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Protection of European domestic pigs from virulent African isolates of African swine fever virus by experimental immunisation

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ABSTRACT

African swine fever (ASF) is an acute haemorrhagic disease of domestic pigs for which there is currently no vaccine. We showed that experimental immunisation of pigs with the non-virulent OURT88/3 genotype I isolate from Portugal followed by the closely related virulent OURT88/1 genotype I isolate could confer protection against challenge with virulent isolates from Africa including the genotype I Benin 97/1 isolate and genotype X Uganda 1965 isolate. This immunisation strategy protected most pigs challenged with either Benin or Uganda from both disease and viraemia. Cross-protection was correlated with the ability of different ASFV isolates to stimulate immune lymphocytes from the OURT88/3 and OURT88/1 immunised pigs.

1. Introduction

African swine fever (ASF) is a highly contagious, haemorrhagic disease of pigs caused by a large, cytoplasmic, icosahedral DNA virus (ASFV) with a genome size of 170–193 kbp. Virulent isolates kill domestic pigs within 7–10 days of infection. In chronic cases ASF causes respiratory disorders and in some cases swelling around the leg joints and skin lesions. Domestic pigs can survive infection with less virulent isolates and in doing so can gain immunity to subsequent challenge with related virulent viruses [1–5].

ASF is endemic in many sub-Saharan African countries as well as in Sardinia. In 2007 ASF was introduced into Georgia and from there spread rapidly to neighbouring countries in the Trans Caucasus region, including Southern European Russia [6]. The virus has continued to spread through the Russian Federation and 18 federal subjects have reported outbreaks (OIE WAHID). Virus has also been isolated a number of times from wild boar in this region and the presence of ASF in this wildlife population is likely to make eradication more difficult [6].

Genotyping of ASFV isolates by partial sequencing of the B646L gene encoding the major capsid protein p72 has identified up to 22 genotypes [7,8]. Many of these are circulating in the long-established sylvatic cycle involving soft ticks of *Ornithodoros* spp. and warthogs in eastern and southern Africa. In many regions the isolates circulating in domestic pigs are genetically more similar.

Previous work has shown that pigs are protected from challenge with related virulent isolates following infection with natural low virulence isolates and with virus attenuated by passage in tissue culture or by deletion of genes involved in virulence [2,3,9,10]. Protection induced by the non-virulent OURT88/3 isolate was shown to require $CD8^+$ T cells since depletion of these cells was shown to abrogate this protection [11]. Passive transfer of antibodies from pigs protected following infection with lower virulence isolates was also shown to protect naïve pigs from challenge with related virulent virus [12]. Although they are effective in inducing protection, there are safety issues related to the release of attenuated live vaccines. For example, following the introduction of ASF to Spain and Portugal in 1960, field isolate viruses were serially passed through primary bone marrow or blood macrophage cell cultures and then used to vaccinate pigs in Spain and Portugal. A substantial proportion of the half million pigs vaccinated in Portugal developed unacceptable post-vaccination reactions, including death [13]. In addition, a large number of carrier animals were generated, hin-

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