シー型肝炎ウイルスを介した肝細胞における鉄沈着調節メカニズムの解明

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研究成果報告書

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目次

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研究成果の概要

Hepatic iron overload is frequently found in chronic hepatitis C (CH-C). Excess amount of cellular iron catalyses the over-production of hydroxyl radicals culminating in cell damage. The iron-mediated cytotoxicity plays an important role in the pathogenesis and carcinogenesis of CH-C. However, the precise mechanism of hepatic iron accumulation in CH-C is still obscure. Hepcidin acts as a key regulator of systemic iron homeostasis through down-regulating ion absorption from small intestine.

We reported that chronic HCV infection is associated with lower levels of serum hepcidin despite hepatic iron accumulation (Mol Med 2007), hepatic iron accumulation is associated with disease progression and resistance to interferon/ribavirin combination therapy in chronic hepatitis C (J Gastroenterol Hepatol 2007), and that iron-related hepatic oxidative DNA damage is associated with increased risk for hepatocellular carcinoma in chronic hepatitis C (Br J Cancer 2008).

Transferrin receptor 2 (TfR2) and interleukin-6 (IL-6) are known regulators of hepcidin. In order to clarify the roles of TfR2 and IL-6 in insufficient hepcidin expression during HCV infection, we investigated modulation of TfR2 and IL-6 expressions using a hepatocyte system transfected with full-genomic HCV-RNA. Our data showed that the holo-

transferrin-mediated transcriptional regulation of hepcidin via TfR2 was lost whereas IL-6 stimulated hepcidin expression in HCV replicon cells, which may partially explain a mechanism for an insufficient hepcidin expression and secretion in CH-C patients.

研究報告

1. Fujita N, Horiike S, Sugimoto R, Tanaka H, Iwasa M, Kobayashi Y, Hasegawa K, Ma N, Kawanishi S, Adachi Y, Kaito M.Hepatic oxidative DNA damage correlates with iron overload in chronic hepatitis C patients.

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