Hepatitis C Virus Core Protein Blocks Interferon Signaling by Interaction with the STAT1 SH2 Domain

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Hepatitis C Virus (HCV) is the major cause of non-A, non-B hepatitis, affecting about 170 million people in the world. It is an enveloped, single stranded RNA virus belonging to the family Flaviviridae. The HCV genome is translated into a polyprotein of about 3,000 amino acids cleaved by cellular and viral proteases into three structural proteins and at least six nonstructural proteins. The structure protein include core and two envelope glycoproteins. (1)

Recent study indicated HCV can discredit the host antiviral response to enhance its persistence. The author previously demonstrated that expression of HCV protein can suppress type I interferon (IFN) signal transduction by the reduction of phosphorylated STAT1. They also demonstrated that HCV core protein can bind to STAT1(2). However, the detail mechanism is still not very clear. Therefore, in this paper the author further demonstrated the STAT1 interaction domain in the N-terminal portion of HCV core (amino acids [aa] 1 to 23). This domain is also required to produce P-STAT1 reduction and inhibit IFN signal transduction. Conversely, the C-terminal region of STAT1, especially the SH2 domain, is required for the interaction of HCV core.

In the end, the author proposed a model by which the binding of HCV core to STAT1 results in decreased P-STAT, blockage of STAT1 heterodimerization to STAT2, and thus a reduction of IFN-stimulated gene factor-3 binding to DNA and disrupted IFN-stimulated gene transcription.

Reference: