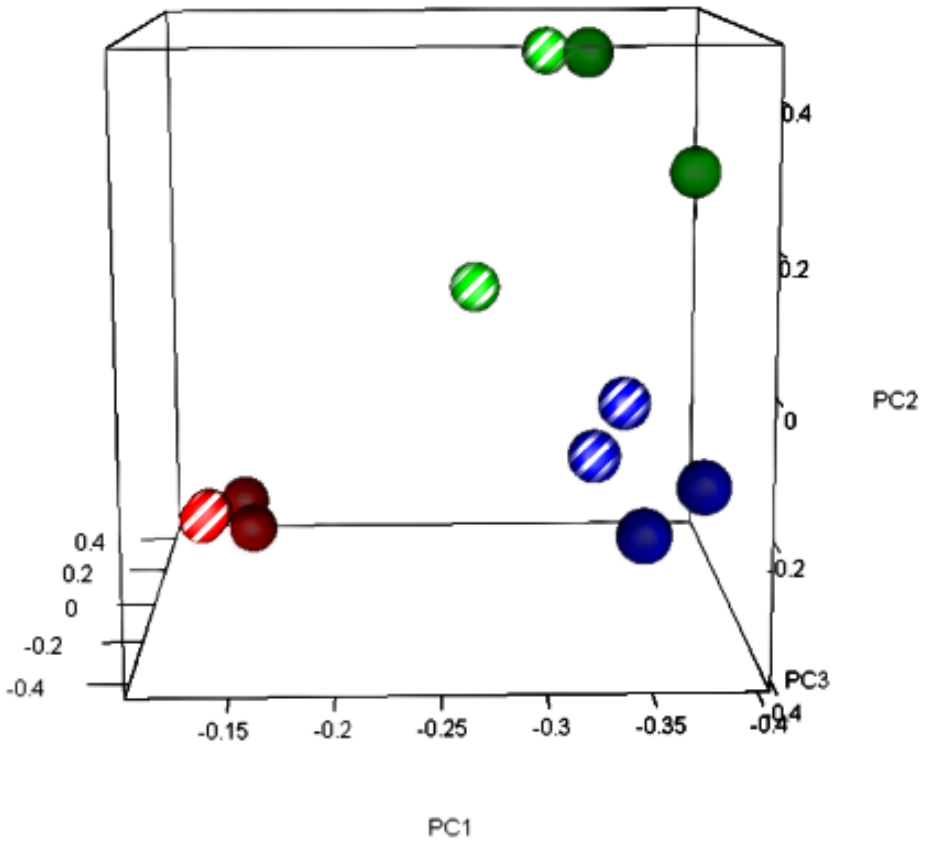
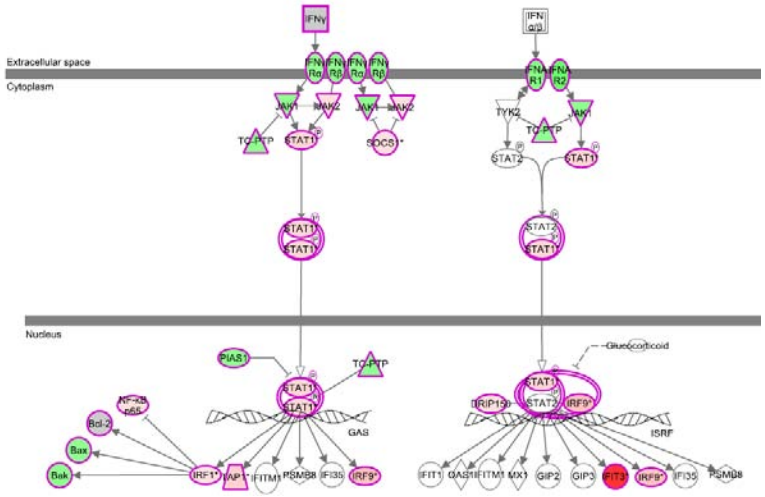


