Vaccine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Evaluation of protection induced by immunisation of domestic pigs with deletion mutant African swine fever virus BeninΔMGF by different doses and routes

Pedro J. Sánchez-Cordón [a,*], Tamara Jabbar [a], Margot Berrezaie [a], Dave Chapman [a,1], Ana Reis [a], Patricia Sastre [b], Paloma Rueda [b], Lynnette Goatley [a], Linda K. Dixon [a]

[a] The Pirbright Institute, Ash Road, Pirbright, Woking, Surrey GU24 0NF, UK
[b] Inmunología y Genética Aplicada S.A. (INGENASA), Hermanos García Noblejas, 39, 28037 Madrid, Spain

ARTICLE INFO

Article history:
Received 13 October 2017
Received in revised form 19 November 2017
Accepted 11 December 2017
Available online xxxx

Keywords:
African swine fever
BeninΔMGF
Pigs
Immunisation routes
Immunoglobulins
Cytokines

ABSTRACT

A live attenuated African swine fever virus (ASFV) vaccine candidate, produced by deletion of several genes belonging to multi-gene families MGF360 and 505 from virulent Benin 97/1 strain (BeninΔMGF), induces protection in pigs against parental virulent strain. In order to better define the safety and efficacy of this attenuated vaccine candidate and to understand protective mechanisms, we extended previous studies by intramuscular immunisation of pigs with the deletion mutant BeninΔMFG at different doses (10^2, 10^3, 10^4 $TCID_{50}$), together with intranasal immunisation at the 10^3 dose. Results demonstrated a strong correlation between both doses and routes of immunisation of BeninΔMFG and the percentage of protection achieved, the onset of clinical signs, the viremia levels reached and the onset of death in non-protected pigs. The results show that the intramuscular route using high doses (10^4 $TCID_{50}$) is the best option for immunisation. Only transient increase in temperature associated with a peak of virus genome levels was observed in most pigs after immunisation. Then, virus genome levels progressively decreased throughout the experiment until reaching low or undetectable levels in those protected pigs that survived after challenge. The IgM antibody responses following immunisation were detected between day 7–10 post-immunisation and remained at elevated levels for 10–18 days in most pigs before dropping. IgG was detected from day 15 to 21 post-immunisation and maintained at increased levels for the remainder of the experiment in most pigs. Induction of IFNγ and IL-10 was detected by ELISA in sera from some pigs immunised with 10^3 $TCID_{50}$ by intramuscular or intranasal route at early times post-immunisation. IL-10 was also detected in serum from some non-protected pigs included in these groups after challenge.

1. Introduction

African swine fever (ASF) is one of the most significant infectious diseases affecting the swine industry, with many isolates causing up to 100% lethality in domestic pigs. ASF is endemic in most sub-Saharan countries in Africa and in Sardinia. Since 2007 ASF has spread from Georgia in the Caucasus, to the Russian Federation and Eastern Europe including EU countries [1]. There is no vaccine for ASF and this limits disease control.

ASF is caused by a complex double-stranded DNA virus, African swine fever virus (ASFV), which encodes up to 167 genes [2,3]. Many genes encode proteins with roles in evasion of host defence's. Amongst these are proteins that inhibit type I interferon induction or responses including a TLR3 agonist, I329L, and members of MGF families 360 and 505/530 [4–6]. Levels of protection up to 100% against virulent virus challenge have been achieved by immunisation with attenuated ASFV. Deletion of multigene family members MGF 36-10L, 11L, 12L, 13L, 14L and 505/530 1R, 2R from the Pr4 isolate or MGF 360-12L, 13L, 14L and MGF 505/530 1R, 2R, 3R from the Georgia 2007 isolate [7] resulted in virus attenuation and induction of protection against challenge. We showed that deletion of these genes plus an additional deletion of MGF 505-3R and interruption of MGF 360-9L and MGF 505-4R from the Benin97/1 isolate (BeninΔMGF) also resulted in

* Corresponding author at: Pathology Department, Animal and Plant Health Agency (APHA-Weybridge), Woodham Lane, New Haw, Addlestone KT15 3NB, UK.
E-mail address: pedro.sanchez-cordon@pirbright.ac.uk (P.J. Sánchez-Cordón).
[1] Current address: Flu Manufacturing Sciences & Technology, MedImmune, AstraZeneca, 13 Renaissance Way, Boulevard Industry Park, Liverpool L24 9JW, UK.

https://doi.org/10.1016/j.vaccine.2017.12.030
0264-410X/