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Rational design of live attenuated Enterovirus 71 vaccine by site-directed mutagenesis and deletion in the 5'-non coding region

The hand, foot and mouth disease (HFMD) is commonly caused by Enterovirus 71(EV-A71) and Coxsackieviruses. EV-A71 infection in young children produces fever, rashes and ulcers but some severe infections can lead to encephalitis, cardiopulmonary failure and even death. The lack of vaccines and antiviral drugs against EV-A71 highlights the urgency of developing preventive and treatment agents. The inactivated vaccine (IV) has been approved for production by the regulatory authority in China. Although the efficacy of the EV-A71 sub-genotype C4a vaccine was more than 90% against mild HFMD, there was only 80.4% efficacy against severe HFMD. The IV elicits only humoral immunity but lacks cellular immunity which is required for long term protection. This has necessitated the search for other vaccines such as viral like particles (VLPs) and live attenuated vaccines. In this study, rational design of the live attenuated EV-A71 was undertaken by substituting nucleotides at positions 158, 475, 487, 5262 and creating a 11 base pair deletion in the 5'NTR (PD mutant). Mutants 475, 486 and PD caused minimal cytopathic effects when compared to mutants 158, 486, and 5262 in Rhabdomyosarcoma (RD) cells. This was consistent with the viral RNA copy number and VP1 for mutants 475, 487 and PD being the lowest observed. A desirable live attenuated vaccine strain can be constructed bearing the 11bp deletion and mutation 487.

Biography

Chit Laa Poh completed her PhD at Monash University(Australia) in 1980 and conducted short periods of postdoctoral training from the Pasteur Institute, Cambridge University and the University College London. She is a Distinguished Professor and Head of the Centre for Biomedical Sciences at Sunway University. She has previously worked in the Yong Loo Lin School of Medicine , National University of Singapore (NUS) for 25 years. She has published more than 85 papers in reputed journals and has been serving as an editorial board member of Journal of Biosceince and Bioengineering, Austin Journal of Tropical Medicine and Hygeine, Journal of Virology and Emerging Diseases. And Annals of Translational Medicine and Epidemiology.

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