

Modulation of HCV replication after combination antiretroviral therapy in HCV/HIV co-infected patients

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Abstract— The hepatitis C virus (HCV) is an important contributor to morbidity and mortality in patients co-infected with HIV. Co-infection results in increased HCV replication and more rapid rates of liver disease progression. The effect of HIV combination antiretroviral therapy (cART) on HCV replication has not been studied in depth. To address this issue, we enrolled a small cohort of HCV/HIV co-infected patients into a cART initiation trial and used dynamic modeling combined with evaluation of immune responses and microarray profiles to determine how effective treatment of HIV affects HCV. Treatment with cART resulted in increased HCV replication and increased alanine aminotransferase (ALT) in a subset of patients. Subjects with evidence of hepatic injury (increased ALT) were more likely to have HCV-specific immune responses directed against HCV epitopes. Over time, HCV viral loads declined. Reproducible and biologically important gene expression changes occurred in co-infected patients who underwent successful cART. The effective suppression of HIV by cART initiated a cascade of early and late events in treated patients. Early events involving down-regulation of interferon-stimulated genes may have led to transiently increased viral replication and hepatic injury. At later time points, HCV viral load declined to levels comparable to those seen in the setting of HCV monoinfection. These findings support early antiretroviral therapy in those with HCV/HIV co-infection.

Index Terms—

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