A hallmark property of the neurotropic herpesviruses is the dissemination of infection following initial exposure of mucosal surfaces to sensory and autonomic ganglia of the peripheral nervous system. The peripheral ganglia serve as the latent virus reservoir and the source of recurrent infections. However, the means by which these viruses routinely invade the nervous system is poorly established. In this lecture, recent findings will be presented that identify neuroinvasive effectors encoded by pseudorabies virus, an alpha-herpesvirus native to swine that is noted for its propensity to cause encephalitic zoonotic infections. These studies are beginning to define the cellular and molecular events that are coordinated by the virus to achieve their remarkable infectious cycle, and how vaccines can be designed to effectively block infection.