A RECOMBINANT APHTHOVIRUS CHIMERA OF THE GLYCOPROTEIN OF VESICULAR STOMATITIS VIRUS AS DNA AND PROTEIN-BASED VACCINE IN CATTLE

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SUMMARY

A chimeric construct conformed by:
- an in tandem-dimer insertion of the antigenic site A (ASA) of VP1 capsid protein of the foot-and-mouth disease virus C3 serotype (FMDV C3, aa 139-149)
- within aa160 and 161 of the vesicular stomatitis virus G protein (VSV-G) was able to display the appropriate ASA conformation/s to elicit anti FMDV-specific neutralizing immune responses in calves.

SUMMARY.

PEPTIDE-based FMDV VACCINES - Overview
- FMDV derived antigens administered as peptide vaccines were unable to induce significant humoral responses and protection in cattle even associated with foreign and FMDV-derived T cell epitope/s (Taboga et al. 1997; Rodriguez et al. 2003)
- However, a dendrimeric peptide containing VP1-ASA and FMDV T-cell epitopes conferred protection in swine (Cubillos et al. 2008)

Introduction (2/19)

1- Several aligned T cell epitopes might be required to induce humoral responses in cattle
2- ASA must be correctly exposed to preserve conformation
3- ASA must be presented as a repetitive motif

HYPOTHESIS

The correct display of epitopes that bind conformational-dependent-neutralizing antibodies aligned with bovine T cell epitopes can circumvent immunological limitations of peptide-based vaccines in cattle:
- difficulty to correctly expose conformational epitopes
- low T-cell induction due to highly polymorphic bovine MHC

RECOMBINANT IMMUNOGEN

VSV-NJ Glycoprotein

STRATEGY

Hypothetical construct conformed by:
- Long sequence
- Must expose Target sequence correctly
- Provide T cell epitopes

Target Constructs:
- Short sequence
- B-cell Epitope/s

Antigenic Site A - “ASA”, VP1 FMDV-C3, Tandem - dimer
Appendix 17

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Open Session of the EuFMD Research Group, Vienna (Austria) 29 September - 1 October 2010
Reactivity with conformational ASA

**WESTERN BLOT**

**IMMUNOPRECIPITATION**

**SERA FROM CHIMERA-VACCINATED ANIMALS STRONGLY REACT WITH WHOLE FMDV PARTICLES**

**FMDV-SPECIFIC ANTIBODIES MEASURED BY VNT and Liquid Phase Blocking ELISA**

**INDIVIDUAL ANIMALS SURPASS PROTECTIVE LEVELS OF ABs (EPP >80%)**

**CONCLUSIONS**

- T-cell epitopes in the chimeric construct could induce T-cell activation in whole blood samples from commercially-vaccinated animals.
- DNA-coded and baculovirus expressed forms of G-ASA induced strong humoral responses in cattle.
- Serum from all G-ASA vaccinated animals recognized conformational ASA in the native FMDV-140S particles.
- 3 out of 5 animals had EPP% values (LP ELISA) above 80% and all DEL-BAC immunized calves showed high serum IgG1 titers, with values comparable to those recorded for protection with inactivated vaccines.

**Reactivity with conformational VP1 epitopes**

**ELISA AGAINST WHOLE AND DENATURED VIRUS**

**SERA FROM CHIMERA-VACCINATED ANIMALS STRONGLY REACT WITH NATIVE FMDV**

**FMDV-specific IgG subtypes**

**CONCLUSIONS**

The association of the FMDV-C3/85 ASA as a tandem dimer to VSV-G N terminal sequence could circumvent limitations of FMDV peptide-based antigens as effective vaccines for bovines.

“New tools and challenges for progressive control”

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