Research Project: Foot-and-Mouth Disease Virus (Fmdv) Countermeasures Discovery

Title: Adenoviral-Based Foot-and-Mouth Disease Virus Vaccine: Effect of Duration of Antigen Expression on Immunogenicity in Swine

Authors:

- Dias, Camila - USDA, PIADC ORISE FELLOW
- Moraes, Mauro
- Koster, Marla
- Grubman, Marvin

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Technical Abstract: An adenoviral (Ad5)-based foot-and-mouth disease virus (FMDV) subunit vaccine, Ad5-A24, is an effective alternative to the current inactivated whole virus vaccine and has a number of advantages including no requirement for infectious FMDV and DIVA (Differentiation of Infected from Vaccinated Animals) capability. Recently, we have also demonstrated that inclusion of the complete coding region of nonstructural protein 2B in the Ad5-A24 vector, Ad5CI-A24-2B, resulted in a more rapid immune response and improved protection in pigs. Nevertheless, the continuous development of this novel vaccine, to overcome high dose requirements and increase the duration of protection, is necessary. In order to address the above concerns, we have constructed a new vector containing two copies of the structural protein coding region of FMDV serotype A (A24 Cruzeiro) separated by an FMDV IRES region and followed by the 3C protease coding region, Ad5-A24-2X. This vector expressed equivalent amounts of structural proteins at 24 hours post Ad5 infection (hpi) in swine and bovine cell lines, but it resulted in reduced cytotoxicity at 48 hpi compared to the Ad5-A24 and Ad5CI-A24 vectors. We also evaluated the immunogenicity of these vectors in swine. Four groups containing 3 pigs per group were vaccinated with 5x10^9 pfu of Ad5-Blue ,Ad5-A24, Ad5- A24-2X and a group with a combination of 2.5x10^9 pfu Ad5- A24-2X plus 2.5x10^9 pfu Ad5CI-A24-2B. Animals were challenged with 10^5 TCID v50 of FMDV A24 at 21 days postvaccination (dpv). All animals were protected, except those that received Ad5-Blue. There were significant differences in the levels of FMDV-specific neutralizing antibodies at 4, 7 and 21 dpv in the group receiving the Ad5 vector combination compared to the Ad5-A24-2X group. The combination group also induced an earlier production of IgG1 and IgG2, but at the day of challenge, the Ad5-A24-2X group showed the highest levels of IgG1 and IgG2. Another promising observation was the sustained levels ofFMDV-specific neutralizing antibodies in the combination group.