

Poster presentation

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PI9-40. Different forms of a lentiviral glycoprotein presented by bivalent measles virus vaccines

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Background

Live attenuated vaccines against measles virus (MV) are among of the safest vaccines and elicit long-term immunity. Recombinant MVs that express foreign proteins at different levels elicit significant immune responses and protection against other pathogens in animal experiments. Interestingly, all but one candidate bivalent vaccine tested by several other groups expressed a soluble form of the foreign antigen. We ask here whether the soluble, membrane-bound or other forms of the antigen presented by recombinant MVs is critical for the quality and strength of the induced immune responses.

Methods

We report here the construction of soluble or stabilized (i.e. non-shedding) forms of the envelope (Env) glycoprotein of simian immunodeficiency virus SIV-smmPBj1.9, a model strain for acute virus pathogenesis. To this end, the Env protein was genetically truncated to express only the Env protein ectodomain or its protease cleavage site was modified to prevent cleavage and allow expression of gp160-Env.

Results

Bivalent recombinant MVs encoding different forms and levels of the SIVsmmPBj1.9 Env protein(s) were rescued, successfully tested for SIV Env expression, and shown to retain similar growth rates as parental MV with titers of up to 1×10^8 TCID₅₀/ml. These bivalent vaccines were inoculated twice intraperitoneally in a prime-boost protocol setting into transgenic IFNARko-CD46Ge mice (1×10^5 TCID₅₀/dose). Transgenic CD46 expression allows MV

replication in the murine cells of these mice in vivo. We are measuring the quality of the cellular and humoral immune responses to different forms and amounts of the SIV-smmPBj1.9 Env proteins presented by MV in mice.

Conclusion

These studies will be used to select optimal candidate bivalent MV-SIV vaccines for the analysis of the immune response and levels of protection in monkeys.