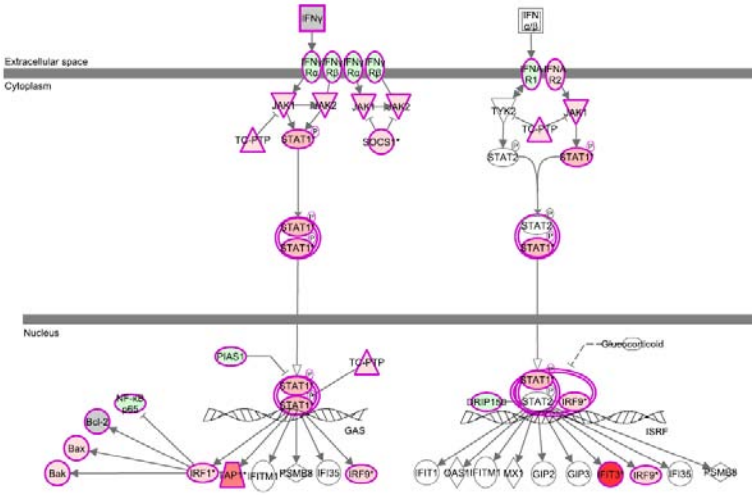
Figure S1. Principle components analysis (PCA). A three-dimensional plot shows the top three principle components derived from gene expression profiles of various differentiation time points and respective IFN-α treatment conditions. The top 1000 genes rank ordered by standard deviation from each condition were used to calculate the top three PCA and plotted using R version 3.0.2 package "rgl" (Vienna, Austria). This unsupervised analysis demonstrates that the clustering of samples in the three-dimensional space were based on biological conditions rather than technical artifacts. Samples were indicated in the plot by either stripped circles (differentiation time point samples) or filled circles (respective IFN-α treated samples). Red circle = Day 5; blue = Day 15; green = Day 21.

Figure S2. Pathway analysis. Genes differentially expressed upon IFN-α treatment at various differentiation time points were subjected to pathway analysis. (A-C) Type I and type II interferon mediated JAK-STAT pathway. (D-F) Pathway involved in viral entry via vesicle-mediated endocytosis. Red shaded genes: upregulated; green shaded genes: down-regulated. (G) Panel shows the pathway legends.

