**Background:** Effective immune responses against hepatitis C virus (HCV) are dependent on CD8+ T cells, yet their function is impaired in chronic infection, which is also a feature of chronic HIV infection. HCV is the most prevalent co-morbidity in HIV, yet the effect of HCV on HIV infection remains largely unknown. This study will determine how CD8+ T cell activity (specifically IL-7 activity) is impaired in chronic HCV infection. IL-7 is critical for CD8+ T cell development, and important for T cell homeostasis, memory cell generation, and cytolytic function. CD8+ T cell responses to IL-7 are dependent on the expression of IL-7 receptor alpha on the cell membrane (mCD127). Reduced mCD127 expression, increased plasma soluble CD127 (sCD127) levels, or cellular deficiencies in IL-7 signalling may contribute to impairment, as we reported in HIV infection. The hypothesis of this study is that HCV infection decreases CD8+ T cell activity, specifically IL-7 responsiveness, in both HCV and HIV-HCV infection.

**Methodology:** CD8+ T cells were isolated from healthy donors (controls) as well as individuals with untreated HCV infection and HAART-controlled (< 40 copies/ml HIV RNA) HIV-HCV co-infection. Expression of mCD127 on CD8+ T cells and plasma sCD127 levels were measured by flow cytometry and immunobead assays, respectively. IL-7-induced signalling (STAT5 phosphorylation), proliferation, and production of the anti-apoptotic molecule Bcl-2 were measured by flow cytometry. Dose responses were assessed by regression analysis (P < 0.05).

**Results:** There was no significant difference in mCD127 expression on blood-derived bulk CD8+ T cells or plasma sCD127 levels between control, HCV and HIV-HCV infection. HCV infection also reduced IL-7-induced STAT5 phosphorylation (p = 0.005) in CD8+ T cells from HCV infection compared to controls, and similar to HIV-HCV co-infected individuals. Cell division of CD8+ T cells cultured with suboptimal amounts of T cell stimulator (PHA) was of lower magnitude in HCV infection than controls. Lastly, the production of Bcl-2 in response to IL-7 was significantly reduced in CD8+ T cells of HCV and HIV-HCV infected individuals compared to controls (p<0.001 and 0.04, respectively).

**Conclusions:** These results suggest that CD8+ T cell impairment in HCV infection is characterized by decreased responsiveness to IL-7, independent of mCD127 expression, in contrast to what is observed in HIV infection. The mechanism of CD8+ T cell impairment may be through IL-7-stimulated signalling, since we know Bcl-2 production is STAT5 dependent. Identifying the mechanisms of CD8+ T cell impairment in HCV infection has implications in the design of novel treatments, namely cytokine directed immunotherapies, to help reduce the burden of HCV effects on HIV infection.