A seven-gene-deleted African swine fever virus is safe and effective vaccine in pigs

16 March 2020

African swine fever (ASF) is a devastating infectious disease in swine and has been catastrophic for the global pig industry. In 2018, ASFV was transmitted to pigs in China and ten other Asian countries, which damaged the pork industry in these areas. The fact demonstrates that ASF is hard to control only by culling infected pigs in China, and the development and application of an efficacious vaccine is urgently needed. Different vaccine strategies for ASF have been evaluated in past decades. Some gene-deleted attenuated ASFVs—but not Inactivated vaccines, DNA vaccines, subunit vaccines, and adenovirus-vectored vaccines—have shown potential as ASF vaccines, while it is not known if they could convert to more virulent strains during their replication in pigs. In the present study, Chen and his colleagues used the Chinese ASFV HLJ/18 as a backbone and generated a series of gene-deleted viruses, and demonstrated that HLJ/-18-7GD (genes encoding MGF505-1R, MGF505-2R, MGF505-3R, MGF360-12L, MGF360-13L, MGF360-14L, and CD2v deleted) is a safe and effective vaccine against ASFV.

The biggest concern with a live attenuated vaccine is whether the vaccine seed virus could convert to a virulent strain during replication in vaccinated animals. To evaluate the biosafety of HLJ/18-7GD, groups of SPF pigs were intramuscularly inoculated with a 100-fold vaccine dose of HLJ/18-7GD and observed for 21 days. Blood samples were collected from the pigs on days 5, 10, and 15 p.i. and spleen and lymph nodes were collected from each pig euthanized on day 21 p.i. to detect viral DNA by qPCR. Viral DNA was not detected in any samples collected. All pigs survived without any ASF clinical signs during the three-week observation period. The authors blindly passed the viral DNA-negative blood of the HLJ/18-7GD-inoculated pigs for four more passages, but viral DNA was not detected in any samples collected from these pigs.

To further investigate the replication of HLJ/18-7GD in pigs, 14 seven-week-old SPF pigs were inoculated with a limit dose (500-fold vaccine dose) of the virus, and two pigs were euthanized on days 2, 5, 8, 10, 12, 16, and 21 p.i., respectively. The blood and organs of these pigs were collected for viral DNA detection. Viral DNA was detected in some lymph nodes of one or two pigs that were euthanized on days 5, 8, 10, 12, and 16 p.i.. The lymph nodes that had the highest viral DNA copies were homogenized and inoculated into four more pigs, and viral DNA was detected in two lymph nodes of one pig that was euthanized on day 10 p.i.. The virus was not detected in any subsequent pigs inoculated with the viral DNA-positive lymph node homogenates. These results indicate that, after intramuscular injection, the HLJ/18-7GD virus is only maintained for a short period in certain lymph nodes of pigs, and does not appear in the blood or any other organs of pigs; therefore, HLJ/18-7GD is highly unlikely to convert to a virulent strain during its replication in pigs.
Chen and his colleagues then evaluated the protective efficacy of HLJ/18-7GD in clean commercial pigs with intramuscular and oral challenge, respectively, as the oral route is how pigs are mainly infected with ASFV in nature. All of the results demonstrated that HLJ/18-7GD provides similar protection in both farmed and SPF pigs. To evaluate the long-term protection of HLJ/18-7GD, a group of pigs were vaccinated once with a 10-fold vaccine dose and challenged the pigs at 10 weeks post-vaccination. These results showed that the long-lasting immunity induced by a single 10-fold vaccine dose of HLJ/18-7GD could provide solid protection against lethal ASFV challenge, which suggests that two administrations of HLJ/18-7GD with the same high dose could protect pigs for their entire lives.

Chen and his colleagues also evaluated the safety of HLJ/18-7GD in pregnant sows, and found that all primiparous sows at different pregnant stages inoculated with a 10-fold vaccine dose of HLJ/18-7GD remained healthy and delivered their piglets on the expected dates, indicating that inoculation with HLJ/18-7GD will not cause disease or abortion in pregnant sows or affect the health of the piglets.

The HLJ/18-7GD does not grow in any cell lines, which means that the vaccine must be produced in primary cells. HLJ/18-7GD grows well in porcine bone marrow cells (PBMs) and at least 200,000 doses of vaccine could be produced from PBMs derived from one piglet. Therefore, using these primary cells for large-scale production of HLJ/18-7GD is feasible and cost-effective.

These important results confidently presented the evidence that HLJ/18-7GD is safe and effective as a live attenuated vaccine in pigs, Science China Life Sciences (2020). DOI: 10.1007/s11427-020-1657-9


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