Lipoprotein Lipase Liberates Free Fatty Acids Exerting Inhibitions of Hepatitis C Virus Infection and Lipid Accumulation in Hepatocytes

Hung-Yu Sun[1*], Pei-Ju Tsai[1], Chiung-Wen Tsao[2], Kung-Chia Young[1]

[1.] National Cheng-Kung university, [2.] Chung Hwa University of Medical Technology

Background/Objective

The lifecycle of HCV is closely associated with hepatic lipid/lipoprotein synthesis pathways. In previous studies, we had demonstrated that the lipoprotein lipase (LPL), an initial enzyme in very-low-density lipoprotein (VLDL) metabolism, might inhibit HCV infection in an enzymatic activity-dependent manner. The LPL lipolytic activity correlated negatively with plasma hepatitis C virus (HCV) viral loads in normolipidemic patients. However, the cellular mechanism of LPL mediated inhibition of HCV infection mediated is remained elusive.

Method

In the present study, we explore the mechanism involved in LPL-mediated inhibition of HCV infection by using PPRE reporter assay and immunofluorescence staining. The HCV core transgenic (coreTg) was applied to investigate the role of LPL in miR-27b expression.

Result

The transactivity and nuclear translocation of PPARalpha was elevated with physiologically ranged LPL treatment of very-low-density lipoprotein or cell-cultured HCV particles. The LPL-induced hepatic PPARalpha activation was alleviated by either blocking the LPL enzymatic activity with inhibitors or preventing the cellular uptake of unbound unsaturated fatty acids with albumin capture and silencing CD36 translocase. Knockdown of PPARalpha and CD36 reversed the LPL-mediated suppression of HCV infection, indicating that PPARalpha and CD36 participated in the LPL-mediated anti-HCV activity. Furthermore, hepatic miR-27b expression was upregulated in both HCV-infected cells and coreTg mice. LPL inhibited miR-27b expression could be restored in cell model, but not in coreTg mice. The result suggested that LPL suppressed miR-27b expression through its anti-HCV property.

Conclusion

LPL might hydrolyze HCV-associated triglyceride and generate unbound free fatty acids which were internalized through CD36, triggered activation of PPARalpha. The PPARalpha inhibits HCV infection and downregulates miR-27b expression, which might relieve HCV induced hepatic lipid accumulation.