, known as the ductular reaction (DR), involves a heterogeneous population of transit-amplifying cells. The clinical relevance of this process is noted by its frequent appearance in a wide variety of human liver diseases including alcoholic and non-alcoholic fatty liver disease. Connective tissue growth factor (CTGF) is important for HPC activation and contributes to the pathogenesis of liver fibrosis. By using the yeast two-hybrid approach, we identified a disintegrin and metalloproteinase with thrombospondin type I motif 7 (ADAMTS7) as a CTGF binding protein. *In vitro* characterization demonstrated CTGF binding and processing by ADAMTS7. Moreover, *Adamts7* mRNA was induced during HPC activation, after the implantation of 2-acetylaminofluorene with partial hepatectomy in rats or on feeding a 3,5 diethoxycarbonyl-1,4-dihydrocollidine (DDC) diet in mice. Co-overexpression of *Adamts7* and *Ctgf* genes was also found during chronic liver injuries caused by the feeding of ethanol or high fat diet in mice that were pre-diabetic after streptozotocin treatment. X-Gal staining showed *Adamts7* expression in hepatocyte nuclear factor 4 α + hepatocytes and desmin+ myofibroblasts surrounding reactive ducts in DDC-treated *Adamts7*^{-/-} mice carrying a knocked-in LacZ gene. *Adamts7* deficiency increased CTGF accumulation, HPC activation and fibrotic response as evidenced by increased levels of α -smooth muscle actin and collagen. These results suggest ADAMTS7 and CTGF as a pair of protease and substrate important for HPC activation and fibrosis during chronic liver injury.

Biography

Liya Pi has completed her PhD in 2005 from Doctor Bryon Petersen at University of Florida. Her PhD study is about mechanisms of liver progenitor/oval cell activation and liver regeneration and has led to the identification of connective tissue growth factor (CTGF) as an important player in liver repair. She has further completed Postdoctoral training under Doctor Edward Scott from 2008-2012 which has broadened her research ventures into CTGF regulation in ocular vascular repair and tumorigenesis. Later she became an Assistant Professor in the Department of Pediatrics at UF and her research has been extended to the field of alcoholic liver disease and aims to understand the molecular mechanism underlying alcoholic cirrhosis.

lp@peds.ufl.edu

Notes: