Veterinary Microbiology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Veterinary Microbiology

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

Evaluation of hydrophobic chitosan-based particulate formulations of porcine reproductive and respiratory syndrome virus vaccine candidate T cell antigens

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ARTICLE INFO

Article history:
Received 2 November 2016
Received in revised form 21 December 2016
Accepted 30 January 2017

Keywords:
Porcine reproductive and respiratory syndrome virus
Chitosan particles
Vaccine formulation
T cell

ABSTRACT

PRRS control is hampered by the inadequacies of existing vaccines to combat the extreme diversity of circulating viruses. Since immune clearance of PRRSV infection may not be dependent on the development of neutralising antibodies and the identification of broadly-neutralising antibody epitopes have proven elusive, we hypothesised that conserved T cell antigens represent potential candidates for development of a novel PRRS vaccine. Previously we had identified the M and NSP5 proteins as well-conserved targets of polyfunctional CD8 and CD4 T cells. To assess their vaccine potential, peptides representing M and NSP5 were encapsulated in hydrophobically-modified chitosan particles adjuvanted by incorporation of a synthetic multi-TLR2/TLR7 agonist and coated with a model B cell PRRSV antigen. For comparison, empty particles and adjuvanted particles encapsulating inactivated PRRSV-1 were prepared. Vaccination with the particulate formulations induced antigen-specific antibody responses, which were most pronounced following booster immunisation. M and NSP5-specific CD4, but not CD8, T cell IFN-γ reactivity was measurable following the booster immunisation in a proportion of animals vaccinated with peptide-loaded particles. Upon challenge, CD4 and CD8 T cell reactivity was detected in all groups, with the greatest responses being detected in the peptide vaccinated group but with limited evidence of an enhanced control of viraemia. Analysis of the lungs during the resolution of infection showed significant M/NSP5 specific IFN-γ responses from CD8 rather than CD4 T cells. Vaccine primed CD8 T cell responses may therefore be required for protection and future work should focus on enhancing the cross-presentation of M/NSP5 to CD8 T cells.

1. Introduction

Porcine reproductive and respiratory syndrome (PRRS) is one of the most important pig diseases worldwide. The causative PRRS virus (PRRSV) is rapidly evolving and there is an urgent need for the development of safer and more efficacious vaccines to improve PRRS control. Efforts to develop improved vaccines have focused primarily on the structural envelope glycoproteins but these have met with limited success and thus alternative approaches are required (Murtaugh and Genzow, 2011; Renukaradhya et al., 2015). While the immunological mechanisms underlying protection against PRRSV remain to be fully defined, there is evidence to suggest that cell-mediated immune responses play an important role (Murtaugh and Genzow, 2011; Zuckermann et al., 2007). Indeed, T cells are crucial to the control of many viruses through cytolysis of infected cells and cytokine secretion. Since clearance of PRRSV infection may not be dependent on neutralising antibodies, we hypothesised that conserved PRRSV T cell antigens should be

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http://dx.doi.org/10.1016/j.vetmic.2017.01.037
0378-1135/