

Construction of a Bartha-K61-like vaccine using the CRISPR/Cas9 method confers complete protective immunity against emerging PRV variant challenge in piglets

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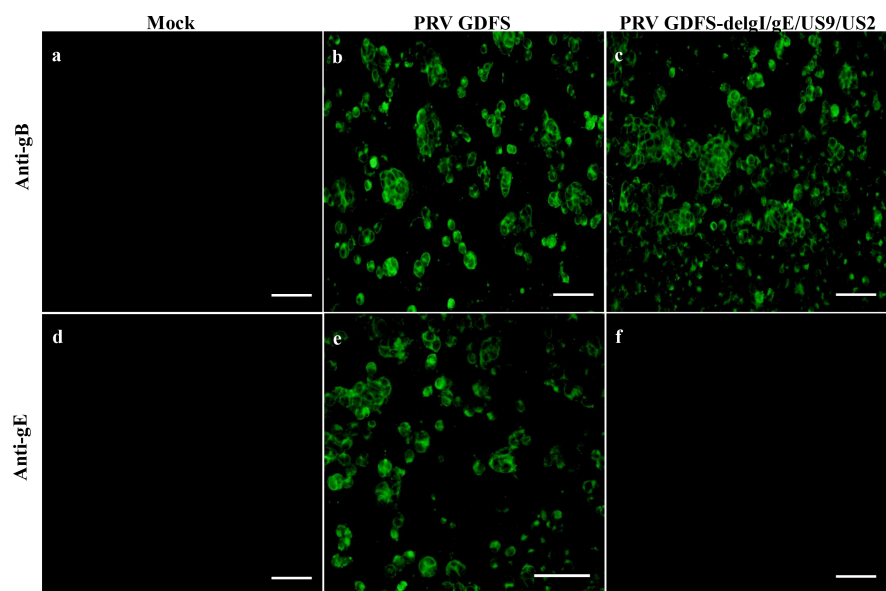
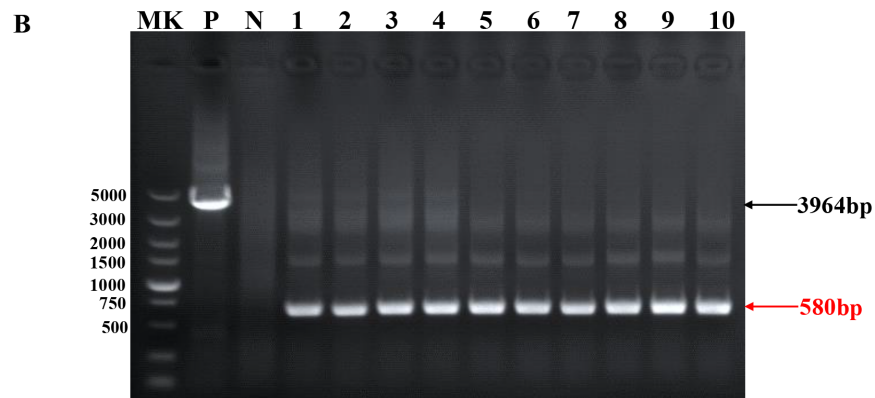
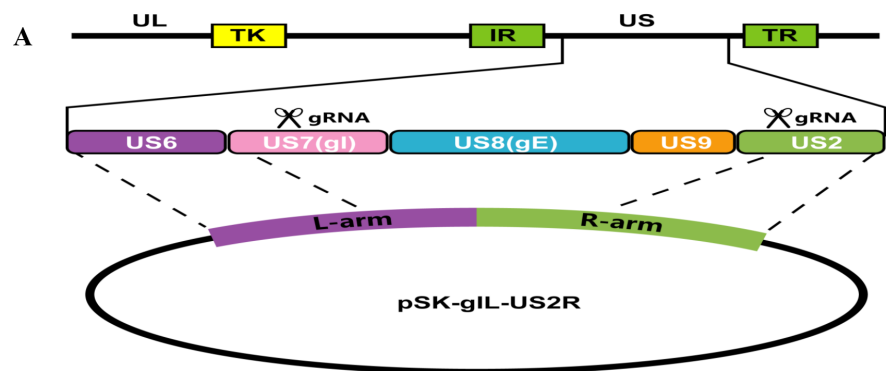
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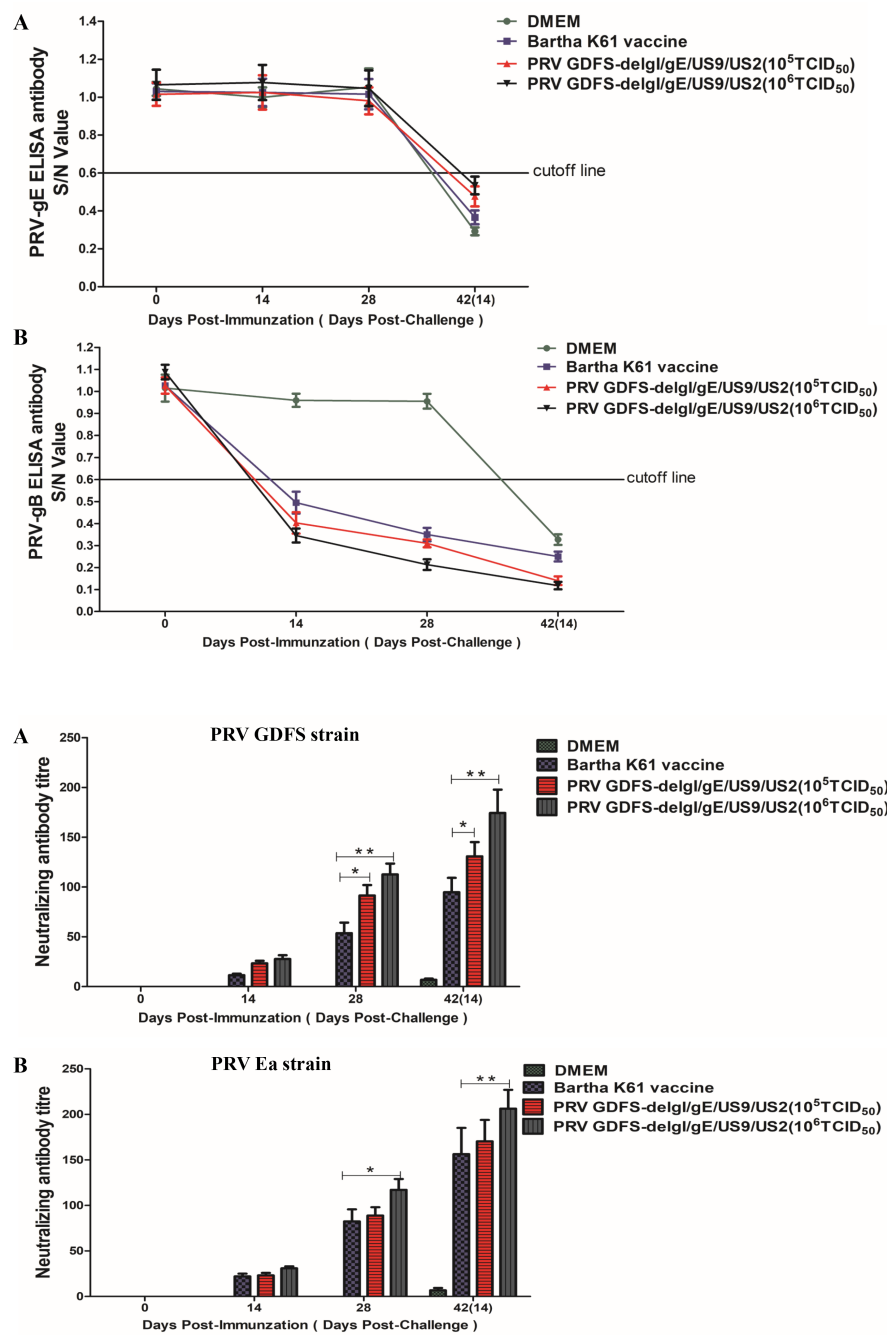
Abstract

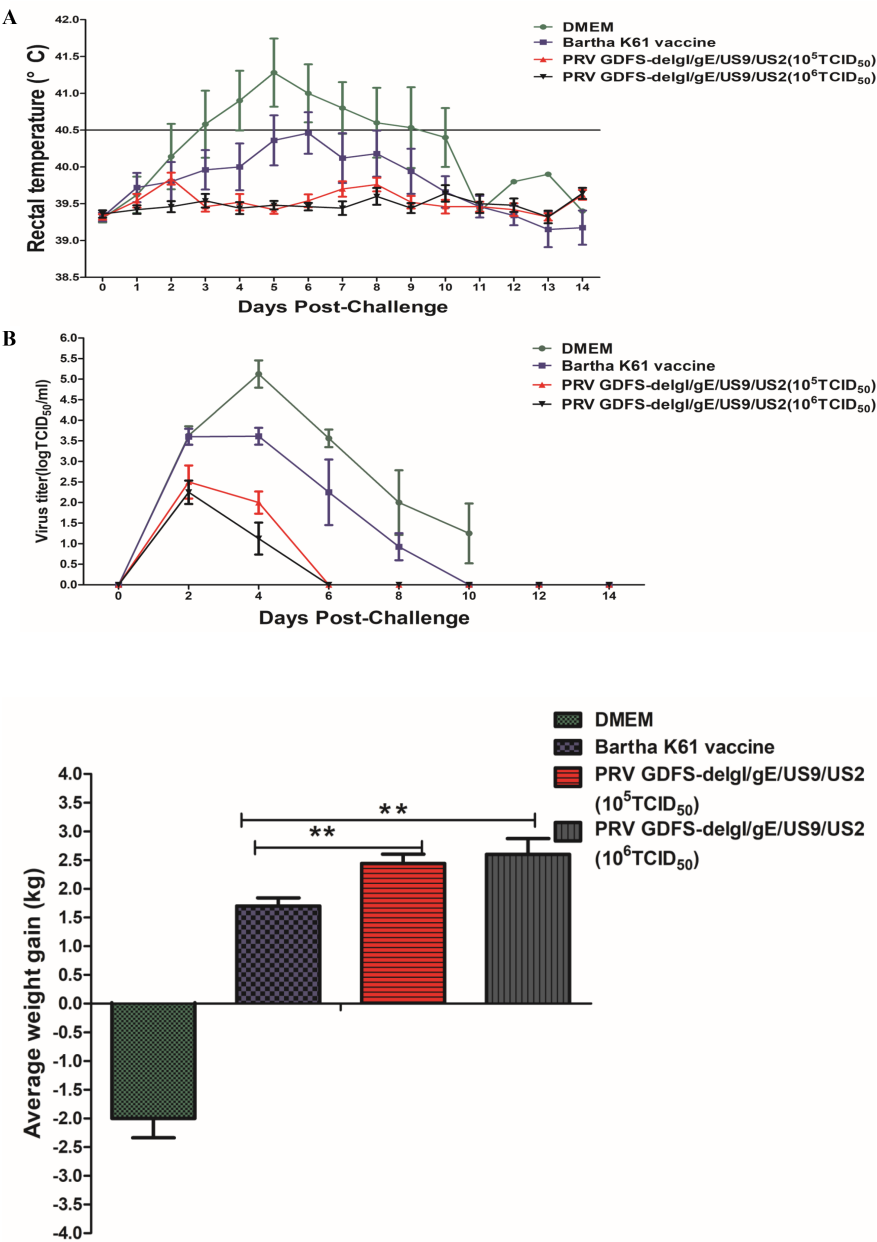
Pseudorabies virus (PRV) causes Aujeszky's disease or pseudorabies (PR) in pigs worldwide, which leads to heavy economic losses to the swine industry. Since 2011, the emerging PRV variant led to the outbreak of PR in Bartha-K61-vaccinated pigs. The PR outbreaks demonstrated that Bartha-K61 vaccine did not provide full protection against the emerging PRV variant. PRV live-attenuated vaccines could control PRV infection, which has become a consensus. In this study, a Bartha-K61-like vaccine based on emerging PRV variant was generated by the CRISPR/Cas9 method, which has deleted the gI, gE, US9, and US2 genes. Safety experiments have confirmed that PRV GDFS-delgI/gE/US9/US2 was safe for 5-7 days-old suckling piglets. The piglets immunized with PRV GDFS-delgI/gE/US9/US2 vaccine did not produce PRV gE-specific antibodies but could generate PRV gB-specific antibodies and high neutralizing titers against PRV GDFS strain (variant PRV strain) or PRV Ea strain (older PRV strain). After emerging PRV GDFS variant challenge, all piglets immunized with PRV GDFS-delgI/gE/US9/US2 vaccine did not show any clinical signs, and the rectal temperature was normal. Moreover, the autopsy and histopathological analyses revealed that the piglets in the PRV GDFS-delgI/gE/US9/US2 vaccine group did not show apparent gross and pathological lesions. Furthermore, the piglets did not present weight loss in the PRV GDFS-delgI/gE/US9/US2 vaccine groups. According to the criteria of OIE terrestrial manual, the results of the experiment confirmed that the PRV GDFS-delgI/gE/US9/US2 vaccine could provide full protection against emerging PRV variant strain in piglets. Therefore, PRV GDFS-delgI/gE/US9/US2 strain is a potential live-attenuated vaccine against emerging PRV variant strain infection in China.

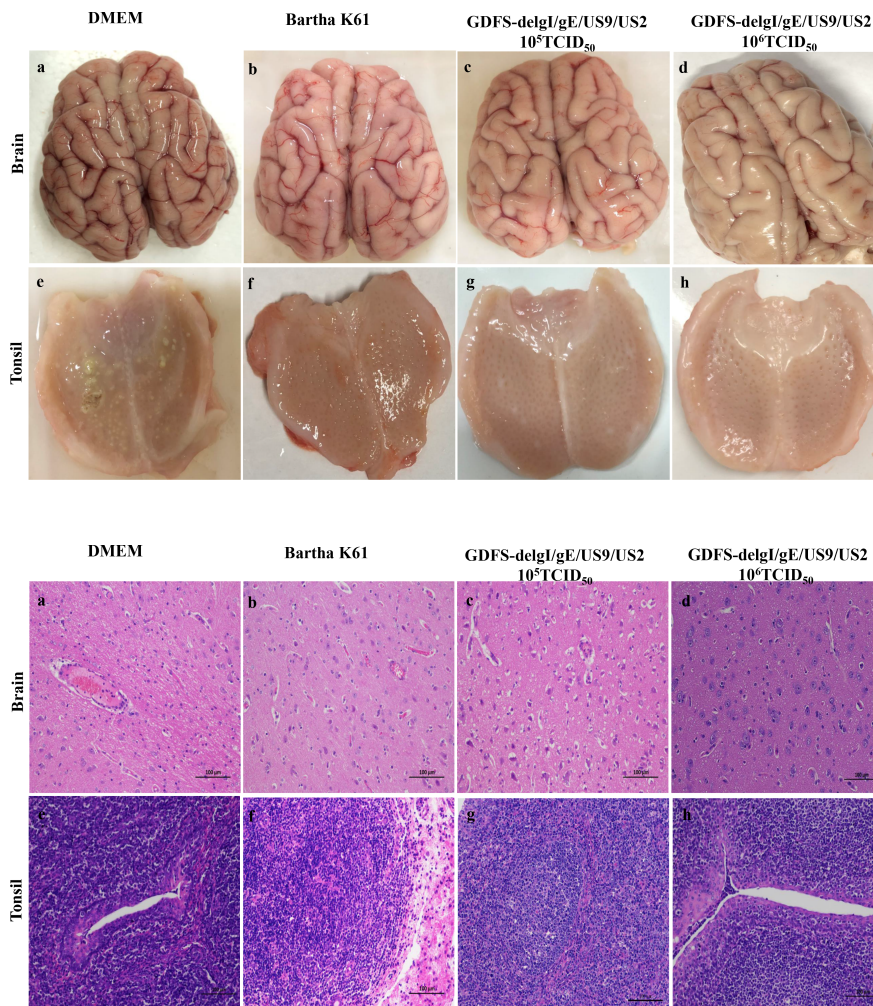
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