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Letters to the editor

The dual role of HCV protein expression in communication between host cells presents potential applications in the treatment of liver fibrosis

Dear Editor,

We read with great interest the study by Dr. Torres and colleagues examining the effects of hepatitis C virus (HCV) NS5A and core proteins on the expression of fibrosis-related genes during co-culture with human hepatic stellate cells (LX2) and human hepatocytes (Huh7) [1]. While previous studies have examined the impact of HCV proteins on the activation of hepatic stellate cells [2–5], this paper provides an in-depth analysis of the effects of HCV NS5A and core proteins on gene expression in co-culture systems at two time points (48 and 72 h). This research reveals the dynamic regulatory role of viral protein-host cell communication in the progression of liver fibrosis. Specifically, NS5A shows higher expression at 48 h, whereas the core protein exhibits increased expression at 72 h, suggesting that different molecular mechanisms may be involved in the early and late stages of liver fibrosis.

Additionally, the changes in gene expression mentioned in the article, such as SERPINE1, SMAD7, and TGFB2, are not only induced in cell models infected with HCV but also align with the gene expression patterns observed in tissues affected by HCV-induced cirrhosis. This suggests that the expression of HCV proteins may promote the development of liver fibrosis by mimicking or influencing the natural regulatory pathways of these genes.

However, it is noteworthy that certain genes, such as IFNG and IL10, exhibited upregulation during the 48-hour co-culture, and these genes are known to have antifibrotic effects [6]. This suggests that the expression of HCV proteins may play a complex role in the liver fibrosis process, potentially promoting fibrosis development while also activating certain antifibrotic mechanisms in host cells.

Recognizing this phenomenon, the author proposes that the “double-edged sword” effect could serve as a foundation for developing new treatment strategies. Specifically, future research could focus on harnessing the unique characteristics of HCV protein expression to enhance the host cell’s anti-fibrotic response through pharmacological or other interventions, while simultaneously inhibiting its pro-fibrotic effects. For instance, investigations could explore whether specific drugs or compounds can modulate the intracellular signaling pathways of HCV protein expression, thereby reducing the expression of fibrosis-related genes and enhancing the cell’s intrinsic repair and anti-fibrotic capabilities without completely suppressing viral replication.

Additionally, this strategy may help address the current challenge of effectively controlling HCV infections while reducing or reversing liver fibrosis caused by the virus. By thoroughly investigating the complex interactions between HCV proteins and host cells, we may identify new therapeutic targets that offer more precise and effective treatment options for patients with chronic HCV infection.

Author contribution

Junxi Liu: Writing – original draft, Writing – review & editing. Boda Zhou: Writing – original draft, Writing – review & editing.

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Declaration of interests

None.

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