Hepatitis C and Human Immunodeficiency Virus Envelope Proteins Cooperatively Induce Hepatocytic Apoptosis via an Innocent Bystander Mechanism

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ABSTRACT

We hypothesized that hepatocytes exposed to hepatitis C virus (HCV) and human immunodeficiency virus (HIV) might be injured via an “innocent bystander” mechanism due to cell-surface binding of viral proteins. To assess this, we studied the effects of HCV envelope protein E2 and T-tropic HIV envelope glycoprotein gp120 on hepatocytes and saw potent apoptosis. Either viral protein alone did not induce this effect. HCV E2 and M-tropic HIV gp120 also induced significant apoptosis. Blocking the CXCR4 receptor led to a reduction in apoptosis. HCV E2 and HIV gp120 acted collaboratively to trigger a specific set of downstream signaling events, including up-regulation of the Fas ligand and dephosphorylation of the anti-apoptotic molecule AKT. These results suggest that hepatic injury may occur in HCV/HIV coinfection through the induction of novel downstream signaling pathways and provide a rationale for therapeutic interventions that interfere with specific receptors and signaling molecules.

Presence of Human Immunodeficiency Virus-1-Specific CD4 and CD8 Cellular Immune Responses in Children with Full or Partial Virus Suppression

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ABSTRACT

The present study assessed antiviral T cell immune responses in 48 human immunodeficiency virus (HIV)-infected children with a stable or decreasing CD4(+) T cell counts and different levels of viral control, in the presence or absence of antiretroviral therapy. Children with full (<40 copies/mL) or partial (<50,000 copies/mL) virus suppression and with a history of stable CD4(+) T cell counts had significantly increased levels of anti-HIV CD4(+) T cell lymphoproliferative responses, lower levels of CD38(+), and higher CD8(+)/CD28(+) T cell percentage, compared with those in treated children with a lack of virus suppression (>50,000 copies/mL). Levels of anti-HIV CD8(+) T cell activity, although higher in treated children with a lack of virus suppression, were not significantly different between the groups. Although levels of anti-HIV CD4(+) and CD8(+) T cell responses were not associated, these levels of responses were associated with the percentage of specific T cell subsets. Overall, a history of stable CD4(+) T cell counts, as a result of therapy that imparted full or partial virus suppression, was associated with increased levels of anti-HIV CD4(+) T helper responses and decreased T cell activation.