**Title: Human SCARB2 Acts as a Cellular Co-receptor for Helping HFMD PathogensInfection Vaccine**

Hand, Foot, and Mouth Disease (HFMD) and acute flaccid myelitis (AFM) are severe childhood infectious diseases. HFMD is caused by various pathogens, with Coxsackie virus A10 (CVA10) being one of them. However, it rarely causes severe neurological symptoms in children. The lack of a reliable animal model is a challenge in studying the manifestations of human diseases caused by CVA10, and current clinical treatments are limited to symptom relief. Recent study indicates that CVA10 does not use common enterovirus 17 (EV71) CVA16 receptor like human SCARB2 (hSCARB2, scavenger receptor class B, member 2), but uses other receptor such as kremen1 for infection. Objective, to determine the CVA10 infection pathophysiology and to evaluate the CVA10 infect and replicate in the mouse cells which expressing human SCARB2 (NIH3T3-SCARB2).. Methods, knock-downing of endogenous human SCARB2 or KREMEN1 by its specific siRNA was able to inhibit CVA10 infection in human RD cells. Immunoprecipitation result confirmed that hSCARB2 could physically interact with VP1 of CVA10 and KREMEN1..The viral challenge study in young-aged hSCARB2- transgenic mice and in wild type mice parallelly. Results, it resulted in severe hind limb paralysis syndromes accompanied with high mortality rate in hSCARB2- transgenic but not in wild type mice.  CVA10 viral loads were evident in the transgenic mice’s tissues from muscle, spinal cord, and brainstem. Transgenic mice pre-immunized with the formalin-inactivated CVA10 vaccine was able to resist the subsequent lethal challenge with CVA10 and reduce the severity of disease. The novelty in this study is a pioneer to report that hSCARB2 served as a co-receptor to help CVA10 cell infection. In addition, hSCARB2-transgenic mice are a useful model for assessing anti-CVA10 medications and for studying the pathogenesis induced by CVA10. Furthermore, utilized this mouse in tests for the AFM animal model and found that it can accurately replicate the pathological features of Enterovirus D68 (EVD68) virus-induced acute flaccid myelitis and other HFMD-pathogens including CVAs in human. In conclusion, applied this mouse to the development of a broad-spectrum hand, foot, and mouth disease (HFMD) vaccine and successfully demonstrated the protective efficacy of the broad-spectrum HFMD vaccine Ad-VLP, preventing fatal doses of EV71, CVA16, and CVA10 challenges in this mouse.