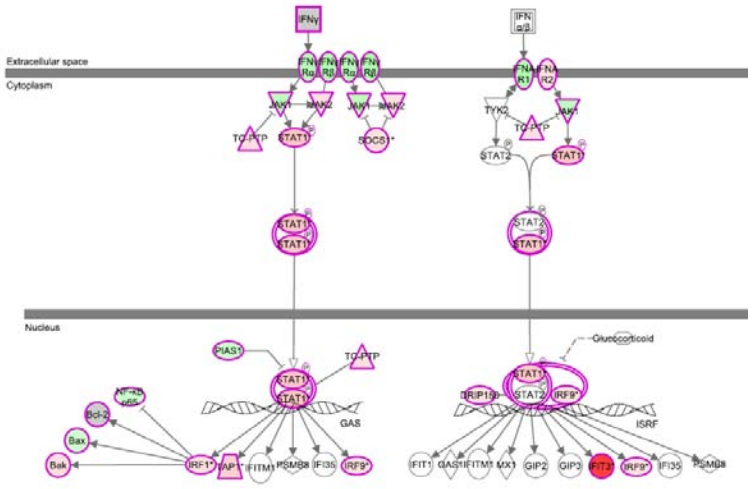
A. Day 5, Control Vs. IFN



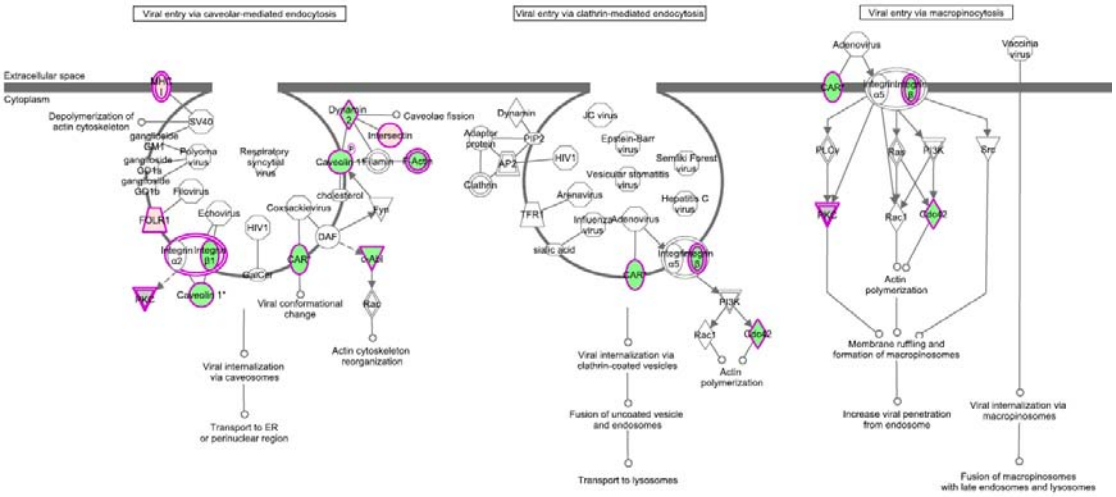
B. Day 15, Control Vs. IFN



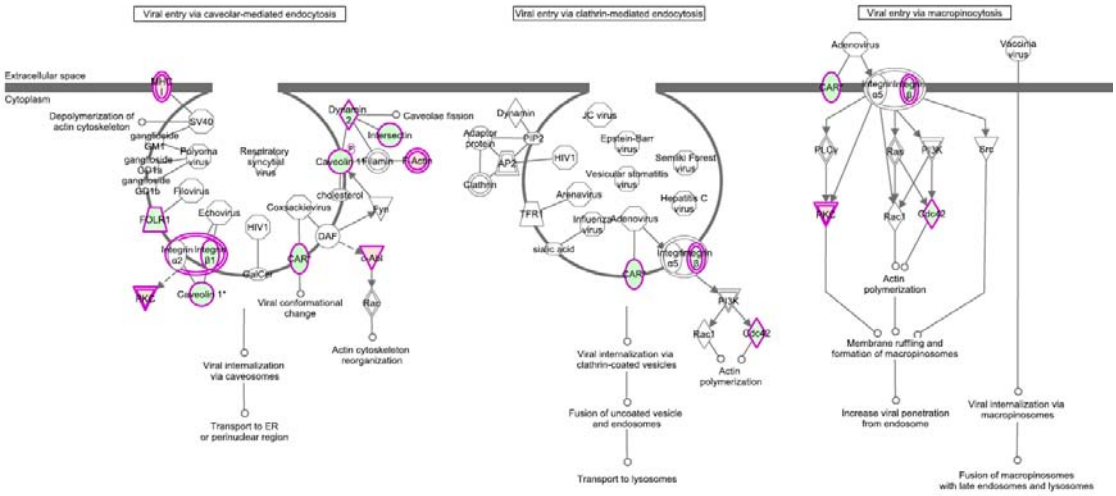
C. Day 21, Control Vs. IFN



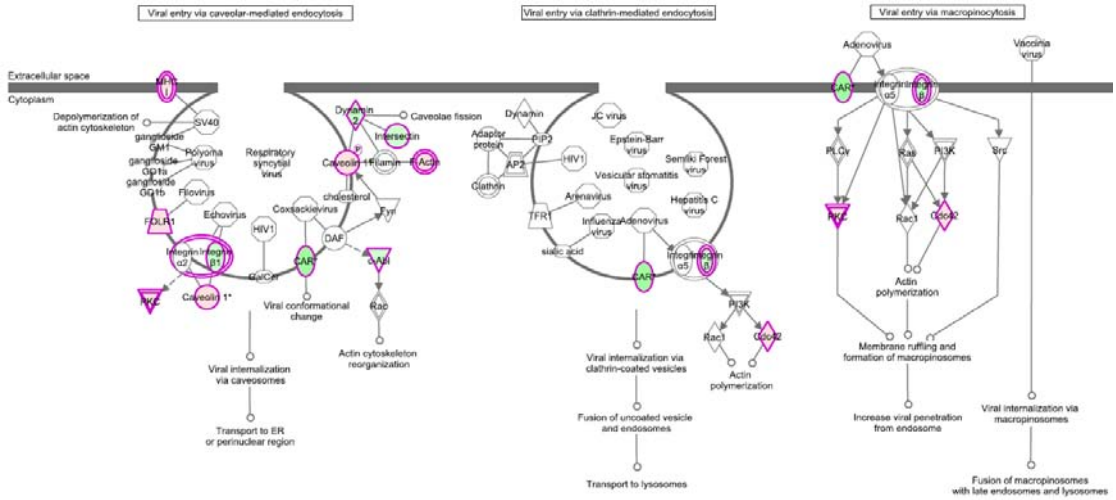
D. Day 5, Control Vs. IFN



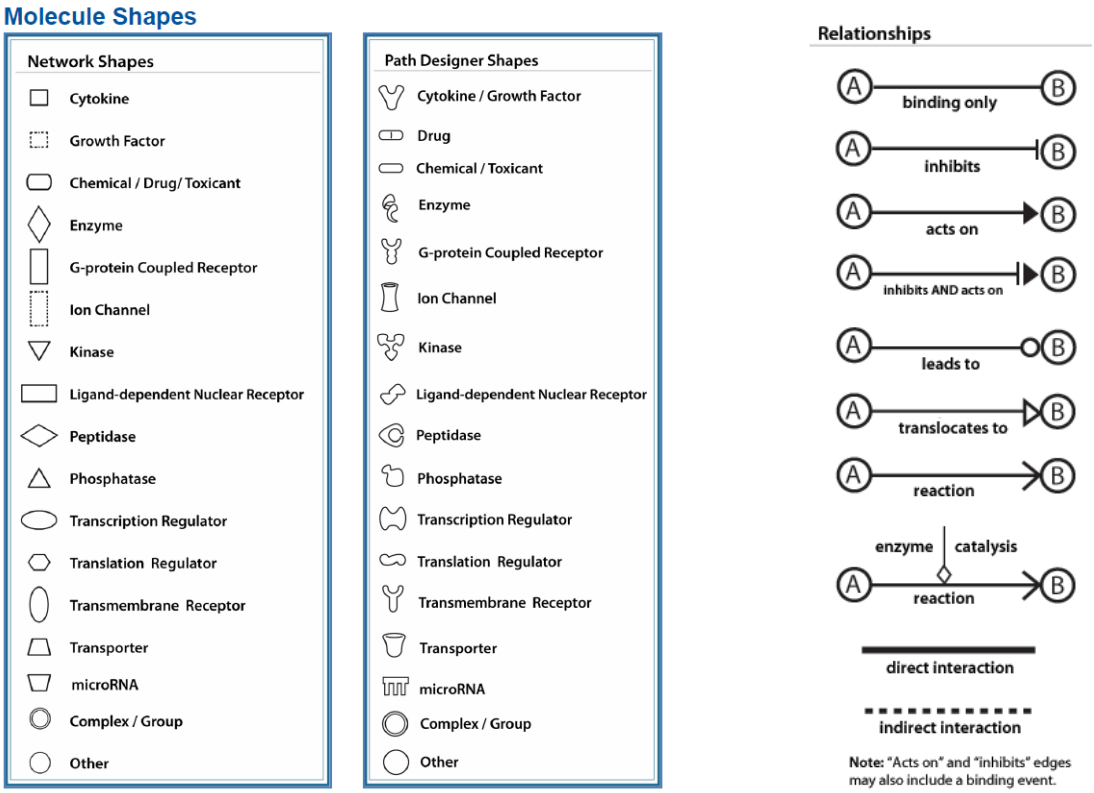
E. Day 15, Control Vs. IFN



F. Day 21, Control Vs. IFN



G. Pathway Legends



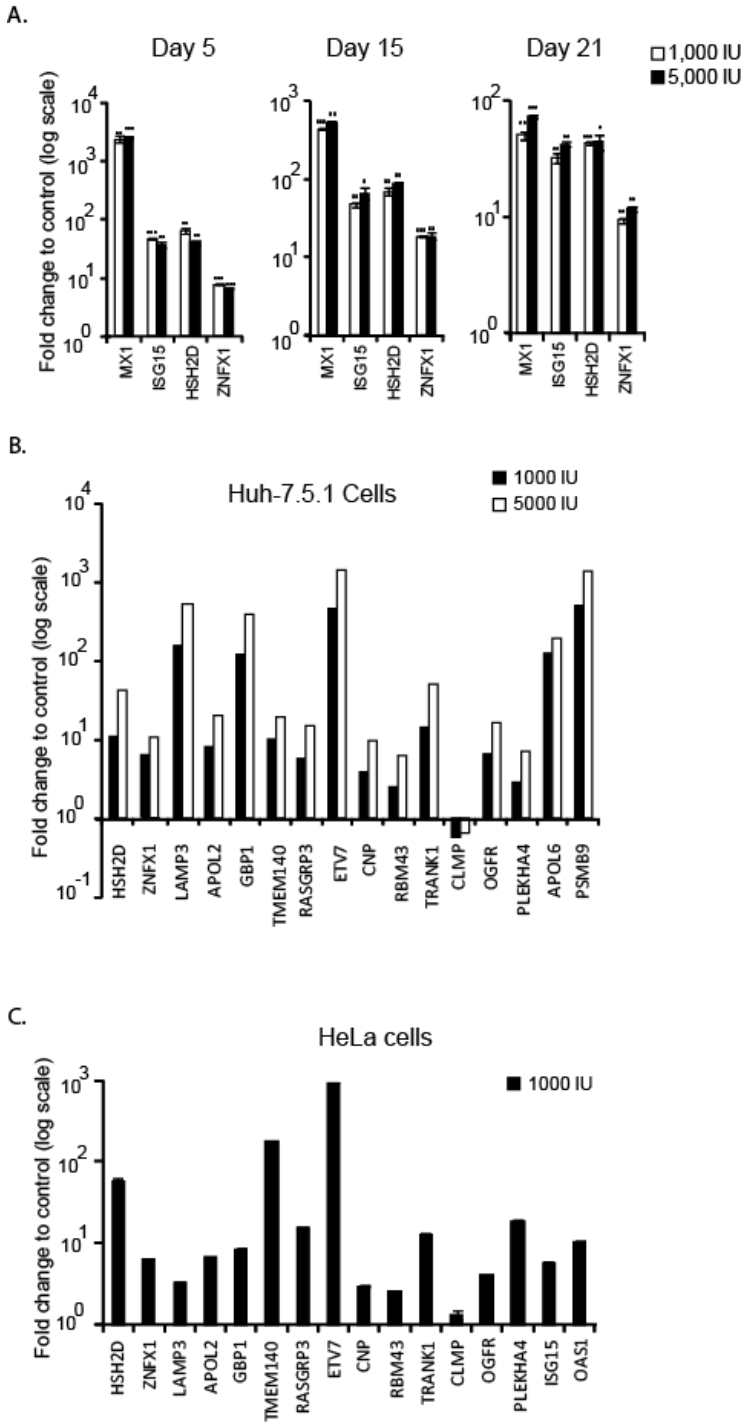


