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Development of Novel Live Attenuated Vaccine Against Enterovirus 71(EV-A71)

Chit Laa Poh¹, Kuan Onn Tan² and Pinn Tsin Isabel Yee¹

¹Research Centre for Biomedical Sciences, School of Science and Technology, Sunway University, Bandar Sunway, Kuala Lumpur, Selangor 47500, Malaysia;

²Department of Biological Sciences, School of Science and Technology, Sunway University, Bandar Sunway, Kuala Lumpur, Selangor 47500, Malaysia.

The hand, foot, and mouth disease (HFMD) is manifested as a mild illness but fatal neurological complications have been observed in young children. Enterovirus 71 (EV-A71) and other enteroviruses causing HFMD have led to over 7 million infections worldwide. With rising concern about the virulence of EV-A71, there is an urgent need for a vaccine against EV-A71. Several EV-A71 strains bearing single nucleotide (nt) mutations were constructed and the contribution of each mutation to virulence was evaluated. The nt(s) that contributed to reduction in virulence *in vitro* were selected and each mutation was individually introduced into the genome to construct the multiply mutated strain (MMS) which carried 6 substitutions of nt(s) at the 5'-NTR (U700C), VP1-E145G, VP1-98E, VP1-244K and G64R in the seed strain that had a partial deletion within the 5'-NTR region (nt. 475-485). A vaccine construct carrying miRNA let-7a and miR-124a target sequences in the EV-A71 genome was also designed. The ability of the MMS and miRNA constructs to act as vaccines in protecting mice against EV-A71 in challenge studies was evaluated. After 2 immunizations, the MMS and miRNA vaccines protected 2-week old ICR mice from weight loss and hind limb paralysis as compared to the PBS-injected mice. In addition, markedly elevated systemic levels of IFN- γ and lower levels of TNF- α /IL-6 were detected. ELISPOT results showed that the MMS demonstrated the highest amount of IFN- γ , indicative that this construct elicits the highest CD8+ T cell response. The MMS is a promising candidate as a vaccine against fatal EV-A71.

Biography

Poh Chit Laa was an instrumental in setting up the Programme of BSc(Hons)Biology with Psychology, taking into account the strength of staff from the Department of Psychology with newly appointed staff in the new Department of Biological Sciences. She has also completed the setting up of a second programme- BSc (Hons) Medical Biotechnology. Currently, she is working with the HOD of the Department of Biological Sciences to develop a PhD Programme in Life Sciences. Her MSc in Life Sciences programme had received approval from Malaysian Ministry of Education.

Mail Id: pohcl@sunway.edu.my

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