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Protective efficacy of a high-growth reassortant H1N1 influenza virus vaccine against the European Avian-like H1N1 swine influenza virus in mice and pigs

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ABSTRACT

Swine influenza A viruses (SIVs) causing outbreaks of acute, highly contagious respiratory disease in pigs also pose a potential threat to public health. European avian-like H1N1 (EA H1N1) SIVs are the predominant circulating viruses in pigs in China and also occasionally cause human infection. In this study, a high-growth reassortant virus (SH1/PR8), with HA and NA genes from a representative EA H1N1 isolate A/Swine/Shanghai/1/2014 (SH1) in China and six internal genes from the high-growth A/Puerto Rico/8/34 (PR8) virus, was generated by plasmid-based reverse genetics and tested as a candidate seed virus for the preparation of inactivated vaccine. The protective efficacy of inactivated SH1/PR8 was evaluated in mice and pigs challenged with wild-type SH1 virus. After primer and boost vaccination, the SH1/PR8 vaccine induced high-level hemagglutination inhibiting (HI) antibodies, IgG antibodies, and neutralization antibodies in mice and pigs. Mice and pigs in the vaccinated group showed less clinical phenomena and pathological changes than those in the unvaccinated group. In conclusion, the inactivated high-growth reassortant vaccine SH1/PR8 could induce high antibody levels and complete protection is expected against SH1 wild type SIV, and protection against heterologous EA H1N1 SIV needs further evaluation.

1. Introduction

Swine influenza (SI) is an economically important infectious disease in swine populations and leads to fever, sneezing, coughing, labored breathing, and bacterial/viral secondary infections. H1N1, H1N2 and H3N2 subtype swine influenza A viruses (SIVs) have been widely reported in pigs frequently associated with clinical disease (Brown, 2000; Kumar et al., 2011; Vincent et al., 2008), and these viruses have remained largely endemic in swine populations worldwide and cause one of the most epidemic respiratory disorders. Since porcine respiratory tract cells possess both avian influenza virus receptor and mammalian influenza virus receptor, pigs have been considered to be a “mixing vessel” for occurring potential influenza virus reassortment derived from different host species (Ma et al., 2010; Neumann et al., 2009). For instance, a unique reassortment of SIVs of North American and Eurasian lineages circulating in the domestic swine populations might be responsible for the emergence of the 2009 novel pandemic influenza H1N1(pH1N1) virus that caused public concern.

SI was first observed in 1918 in US, Hungary, and China. The classical H1N1 subtype swine influenza virus (SIV), isolated in the USA in 1930 (Shope, 1931; Webster, 2002), is thought to be a descendant of 1918 pandemic influenza virus. Since 1979, the dominant H1N1 SIVs circulating in Europe have become ‘avian-like’ H1N1 viruses which are antigenically and genetically distinguishable from the classical H1N1 SIVs (Dunham et al., 2009; Scholtissek et al., 1983), but are related closely to H1N1 viruses isolated from ducks. These European avian-like

