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MicroRNA reduction of enterovirus 71 viral replication attenuates and confers protective immune response in mice

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The hand, foot, and mouth disease (HFMD) is generally manifested as a subclinical infection, but fatal neurological complications can occur in young children. Epidemiological surveillance in China from 2008-2014 showed that 43.73% of HFMD cases were due to EV-A71. Up to date, there is no WHO-approved vaccine against EV-A71. This study demonstrated a novel miRNA vaccine construct for EV-A71 which decreased viral replication *in vitro*, whilst conferring a protective immune response in four-week old ICR mice. A vaccine construct was engineered to carry microRNA (miRNA) target sequences let-7a and miR-124a in the EV-A71 genome, allowing endogenous RNA silencing in specific cell types. The viral RNA copy number of the miRNA vaccine strain was much lower in RD (1.2×10^2) and SHSY-5Y cells (7.7 X 10) that expressed let-7a and miR-124a, respectively. The miRNA vaccine construct caused much reduction in plaque number (3.5×10^4 PFU/ml) in the SHSY-5Y cells as compared to the wild type virus (5.0×10^8 PFU/ml). No weight loss and hind limb paralysis were observed in the miRNA vaccine-administered mice (n=5) in comparison to the naïve group of mice (n=5). Significantly elevated systemic levels of IFN-γ and lower levels of pro-inflammatory cytokines TNF-α and IL-6 were detected. Higher $CD8^+$ T cell response was elicited by the miRNA vaccine strain in mice as compared to the inactivated vaccine. The miRNA vaccine construct was able to confer protective immunity against EV-A71 sub-genotypes B3, C3 and C4. Ten serial passage studies to determine the genetic stability of the target sequences let-7a and miR-124a showed that the sequences did not revert to wild type virulence. Overall, the miRNA vaccine construct is an effective attenuation strategy for vaccine development.

Biography

Dr. Chit Laa Poh is a Distinguished Professor and Head of the Centre for Biomedical Sciences at Sunway University. She 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 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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