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## **American Liver Foundation Research Award: Role of the Innate and Adaptive Immune System in the Pathogenesis of Acute and Chronic Hepatitis B-Induced Liver Injury**

by Jody Lynn Baron, MD, PhD

The immune system serves to rid our bodies of infectious disease and to prevent the recurrence of disease. In the past two decades, our understanding of the immune system has increased dramatically. In general, our immune system has two major components, each with specific functions. The first, the innate immune system, is rapidly mobilized to combat infection. The second, the adaptive immune system, is specific for each particular infection but takes days to weeks to generate. Our immune system, however, is not infallible and it is not infrequent that the immune response itself is responsible for causing the disease. This is the case for infection with human hepatitis B virus (HBV).

The scientific questions that our laboratory is addressing are: what are the immune mechanisms underlying chronic HBV infection, and how do these mechanisms differ from the immune mechanisms generated during successful viral clearance?

Hepatitis B virus is a virus that causes acute and chronic liver injury (hepatitis). Although the majority of adults infected with HBV generate an effective immune response that allows the body to rid itself of infection, 5% of infected adults cannot clear their bodies of infection. This chronic infection can lead to liver failure and liver cancer. **Failure to eliminate HBV from the body is an even more striking problem in infected newborns, who develop a chronic infection in as many as 90% of cases.** Because viral transmission from mother to child is common in highly populated areas of Asia and Africa, it is estimated that 300 million people throughout the world will have chronic HBV infections; yet, current treatments have limited effectiveness. **Hepatitis B virus itself does not cause the liver injury. It is the body's immune response to hepatitis B that is believed to be responsible for chronic infection, liver injury and liver cancer.**

It is thus important to be able to study this immune response to HBV in order to understand how the injury occurs and to develop effective treatment. However, study of the immune response to HBV has been limited, due to the lack of a good experimental system in which to study this immune response. Our laboratory has developed a new mouse model of acute and chronic hepatitis B infection that mimics human disease. With this model, we are able to address many of the important questions about both effective and destructive immune responses to hepatitis B virus. The model allows us to characterize different immune responses to the virus and to see what types of immune response help the body eliminate the virus, and what types of immune response lead to liver injury. For example, initial experiments have uncovered a novel immune response to HBV that causes an acute hepatitis and is mediated by the innate immune system; a role for the innate immune system in response to HBV was previously unsuspected. We are now in the process of characterizing this innate immune response to understand its role in both liver injury and in recovery from the virus. Experiments such as these will lead to a greater understanding of protective and destructive immune responses, and allow us to design treatments that can direct the immune system to rid the body of the virus without causing the disease itself.

*Dr. Baron is an Assistant Professor in the Division of Gastroenterology at the University of California, San Francisco. She received a \$150,000 Liver Scholar Award from the American Liver Foundation in 2004.*