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## PREVENTION OF FOOT-AND-MOUTH DISEASE IN CATTLE USING A PRIME-BOOST-VACCINATION STRATEGY

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Foot-and-mouth disease (FMD) is one of the most economically important infectious diseases of production animals globally. Vaccination can help to control this disease, however, current vaccines are imperfect. They are made using chemically inactivated FMD virus (FMDV) that is produced in mammalian cell culture under high containment. Here, we have expressed the FMDV capsid protein precursor (P1-2A) of strain O1 Manisa alone or with the FMDV 3C protease (3C<sup>pro</sup>) using a “single cycle” packaged alphavirus self-replicating RNA based on Semliki Forest virus (SFV). When the FMDV P1-2A was expressed with 3C<sup>pro</sup> then processing of the FMDV capsid precursor protein is observed within cells and the proteins assemble into empty capsid particles. In cattle vaccinated once with these rSFV-FMDV vectors alone, anti-FMDV antibodies were elicited but the immune response was insufficient to give protection against FMDV challenge. However, the prior vaccination with these vectors resulted in a much stronger immune response against FMDV post-challenge and the viremia observed was decreased in level and duration. In subsequent experiments, cattle were sequentially vaccinated with a rSFV-FMDV followed by recombinant FMDV empty

capsid particles, or *vice versa*, prior to challenge. Animals given a primary vaccination with the rSFV-FMDV vector and then boosted with FMDV empty capsids showed a strong anti-FMDV antibody response prior to challenge. Following challenge with FMDV, the cattle were protected against disease and no FMDV RNA was detected in their sera. Initial inoculation with empty capsids followed by the rSFV-FMDV was much less effective at combating the FMDV challenge and a large post-challenge boost to the level of anti-FMDV antibodies was observed and clinical disease occurred. This prime-boost system, using reagents that can be generated outside of high-containment facilities, offers significant advantages to achieve control of FMD by vaccination.