Molecules help the immune system to detect cells infected with West Nile virus

February 5 2009

New research reveals a model of host-pathogen interaction that explains how the immune system finds and destroys cells infected with a potentially lethal brain virus. The study, published online on February 5th in *Immunity*, a Cell Press publication, may lead to new treatments for West Nile virus (WNV) and other similar viral infections.

WNV is a single-stranded (ss)RNA virus that is the most common cause of viral inflammation of the brain (encephalitis) in North America, and it has emerged as a significant worldwide public health concern. Infection with the virus, which is spread by mosquitoes, is often asymptomatic but can lead to a potentially fatal inflammation of the brain. "An approved therapy for use in humans does not currently exist, and viral pathogenesis is incompletely understood," says senior study author Dr. Richard A. Flavell from the Yale University School of Medicine.

Dr. Flavell and colleagues had previously shown that Toll-like receptor 7 (TLR7), a molecule known to play an important role in innate immunity (the body's first line of defense against infection), is involved in helping the immune system to recognize ssRNA viruses. His team sought to demonstrate a functional role for TLR7 in the control of WNV infection.

The researchers examined WNV infection in mice lacking either TLR7 or MyD88, an adaptor molecule used by TLR7 for detecting infection with a ssRNA virus. Mice lacking TLR7 or MyD88 exhibited increased

susceptibility to lethal WNV encephalitis. The mice had increased levels of WNV and, unexpectedly, increased levels of most of the innate immune system chemicals that are thought to be critical for host anti-viral immunity.

In contrast, mice lacking TLR7 or MyD88 had reduced levels of other key chemicals, including interleukin-23 (IL-23). Additional studies revealed that macrophages, immune cells that ingest and kill virus-infected cells, failed to home to WNV-infected cells in mice lacking TLR7. This suggests that TLR7 and IL-23-dependent WNV responses play a critical role in the ability of the host innate immune system to locate infected cells.

" Taken together, our results show that TLR7 is a critical host sensor of WNV required for IL-23-dependent immune cell homing to infected target cells, and they suggest that pharmacotherapy aimed at promoting TLR7/IL-23 signaling will be beneficial for treatment of WNV and perhaps other viruses that cause encephalitis," concludes Dr. Flavell.

Source: Cell Press