MVA-NS1 vaccine candidate confers protection in IFNAR (-/-) mice against a homologous challenge with EHDV-8

Alejandro Carra-Valenzuela*, Luis Jiménez-Cabello, Iván Belinchón-Esteban, Iván Mazuecos-Aragonés, Sergio Utrilla-Trigo, Javier Ortego, Eva Calvo-Pinilla
Centro de Investigación en Sanidad Animal, INIA-CSIC, Valdeolmos, 28130 Madrid, Spain.
*alejandro.carra@inia.csic.es

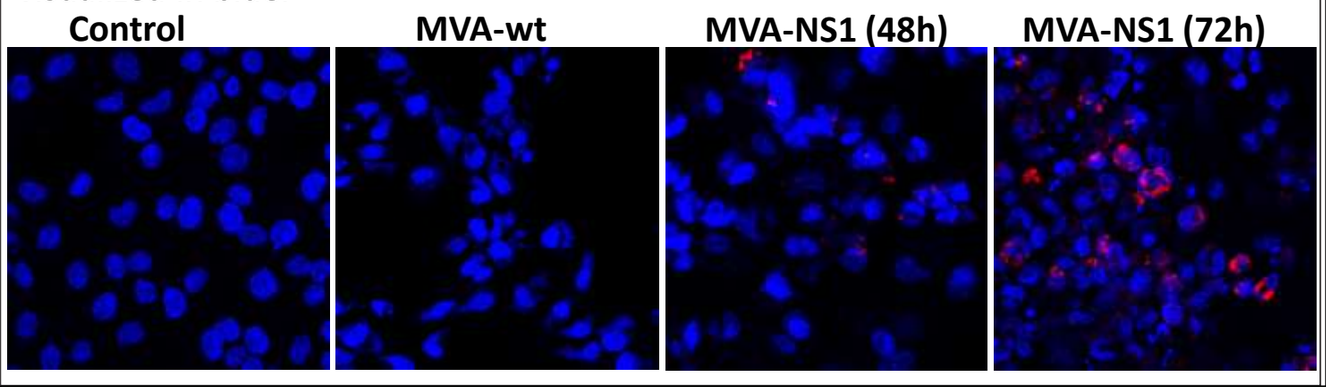
SUMMARY

Vaccination campaigns are an effective tool to control and prevent infections and diseases caused by Orbivirus, such as Bluetongue (BTV) or Epizootic hemorrhagic disease virus (EHDV). Both virus affects wild and domestic ruminants and causes important economic losses in livestock industry. In this study, we designed and generated a novel vaccine candidate against EHDV based on recombinant MVAs that express the non-structural protein NS1 from EHDV serotype 8. We confirmed the potential of this vaccination strategy in conferring robust protection against EHDV-8 in IFNAR (-/-) mice. Despite did not confer complete protection against a heterologous challenge with EHDV-6, it delayed the onset of clinical signs and death.

MATERIALS AND METHODS

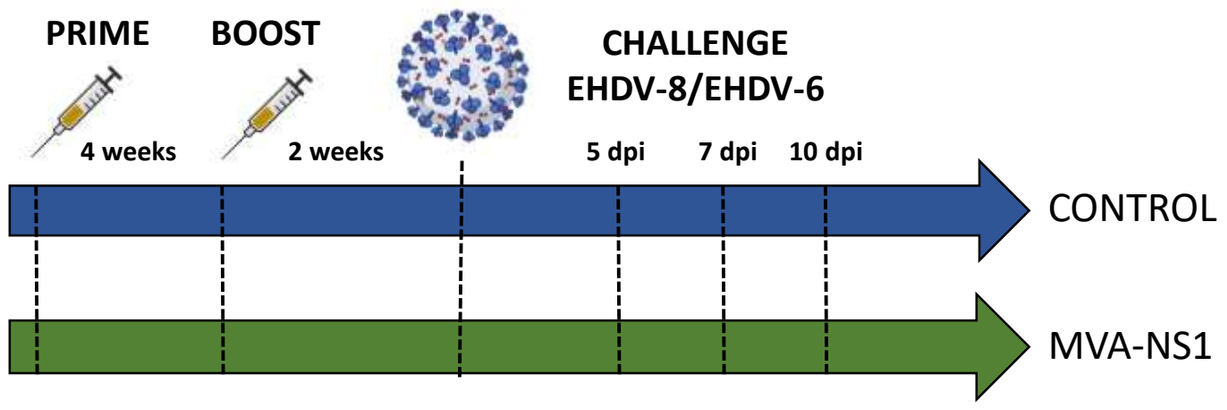
Generation of rMVA-NS1

We generated a recombinant MVA (Modified Vaccinia Ankara virus) that express the non-strcutural protein NS1 from EHDV-8. Recombinant virus was obtained by homologous recombination of NS1 gene in F13L locus of MVA. The efficient expression of the protein was confirmed by immunofluorescent assay (IFA) employing hyper immune sera from sheep infected with EHDV, and a anti-sheep IgG conjugated with Alexa Fluor 594. NS1 was correctly observed in red. Nuclei are visualized in blue.



