Helper T cells, not killer T cells, might be responsible for clearing hepatitis A infection

July 16 2012

Helper cells traditionally thought to only assist killer white blood cells may be the frontline warriors when battling hepatitis A infection. These are the findings from a Nationwide Children's Hospital study appearing in a recent issue of the *Journal of Experimental Medicine*.

Hepatitis A is a highly contagious liver infection caused by the hepatitis A virus. Despite the availability of an effective vaccine, the virus infects millions of people worldwide each year and remains a global public health problem, especially in underdeveloped countries.

Unlike the hepatitis C virus, the hepatitis A virus does not establish a persistent infection. Yet, up to 20 percent of patients can relapse several weeks after virus growth and after symptoms have disappeared.

"Mechanisms of immunity that protect against relapse, and why they occasionally fail, are unknown," said the study's lead author Christopher M. Walker, PhD, director of the Center for Vaccines and Immunity at The Research Institute at Nationwide Children's Hospital.

Research has shown that white blood cells known as CD8+ killer T cells play a critical role in controlling hepatitis C and hepatitis B virus infections. These T cells act by killing infected liver cells, a process that damages the liver, but is necessary to effectively shut off production of new viruses.

A study published more than 20 years ago suggested that killer T cells

also control hepatitis A virus infection in humans. However, Dr. Walker observed a very different pattern of immunity while studying acute hepatitis A virus infection in animals.

He found that the infection was controlled well before an effective killer T cell response was generated. Hepatitis A virus growth was instead controlled by CD4+ T helper cells, a different type of white blood cell that normally assists in the activation killer T cells but, is not thought to directly engage virus-infected cells. In the two infected animals infected with the hepatitis A virus, helper T cells secreted factors that suppressed virus growth without causing serious liver damage or inflammation that is an undesirable byproduct of a killer T cell response.

Moreover, the helper T cells responded to resurgence in hepatitis A virus growth after initial control of the infection, and remained strong until the virus was finally eliminated from the liver several months later. These findings suggested that CD8+ T cells are not necessarily required to control hepatitis A virus infection. Instead, it appears that CD4+ T cells have a more direct role in stopping replication of the hepatitis A virus by mechanisms that do not involve severe damage to the liver.

"This is quite an unusual discovery," said Dr. Walker, also a faculty member at The Ohio State University College of Medicine. "These findings document a previously unappreciated role for CD4+ T cells in resolving acute hepatitis A, and perhaps in surveillance against a relapse in virus growth and liver disease that sometimes occurs in those with weak immune systems, particularly the very young and old."

If CD4+ T cells are found to play a similar role in humans, they could serve as a new target for preventing relapse of hepatitis A virus infection. An inefficient helper T cell response might explain why some patients relapse after clearing the infection.

"If CD4+ T cells have an immune surveillance function, as suggested by our findings, patients at greatest risk of relapsing liver disease may benefit from a vaccine that would boost helper T cell activity until the virus is finally cleared from the liver," said Dr. Walker.

Provided by Nationwide Children's Hospital