My laboratory studies the pathogenesis of neurotropic viruses, herpes simplex virus (HSV) and enterovirus 71 (EV71). HSV-1 infection is the most common cause of sporadic, fatal encephalitis, but current understanding of how the virus interacts with cellular factors to regulate disease progression is limited. In our recent work published in the *Journal of Clinical Investigation*, we show that HSV-1 infection induced the expression of the cellular transcription factor, early growth response 1 (Egr-1). Egr-1 increased viral replication by activating promoters of viral productive cycle genes through binding to its corresponding sequences in the viral promoters. Furthermore, Egr-1 deficiency or knockdown of *Egr-1* by a DNA-based enzyme greatly reduced the mortality of HSV-infected mice by decreasing viral loads in tissues. This study provide the first evidence that Egr-1 increases the mortality of HSV-1 encephalitis by enhancing viral replication. Moreover, blocking this cellular machinery exploited by the virus could prevent host mortality.

EV71 infects the central nervous system and causes death and long-term neurological sequelae in hundreds of thousands of young children, but its pathogenesis remains elusive. In our recent work published in the *Journal of Virology*, we show that virus and three types of lymphocytes, B cells, CD4 T cells, and CD8 T cells are detected in the spinal cord of an EV71-infected patient who died. Our mouse studies show that the levels of virus and lymphocytes in brains and antibody titers in sera were elevated while the infected mice succumbed to death in a phenomenon analogous to that observed in patients. We also demonstrated that after infection, the disease severity, mortality, and tissue viral loads of mice deficient in B, CD4 T, or CD8 T cells were increased. In addition, treatment with a virus-specific antibody, but not a control antibody, before or after infection significantly reduced the disease severity, mortality, and tissue viral loads of mice deficient in B cells. Our results show that both lymphocyte and antibody responses protect mice from EV71 infection.

**Selected Publications**