

Our research is focused on investigating the mechanisms of RNA virus-host interaction, viral regulation of host immunity, and viral pathogenesis. We create and utilize small animal models and tissue culture systems for infection with RNA viruses such as influenza virus and lymphocytic choriomeningitis virus (LCMV). Our study should assist in the development of novel therapies including anti-viral drugs and immune therapeutics to remedy diseases caused by viral infections.

1. Influenza-host interaction: Influenza continues to threaten humans and remains a major worldwide health concern. Thus, identifying new therapeutic targets and understanding the mechanisms of host-virus interactions are important biomedical goals. The sphingolipids regulate diverse cellular conditions and display therapeutic potential in treating human diseases. We have found that sphingosine kinase that generates sphingosine 1-phosphate (S1P) promotes the replication of influenza virus. In contrast, S1P-degrading enzyme S1P lyase inhibits influenza viral propagation and virus-induced cytopathic effects. Thus, S1P-metabolizing enzymes are new therapeutic targets for the treatment of diseases caused by influenza virus infection. We are investigating the molecular mechanisms behind the phenomena. We are also interested in investigating influenza viral strategies to evade host innate immunity. Interferons (IFNs) are renowned as the most powerful of antiviral molecules, as they obstruct the replication of numerous viruses. We have found that influenza viral hemagglutinin protein induces degradation of type I IFN receptor and inhibit the antiviral IFN responses. The impact of this pathway on influenza and investigating the viral mechanism are the focus of our current study. The project could elucidate novel mechanisms by which influenza virus escapes the host immunity and help us design new therapeutics or advanced vaccine to control influenza.

2. Virus-induced immune suppression and viral persistence: LCMV Clone 13 suppresses host immune responses such as antiviral T cell immunity, which allows the virus to persist in mice. Therefore, LCMV Clone 13 infection represents an excellent model system for studying the interplay between chronic viral infections and host immunity. Our data suggest that the sphingolipid system plays an important role in virus-mediated immune suppression, viral immunopathology, and viral persistence. Thus, the study could enhance our understanding of sphingosine regulation of the host immunity to virus infection and provide the basis for developing immunotherapeutic approaches to terminate persistence of viruses such as human immunodeficiency virus and hepatitis C virus in humans.