INTERFERON RESPONSES IN CELLS EXPRESSING THE FULL LENGTH HEPATITIS C VIRUS (HCV) POLYPROTEIN

Abstract

To develop efficient therapies, the molecular interactions between hepatitis C virus (HCV) proteins and the host cell must be fully understood. In this regard resistance of HCV to interferon (IFN) treatment is a widespread clinical problem. However because of the lack of a suitable tissue culture system, which supports HCV replication, efforts to study the detailed mechanisms of IFN resistance in cells infected with HCV have been hindered. To address this problem, we have developed an efficient baculovirus delivery system to introduce the whole genome of HCV into hepatoma cells. This construct lacks the 3'UTR that is responsible for HCV replication. Thus it enables us to look for the effects of HCV proteins on IFN signaling. The expression of the HCV polyprotein was under the control of an inducible tetracycline-responsive promoter coupled to the HCV 5'UTR. Thus the tetracycline controlled construct confirmed use for regulable expression of proteins. The effect of this construct on the induction of IFN promoter and on the inhibition of IFN signalling pathway has been analysed. In conclusion, under our conditions it seems that HCV, either full length or sub-genomic replicon, has no effect on induction of IFN promoter or on transcriptional regulation of interferon stimulated response element (ISRE) by IFN. Moreover, baculovirus as a vector seems to have a marginal effect on the IFN promoter.