

IFN- α , which is classed as a type I interferon, is secreted by almost all virus-infected cells (47) and in higher amounts by plasmacytoid dendritic cells (48,49).

Expression of IFN- γ (the only type II interferon) is restricted to T cells, NK cells, and macrophages (50).

h. What IFN- γ does during HCV infections

IFN- γ contributes to HCV clearance in several ways. First, IFN- γ enhances NK cell activity. Second, IFN- γ promotes the processing and presentation of antigens, that is, processing by DCs and presentation by DCs to T cells. Dendritic cells use MHC Class I to present antigens to CD8⁺ T cells, and MHC Class II to present antigens to CD4⁺ T cells. IFN- γ stimulates expression of various components of the MHC complex of proteins. Thus, according to Meissner et al. (51) both MHC class I and class II genes are inducible by IFN- γ stimulation. Third, IFN- γ facilitates T cell homing from lymph nodes and peripheral blood to the site of infection by way of inducing chemokines (52). Finally, IFN- γ may directly inhibit replication of HCV.

i. What T cells do during HCV infections where the patient spontaneously recovers

In acute self-limited hepatitis C, the HCV-specific responses by CD4⁺ T cells and CD8⁺ T cells can be vigorous with more than 10% of all the peripheral blood lymphocytes recognizing HCV antigens (53). In patients spontaneously recovering from an acute HCV infection, T cells express IFN- γ , where this IFN- γ is thought to be critical for clearing the HCV infection (54).

⁴⁷ Frese M, Schwärzle V, Barth K, et al. Interferon- γ inhibits replication of subgenomic and genomic hepatitis C virus RNAs. *Hepatology*. 2002;35:694–703.

⁴⁸ Cella M, Jarrossay D, Facchetti F, et al. Plasmacytoid monocytes migrate to inflamed lymph nodes and produce large amounts of type I interferon. *Nat Med*. 1999;5:919–923.

⁴⁹ Dolganiuc A, Chang S, Kodys K, et al. Hepatitis C virus (HCV) core protein-induced, monocyte-mediated mechanisms of reduced IFN- α and plasmacytoid dendritic cell loss in chronic HCV infection. *J Immunol*. 2006;177:6758–6768.

⁵⁰ Frese M, Schwärzle V, Barth K, et al. Interferon- γ inhibits replication of subgenomic and genomic hepatitis C virus RNAs. *Hepatology*. 2002;35:694–703.

⁵¹ Meissner TB, Li A, Biswas A, et al. NLR family member NLRC5 is a transcriptional regulator of MHC class I genes. *Proc Natl Acad Sci USA*. 2010;107:13794–13799.

⁵² Shin EC, Protzer U, Untergasser A, et al. Liver-directed gamma interferon gene delivery in chronic hepatitis C. *J Virol*. 2005;79:13412–134120.

⁵³ Ahlenstiel G, Titerence RH, Koh C, et al. Natural killer cells are polarized toward cytotoxicity in chronic hepatitis C in an interferon- α -dependent manner. *Gastroenterology*. 2010;138:325–335.

⁵⁴ Ahlenstiel G, Titerence RH, Koh C, et al. Natural killer cells are polarized toward cytotoxicity in chronic hepatitis C in an interferon- α -dependent manner. *Gastroenterology*. 2010;138:325–335.