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Role of ORF 7 in varicella-zoster virus tissue tropism and potential for novel vaccine

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A fter the primary infection, varicella-zoster virus (VZV) remains latent in sensory ganglia and reactivates upon weakening of the immune system, erupting from sensory neurons and infecting surrounding skin tissue. The factors involved in neuronal invasion and establishment of latency are still elusive. In our previous work, we employed a VZV BAC system in order to characterize a comprehensive library of VZV single ORF deletion mutants. We reported 18 ORFs to be fully dispensable in melanoma cells, which we postulated to encode elements responsible for specific tissue tropism. We now, demonstrate that screening of these 18 dispensable gene mutants in differentiated neurons led to the identification of ORF7 as a neurotropic factor. This finding adds to our previous report that ORF7 is also a skin tropic factor. ORF7 is a virion component localized to the Golgi compartment in infected cells, whose deletion causes loss of poly-karyon formation *in vitro* and severely impairs viral spread in human nervous tissue *ex vivo*. Interactions between ORF7 and other virion proteins are under investigation. Furthermore, ORF7 is required for VZV replication in xenografts of human skin and dorsal root ganglia in a SCID-hu mouse model. Here we show that an ORF7 deletion virus is able to infect dendritic cells, which in turn can infect T cells. This unique set of characteristics lends an ORF7 deletion mutant the potential to become an excellent VZV vaccine candidate. This neuroattenuated vaccine would cause neither the primary chickenpox nor the secondary herpes zoster diseases. Finally, given that ORF7 is essential for VZV initial infection of neurons and replication therein, it may also be a critical trigger of reactivation from latency.

Biography

Hua Zhu is an Associate Professor of Department of Microbiology, Biochemistry and Molecular Genetics, New Jersey Medical School, Rutgers University. He has received a PhD from the Columbia University, New York NY in 1993. He has completed his Postdoctoral training in herpes viruses in Princeton University, NJ in 1998. He is serving as an Editorial Board Member of the *Journal of Anti-virals and Anti-retrovirals* and Reviewer of 6 journals. He published over 60 research articles, reviews and book chapters.

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