Zika Virus Neurotropism and Vaccine Development

Professor Qin Cheng-Feng
Director and Professor
Department of Virology,
State Key Laboratory of Pathogen and Biosecurity,
Beijing Institute of Microbiology and Epidemiology,
Academy of Military Medical Sciences,
Beijing, China

Abstract
Zika virus (ZIKV) is a mosquito-transmitted flavivirus that has emerged as a global health threat since 2015. Based on the pregnancy mouse models, we demonstrated that ZIKV preferentially infects neural progenitor cells (NPC), causing cell death and reduced proliferation, which results in impaired brain development in the fetus. Further, we found a single serine to asparagine substitution (S139N) in the viral polyprotein substantially increased the tropism to human and mouse NPCs, led to more significant microcephaly, and higher mortality in neonatal mice. This functional adaption thus substantially contributes to the increased incidence of microcephaly in recent ZIKV epidemics. Furthermore, we developed a recombinant live-attenuated chimeric ZIKV vaccine candidate (termed ChinZIKV) that expresses the prM-E proteins of ZIKV using the licensed Japanese encephalitis live-attenuated vaccine SA14-14-2 as the genetic backbone. ChinZIKV retained its original tropism and genetic stability in vitro, whilst exhibiting an attenuation phenotype in multiple animal models. Remarkably, immunization of mice and rhesus macaques with a single dose of ChinZIKV elicits robust and long lasting immune responses and confers complete protection against ZIKV challenge in multiple animal models.


