VIRAL HEPATITIS

New strategy by which HCV evades host immune defences

In acute HCV infection, CD8⁺ T cells are known to mount a robust response, helping to eliminate infected cells. However, in patients with chronic hepatitis C, these cells become exhausted and are unable to control viral replication.

“Importantly, hepatocytes assist in the stimulation of CD8⁺ T cells by producing immunostimulatory cytokines such as IL-7, IL-15 and its high-affinity receptor IL-15R α ,” explain Jesús Prieto and Esther Larrea. “Given the remarkable ability of HCV to evade antiviral immune defence mechanisms, we decided to study whether the expression of IL-7, IL-15 and IL-15R α was impaired in chronic HCV infection.”

The researchers measured levels of IL-7, IL-15 and IL-15R α in patients with chronic hepatitis C and investigated the production of these molecules in Huh7 cells sustaining HCV replication (all genotype 1). Prieto, Larrea and colleagues also studied the levels of interferon regulatory factors (IRF1 and IRF2), as these factors have been shown to stimulate IL-7 and IL-15R α .

Immunostaining for IRF2. Courtesy of J. Prieto and E. Larrea.

“Our results revealed downregulation of both IL-7 and IL-15R α in livers from patients with chronic hepatitis C,” note Prieto and Larrea. Studies in the Huh7 cells demonstrated that this downregulation is a result of blocked expression of IRF2 (the levels of which were also found to be reduced in the livers of patients infected with HCV). Furthermore, the researchers found that, in line with previous studies, the combination of IFN- α and oncostatin M upregulated IL-7 and IL-15R α .

The authors suggest that their findings highlight a new mechanism by which HCV evades host immune defences. “We would like to stimulate translational efforts combining oncostatin M and IFN- α in chronic viral hepatitis,” they say.

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Original article Larrea, E. *et al.* Dysregulation of interferon regulatory factors impairs the expression of immunostimulatory molecules in hepatitis C virus genotype 1-infected hepatocytes. *Gut* doi:10.1136/gutjnl-2012-304377