As reviewed by Saito et al. (110), recovery from hepatitis C (HCV) infection requires responses by both $CD8^+$ T cells and $CD4^+$ T cells. Moreover, what is required is response by T cells that are specific for, and recognize, a *variety* of epitopes from HCV (not just one epitope). In other words, if the T-cell response involved only T cells specific for one particular epitope, for example, the epitope of RLGVRATRK, the infected person would not be able to effectively combat the infection. Semmo and Klenerman (111) provide a detailed account of the most stimulatory epitopes of the HCV polyprotein.

b. Methodology Tip—GenBank

The following information is relevant to acquiring the primary sequence of nucleic acids and polypeptides from any organisms, including mammals, plants, yeasts, bacteria, archaea, and viruses, including hepatitis C virus. GenBank is a database, provided by the US Government, which can be accessed on the internet at: www.ncbi.nlm.nih.gov.

Where a person has a sequence of a nucleic acid in hand, and where the goal is to find other nucleic acids having a similar sequence, or related sequence, this goal can be accomplished by inputting that sequence at this website. Where a person has the sequence of an oligopeptide or polypeptide in hand, the same goal can be accomplished using search tools at this website.

Where a researcher is interested in comparing the primary sequences of two polypeptides, this comparison can be accomplished using computer software programs available from the *Expasy Proteomics Server* of the Swiss Institute of Bioinformatics, or by using the *Accelrys* program, available from Biovia, San Diego, CA. Side-by-side comparisons of primary sequences can be used, for example, for determining whether the same oncogene from two different tumors contains the same collection of antigenic epitopes, for determining whether two different viral isolates have acquired the same mutations, or for determining the function of a newly discovered cytokine.

c. Dendritic Cells and Antigens of HCV

At the start of HCV infection, dendritic cells (DCs) take up the virus. The DCs process the HCV polyprotein, and present peptides by way of MHC class I and MHC class II. The peptides bound to MHC class I are presented to $CD8^+$ T cells, resulting in the activation and propagation of these T cells. These T cells eventually kill liver cells that are infected with HCV. The peptides bound to MHC class II are presented to $CD4^+$ T cells, resulting in the activation and propagation of these T cells, where the result is that these helper T cells stimulate the $CD8^+$ T cells. The following accounts for the ability of $CD8^+$ T cells to specifically kill infected hepatocytes. Normal liver cells do not contain HCV proteins on the cell membrane, because normal liver cells do not contain the HCV. But when HCV infects a liver cell, epitopes from the virus are processed and presented on the MHC class I of the liver cell. Thus, the complex of MHC class I/HCV

[110]Saito K, Ait-Goughoulte M, Truscott SM, et al. Hepatitis C virus inhibits cell surface expression of HLA-DR, prevents dendritic cell maturation, and induces interleukin-10 production. J. Virol. 2008;82:3320–28.

[111]Semmo N, Klenerman P. CD4 + T cell responses in hepatitis C virus infection. World J. Gastroenterol. 2007;13:4831–38.