

# 学 位 論 文 の 要 旨

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<p>主論文の題名</p> <p>Substitution in Amino Acid 70 of Hepatitis C Virus Core Protein Changes the Adipokine Profile via Toll-Like Receptor 2/4 Signaling</p> <p>主論文の要旨</p> <p>Amino acid (aa) substitution at position 70 from arginine (70R) to glutamine (70Q) in the genotype 1b hepatitis C virus (HCV) core protein is associated with insulin resistance and worse prognosis. However, the precise mechanism is still unclear. The aim of this study was to investigate the impact of the substitution in HCV core protein (R70Q) on adipokine production by adipocytes.</p> <p>The influence of HCV core protein (70R or 70Q) on adipokine production by both 3T3-L1 and human adipocytes were examined with real-time PCR and enzyme-linked immunosorbent assay (ELISA), and triglyceride content was also analyzed. The effects of toll-like receptor (TLR)2/4 inhibition on IL-6 production by 3T3-L1 induced by HCV core protein were examined.</p> <p>IL-6 production was increased and adiponectin production was reduced without a change in triglyceride content by treatment with 70Q compared to 70R core protein in both murine and human adipocytes. IL-6 induction of 3T3-L1 cells treated by 70Q protein was inhibited with anti-TLR2 antibody by 42%, and by TLR4 inhibitor by 40%.</p> <p>Our study suggests extracellular HCV core protein with substitution enhance IL-6 production and reduce adiponectin production from visceral adipose tissue, which can cause insulin resistance, hepatic steatosis, and ultimately development of HCC.</p>			