Immunization of IFNAR (-/-) mice

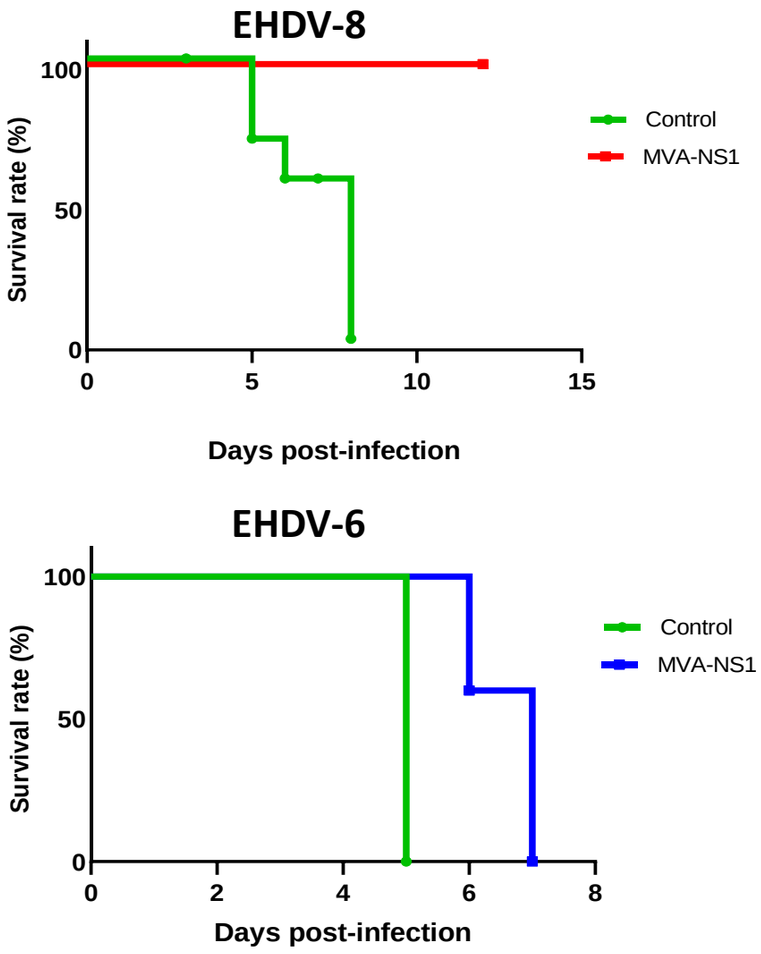
Groups of IFNAR(−/−) mice (*n* = 5) were immunized with two doses of MVA-NS1 (10^7 pfu/ml). Immunized and non-immunized mice were challenged with a lethal dose (100 PFU) of EHDV-8 or EHDV-6. In both cases, a group was non-immunized (control). Blood samples were collected at days 5, 7 and 10 post-infection to analyze viremia and mice were daily monitorized.



