HEPATITIS C VIRUS: FROM REPLICATION TO INFECTION OUTCOME

(i)Guaniri Mateu[1] and Arash Grakoui[1,2]
(ii) Hirotomo Nakahara[1], Holly L. Hanson[1] and Arash Grakoui[1,2]
(iii) Hank Radziewicz[1,2], Chris Ibegbu[1], Kimberly A. Workowski[2], Gordon Freeman[3], Rafi Ahmed[1] and Arash Grakoui[1,2]

[1]Emory Vaccine Center and Department of Microbiology and Immunology, and [2]Department of Medicine, Emory University School of Medicine, Atlanta, GA, 30322; [3]Department of Medical Oncology, Dana-Farber Cancer Institute, Department of Medicine, Harvard Medical School, Boston, MA 02115

Hepatitis C virus (HCV) establishes chronic infection in the liver of nearly 80% of those infected and in addition to causing hepatitis, may cause liver cirrhosis and hepatocellular carcinoma. These detrimental long-term sequelae of persistent HCV infection now comprise the leading indication for liver transplantation in the United States. Defining the elements of the immune response that fail or are insufficient to mediate HCV infection resolution in the majority of those infected is critical for advancing our understanding of how to therapeutically intervene in HCV disease pathogenesis. Three important topics spanning viral replication to the host response will be discussed: (i) development of an infectious in vitro model system in which we have generated chimeric HCV genotype 2a infectious clones capable of efficient replication and virion production; (ii) determination of the ability of MHC class II-expressing antigen presenting cells to productively prime and maintain HCV-specific CD4+ T helper cells, a cell population critical for infection resolution; and (iii) elucidation of the role of the co-inhibitory molecule PD-1on HCV-specific CD8+ T cells that demonstrate an exhausted phenotype which can be partially reversed with blockade of the PD-1/PD-L1 interaction.
Key words: HCV, antigen presentation, T cells