Porcine Research

A brief review of recent advances in African swine fever vaccine development

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Abstract. African swine fever (ASF) is a highly contagious and lethal disease affecting domestic pigs and wild boars, caused by the African swine fever virus (ASFV). The disease poses significant socio-economic challenges globally, with no commercially available vaccines to date. This review explores recent advancements in ASF vaccine development, focusing on four primary approaches: live-attenuated vaccines (LAVs), gene-deleted and rationally designed vaccines, subunit and DNA vaccines, and innovative delivery methods. Live-attenuated vaccines have shown promise in eliciting robust immune responses, with candidates like ASFV-G-ΔI177L demonstrating sterile immunity. Gene-deleted vaccines leverage genomic editing to enhance safety, while subunit and DNA vaccines offer safer alternatives but face challenges in achieving consistent efficacy. Novel delivery methods, such as oronasal administration, hold potential for large-scale deployment, particularly for wildlife reservoirs. Despite progress, vaccine development is hindered by ASFV's complex genome, immune evasion strategies, and safety concerns regarding live vaccines. The absence of a differentiating infected from vaccinated animals (DIVA) strategy further complicates disease monitoring and control. Future research must integrate advanced genomic tools, immunological insights, and innovative delivery platforms to overcome these challenges and develop safe, effective vaccines capable of mitigating the global threat of ASF.
Key Words: ASF, DIVA, LAV.

Introduction. African swine fever (ASF) is a contagious viral disease caused by the African swine fever virus (ASFV), a large, double-stranded DNA virus belonging to the Asfarviridae family (Galindo & Alonso 2017). First identified in Kenya in 1921 (Montgomery 1921), ASF has since spread across Africa, Europe, Asia, and most recently into the Americas, causing devastating outbreaks in domestic pig populations and wild boar reservoirs (Han et al 2023). The epidemiology of ASF is characterized by its ability to persist in the environment and its transmission through direct contact, contaminated fomites, and infected wild boars. The disease has catastrophic consequences for the global swine industry, with mortality rates reaching 100% in its acute form, resulting in billions of dollars in economic losses and threatening food security worldwide (Urbano & Ferreira 2022).

The pathogenesis of ASF is complex, involving widespread viral replication in macrophages, which disrupts immune function and triggers severe hemorrhagic fever. Infected pigs experience rapid-onset clinical signs such as fever, anorexia, cyanosis, and internal bleeding. The virus's ability to evade host immune responses through mechanisms like immune modulation and apoptosis of lymphocytes further complicates its containment (Revilla et al 2018). The immune evasion strategies of ASFV, coupled with its genetic diversity across at least 24 genotypes, pose significant challenges to vaccine development (Turlewicz-Podbielska et al 2021).

Even if during the last decades several research groups tried to work on a solution, the development of a safe and effective vaccine has been burdened with setbacks. Traditional vaccine platforms, including inactivated and subunit vaccines, have failed to confer reliable protection, largely due to the virus’s ability to bypass neutralizing antibody responses and its reliance on cellular immunity for effective control (Teklue et al 2020). Live-attenuated vaccines (LAVs), although promising in terms of efficacy, carry the risk of

reversion to virulence, raising concerns about their safety and suitability for large-scale use (Borca et al 2019). Furthermore, the lack of a differentiating infected from vaccinated animals (DIVA) strategy limits the applicability of current vaccine candidates in disease surveillance and eradication programs (Han et al 2023).

This review explores recent advances in ASF vaccine development, focusing on the innovative strategies employed to overcome these challenges and the persistent obstacles that hinder progress. By understanding the epidemiology, pathogenesis, and current limitations of ASF vaccines, researchers can pave the way for effective solutions to mitigate this global threat.

Progress in vaccine strategies

Live-attenuated vaccines (LAVs). Live-attenuated vaccines (LAVs) have gained significant attention in ASF vaccine development due to their ability to induce robust immune responses by mimicking natural infection. Recent advances in this field include the rational attenuation of ASFV strains through genetic deletions. For instance, ASFV-G-ΔI177L, developed by deleting the I177L gene, demonstrated complete sterile immunity against the virulent ASFV Georgia strain, with no adverse effects even at high dosages. This vaccine represents a critical step forward, offering a balance between safety and efficacy (Borca et al 2019).

