**Human SCARB2 Acts as a Cellular Coreceptor for helping HFMD pathogens infection**

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**ABSTRACT** (250-300 words)

**Hand, Foot, and Mouth Disease (HFMD) and acute flaccid myelitis (AFM) are severe childhood infectious diseases. HFMD is caused by various pathogens, with Coxsackievirus 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. We tried to discovery CVA10 infection mechanism and found that CVA10 could infect and replicate in the mouse cells which expressing human SCARB2 (NIH3T3-SCARB2) but not in parental NIH3T3 cells. 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. We previously generated a novel EV71-infectious model with hSCARB2-transgenic mice expressing the discovered receptor hSCARB2.We performed the viral challenge study in young-aged hSCARB2- transgenic mice and in wildtype mice parallelly. It resulted in severe hind limb paralysis syndromes accompanied with high mortality rate in hSCARB2- transgenic but not in wildtype 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, we have 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. We have 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. In the future, we will complete the exploration of the immune mechanisms of this vaccine and the development of other hand, foot, and mouth disease-related virus infection models.**

**BIOGRAPHY** (100-150 words)

* Dr. Shu-Ling Yu possesses specialized knowledge in virology and immunology related to animal experiments, along with a passion for improving health and preventing infections. She has dedicated many years to exploring HFMD and AFM animal models, as well as the broad-spectrum vaccine immune mechanisms. Leveraging her extensive research experience, she has established this model. Reinterpreting the function of the receptor hSCARB2 in virus infections opens a new avenue for research in the field of infection pathways.
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