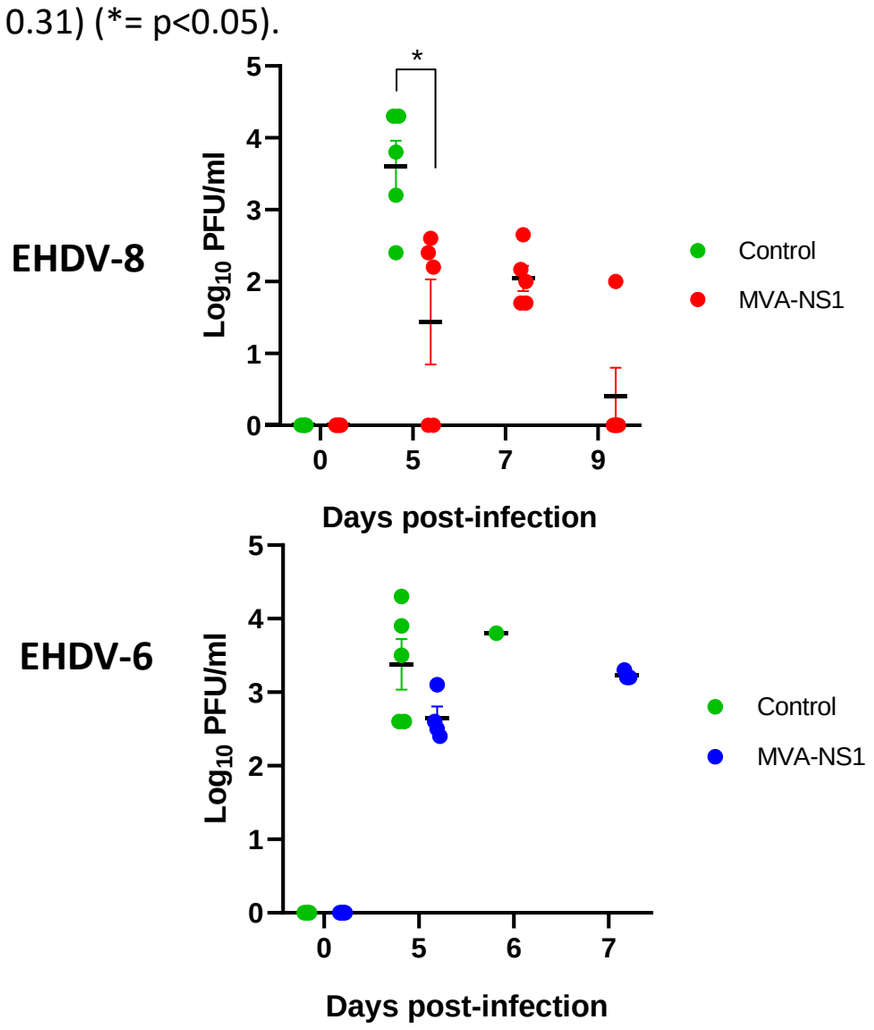
RESULTS

Protection against EHDV

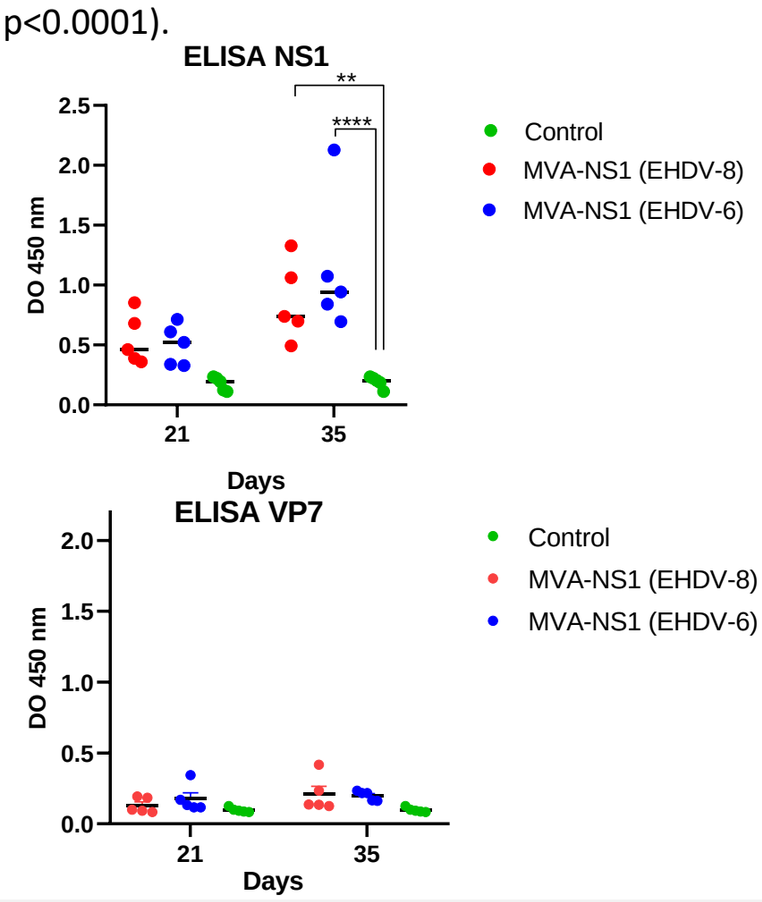
Control mice succumbed to infection against both EHDV challenges. Immunization with MVA-NS1 conferred a complete protection against a homologous challenge with EHDV-8 and delayed the onset of clinical signs and death in EHDV-6 challenge.



Control mice displayed high titers of infectious virus at day 5 post-challenge (mean value= 3.60 ± 0.80 $\log_{10}$PFU/ml) with EHDV-8. In contrast, mice immunized with MVA-NS1 showed a reduction in the titers of infectious virus (mean value =1.44 ± 1.32). In challenge with EHDV-6 the results are similar, with a mild reduction in vaccinated mice. Control (mean value= 3.38 ± 0.76) and vaccinated (2.65 ± 0.31) (*= p<0.05).



We analyzed the DIVA (Differentiating Infected from Vaccinated Animals) potential of our MVA-based vaccine candidate by an in-house ELISA test to detect antibodies specific of NS1 or VP7 proteins. We observed that after two doses of MVA-NS1, animals displayed significant antibody levels specific of NS1 but not specific of VP7. This confirm the DIVA characteristic of our vaccine. Non-immunized mice present basal levels. (**= p<0.01; ****= p<0.0001).



CONCLUSIONS

This study presents safe and adjuvant-free MVA-based vaccine candidates compatible with a DIVA strategy. The prime-boost immunization with MVA-NS1 confers full protection against a homologous challenge with EHDV-8, and controls partially the infection with an heterologous serotype. Future works will focus on the improvement of the vaccine to afford compete heterologous protection.

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