Reduced IFNλ4 activity is associated with improved HCV clearance and reduced expression of interferon-stimulated genes

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Abstract

Hepatitis C virus (HCV) infections are the major cause of chronic liver disease, cirrhosis and hepatocellular carcinoma worldwide. Both spontaneous and treatment-induced clearance of HCV depend on genetic variation within the interferon-lambda locus, but until now no clear causal relationship has been established. Here we demonstrate that an amino-acid substitution in the IFNλ4 protein changing a proline at position 70 to a serine (P70S) substantially alters its antiviral activity. Patients harbouring the impaired IFNλ4-S70 variant display lower interferon-stimulated gene (ISG) expression levels, better treatment response rates and better spontaneous clearance rates, compared with patients coding for the fully active IFNλ4-P70 variant. Altogether, these data provide evidence supporting a role for the active IFNλ4 protein as the driver of high hepatic ISG expression as well as the cause of poor HCV clearance.

Reference


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Corrigendum: Reduced IFNλ4 activity is associated with improved HCV clearance and reduced expression of interferon-stimulated genes

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In this Article, Rune Hartman was omitted as joint supervisor of this work. The correct list of joint supervisors is: Markus H. Heim, Pierre-Yves Bochud and Rune Hartmann.