**Natural killer T cells play a significant role in preventing Coxsackievirus A10 infection through an adeno-based vaccine expressing enterovirus-like particles**

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**Abstract:**

Enterovirus A71 (EV-A71) and coxsackievirus A (CVA) were the primary causative agents of hand, foot, and mouth disease (HFMD), the heightened occurrence of HFMD outbreaks associated with CVA10 worldwide has questioned this perspective. Due to the absence of an effective vaccine or antiviral treatment, HFMD caused by CVA10 has emerged as a significant global public health issue. We study a potent-valent vaccine based on adenovector expressing enterovirus A71 (EV-A71) viral like particle (AdVLP) which elicits a multivalence against not only EV71 but also other coxsackieviruses such as A10. In young-aged human scavenger receptor class B, member 2 –transgenic ((hSCARB2-Tg) mice received two-dose of vaccine following challenge with CVA10, AdVLP immunization significantly reduced muscle, spinal cord, and brain’s viral amounts and protected animal from disease occurrence. In contrast, massive CVA10 accumulated in these tissues that resulted in severe diseases and death in the control vector-received mice. Passive immunization of Tg mice with AdVLP-immunized serum after challenge with CVA10 confirmed that the antibodies present in the serum, while lacking neutralizing capabilities, demonstrated viral-binding activity and complement-dependent responses. These components were found to effectively protect against CVA10 infection in AdVLP-immunized serum. We also assess the efficacy of the formalin-inactivated CVA10 (FI-CVA10) vaccine against CVA10 infection, the FI-CVA10-immunized serum was shown to raise neutralizing antibodies and was subsequently tested in a passive immunization study to demonstrate its potency in preventing CVA10 infection. Notably, the results of passive immunization with AdVLP-immunized splenic lymphocytes versus invariant natural killer T (iNKT) cell-depleted lymphocytes in Tg mice before CVA10 challenge revealed a significant difference. Tg mice that passively received iNKT-depleted lymphocytes were nearly all deceased by day 8 post-challenge, whereas those receiving AdVLP-immunized lymphocytes exhibited a 100% survival rate. Conversely, Tg mice that passively received FI-CVA10-immunized splenic lymphocytes did not show resistance to CVA10 challenge, indicating that neutralizing antibodies rather than cellular immunity played a key role in protecting against CVA10 infection. In conclusion, AdVLP vaccine demonstrates multivalent efficacy against both EV71 and CV. AdVLP induces iNKT cells as well as antibody-mediated cellular responses, which serve as major protective mechanisms against CVA10 infection. The neutralizing antibodies induced by the traditional FI-CVA10 vaccine also plays a significant role in controlling CVA10 infection.

**What will audience learn from your presentation?**

* Enterovirus A71 (EV-A71) and coxsackievirus A (CVA) were the primary causative agents of hand, foot, and mouth disease (HFMD)
* A potent-valent vaccine based on adenovector expressing enterovirus A71 (EV-A71) viral like particle (AdVLP) which elicits a multivalence against not only EV71 but also other coxsackieviruses such as A10.
* AdVLP induces iNKT cells as well as antibody-mediated cellular responses, which serve as major protective mechanisms against CVA10 infection
* The neutralizing antibodies induced by the traditional FI-CVA10 vaccine induces the neutralizing antibodies to resist from CVA10 infection