Figure S3. Quantitative analysis of selected IFN-induced genes in (A) differentiating hESCs, (B) Huh-7.5.1 cells (human hepatoma cell line) and (C) human cell line HeLa. The cells were treated with or without IFN-α for 6 hrs. The cDNA generated from the harvested RNA was subjected to RT-qPCR analysis. The normalized gene expression values of IFN-α treated cells were compared to that of untreated control cells. The fold changes are shown in the bar graph.

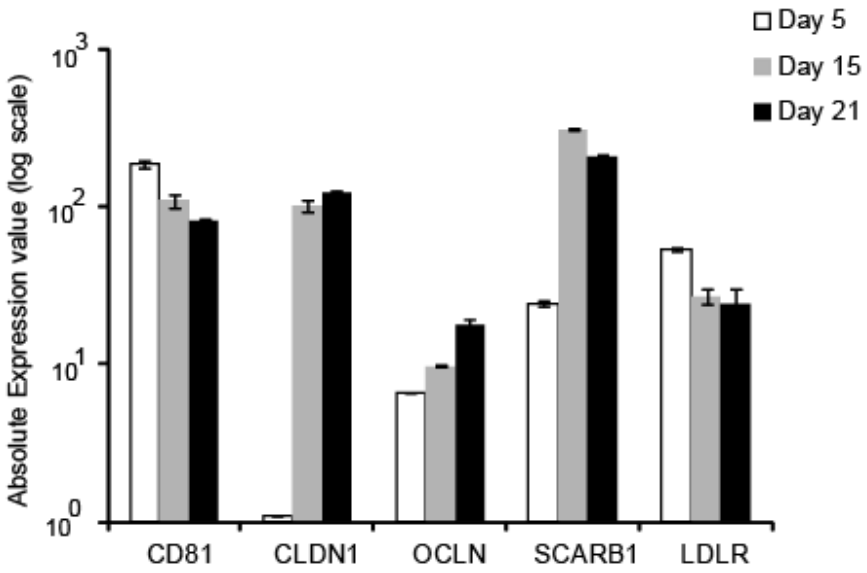


Figure S4. RNA sequencing expression data for HCV cell entry receptors. Differentiated hepatic cells at Day 15 and Day 21 highly expressed all the key receptors, CD81, claudin 1 (CLDN1), occludin (OCLN), scavenger receptor class B member 1 (SCARB1) and low-density-lipoprotein receptor (LDL). CLDN1 and OCLN are tight junction proteins involved in cell-cell interaction and internalization of HCV viral particles. Note: CLDN1 expression level was very low at Day 5 endodermal phase.