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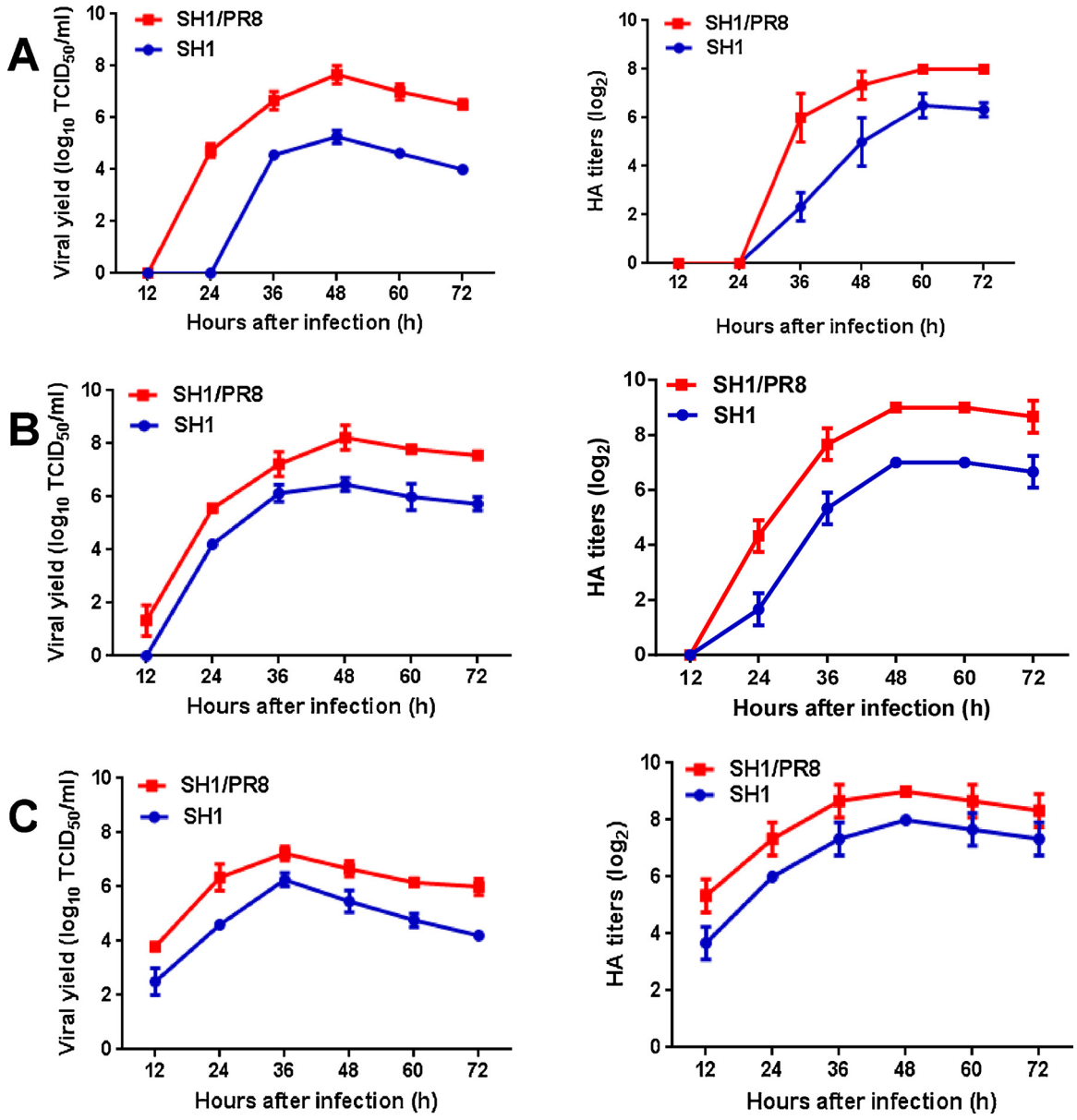

Fig. 1. Growth properties of SH1/PR8 virus and SH1 virus in MDCK cells. MDCK cells were inoculated with reassortant virus SH1/PR8 and wild-type virus SH1 at an MOI of 0.0001 (A), 0.001 (B), 0.01 (C). The HA titers and $TCID_{50}$ were determined at 12, 24, 36, 48, 60 and 72 h post-infection. Each value is shown as the mean of three independent experiments performed in triplicates; standard deviations (SDs) are indicated by the error bars.

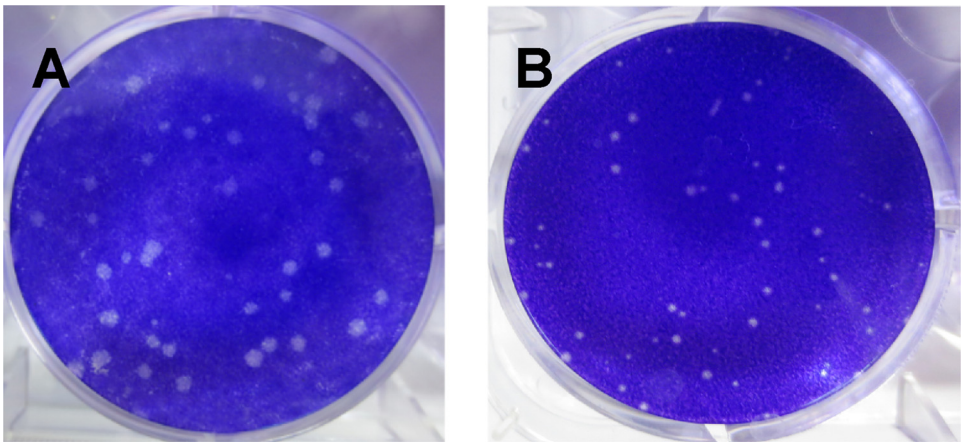

Fig. 2. Plaque size in MDCK cells at 48 h post-infection. The replication abilities of reassortant virus SH1/PR8 (A) and wild-type virus SH1 (B) were determined by plaque assays in MDCK cells.