

## **Identification of Varicella Zoster virus tissue-tropic genes for developing a neuroattenuated vaccine against chickenpox and shingles**

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Varicella zoster virus (VZV) is the causative agent of varicella (chickenpox) and herpes zoster (shingles). After primary infection, VZV establishes latent infection in sensory ganglia, and reactivates upon weakening of the immune system due to various conditions, resulting in a productive infection of sensory neurons and the surrounding skin tissue. However, little is known about the molecular basis of VZV latency and reactivation. In our previous work, we employed a VZV bacterial artificial chromosome system containing a green-fluorescent protein and a luciferase marker (VZV BAC luc) in conjunction with live bioluminescence imaging to create and characterize a comprehensive library of VZV single open reading frame (ORF) deletion mutants. We reported three VZV gene categories based on their requirement for viral replication in melanoma cells: essential (44 ORFs), non-essential with severe growth defects (8 ORFs) and fully dispensable (18 ORFs). We postulated that the latter category is comprised of elements responsible for specific tissue tropism. We now demonstrate that ORF7 is required for VZV replication in xenografts of human skin and dorsal root ganglia (DRG) in a severe combined immunodeficiency (SCID) mouse model. The ORF7 protein is a virion component and localizes to the Golgi compartment in infected cells. Loss of ORF7 function in the VZV mutant may serve the basis for the development of a new neuroattenuated varicella vaccine. Our studies also demonstrate the potential utility of this VZV replicating expression vector to develop recombinant vaccines against other important microbial pathogens such as HIV.

### **Biography**

Hua Zhu has completed his Ph.D. from Columbia University and postdoctoral studies from Princeton University. He has been working on human cytomegalovirus and varicella zoster virus for most 20 years. He has published more than 40 research papers, review articles and book chapters, and serving as an Editor-in-chief of Journal of Antivirals & Antiretrovirals.

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