Another notable candidate, VNUA-ASFV-LAVL2, was developed by serially passaging ASFV in porcine alveolar macrophages. This vaccine provided 100% protection against field isolates, making it a strong candidate for commercial development (Truong et al 2023). Despite these advances, concerns about reversion to virulence and incomplete understanding of ASFV's immune evasion mechanisms remain significant challenges for LAV deployment on a large scale.

Gene-deleted and rationally designed vaccines. The advance of genomic editing tools has enabled the development of gene-deleted vaccines that offer enhanced safety profiles compared to traditional LAVs. These vaccines target specific virulence genes, attenuating the virus while preserving its immunogenicity. ASFV-ΔH240R-Δ7R, a gene-deleted vaccine, achieved complete protection in pigs while maintaining stability after multiple passages, addressing concerns about genetic reversion (Li et al 2023).

Similarly, ASFV-Δ110-9L/505-7R showed that targeted deletions could modulate host immune responses by promoting type I interferon production, a critical pathway for antiviral defense (Zhu et al 2023). These findings underscore the potential of rationally designed vaccines to combine safety with efficacy, paving the way for next-generation ASF vaccines.

Subunit and DNA vaccines. Subunit and DNA vaccines represent safer alternatives to live vaccines, leveraging specific viral antigens to stimulate immunity. Subunit vaccines focus on key immunogenic proteins, such as p72, p30, and p54, which are essential for triggering protective immune responses. Although these vaccines have shown promise in preclinical studies, their efficacy has been limited due to the inability to fully mimic the immune response elicited by live virus exposure (Revilla et al 2018).

DNA vaccines, which use genetic material to encode viral antigens, offer the advantage of inducing both humoral and cellular immunity. However, their protective efficacy remains suboptimal, necessitating improvements in delivery systems and antigen design (Ma et al 2023). Combining subunit and DNA vaccine approaches with novel adjuvants and delivery platforms could enhance their effectiveness.

Innovative delivery methods. Delivery methods play a pivotal role in vaccine efficacy, particularly in managing wildlife reservoirs of ASFV, such as wild boars. Oronasal administration has emerged as a promising strategy for wildlife vaccination. ASFV-G-ΔI177L, when administered orally or nasally, provided robust protection comparable to intramuscular delivery, making it a practical solution for large-scale wildlife immunization (Borca et al 2021).

Oral vaccination strategies for ASFV, particularly in wild boar, face unique challenges, including ensuring vaccine stability in field conditions and achieving sufficient uptake through bait consumption. Recent studies emphasize the importance of formulating palatable baits and conducting cross-protection evaluations to ensure efficacy against diverse ASFV genotypes in wild boar populations (Cadenas-Fernández et al 2024).

Additionally, vesicular stomatitis virus (VSV)-based vectors have been explored as delivery systems for ASF antigens, demonstrating strong immune responses in preclinical models. These systems hold promises for addressing challenges in antigen stability and immune stimulation (Ma et al 2023).

Challenges in ASF vaccine development. ASF vaccine development faces numerous obstacles, stemming from the virus's complex genome and immune evasion strategies. ASFV's ability to suppress type I interferon production and induce apoptosis in immune cells hampers the development of vaccines that can generate robust and long-lasting immunity (Revilla et al 2018). The lack of continuous cell lines for large-scale production and concerns about vaccine safety, particularly for live-attenuated strains, further complicate the process (Han et al 2023).

One of the key challenges in ASF vaccine development is evaluating cross-protection in wild boar populations. Given the genetic diversity of ASFV, oral vaccines must demonstrate efficacy across multiple genotypes under field conditions, which introduces additional complexity to vaccine trials. The absence of robust cross-protection data risks leaving certain genotypes unaffected, limiting the overall impact of vaccination programs (Cadenas-Fernández et al 2024).

Moreover, the absence of a DIVA-compatible vaccine remains a significant limitation, as it impedes disease monitoring and control efforts in vaccinated populations. Addressing these challenges requires interdisciplinary collaboration and continued investment in ASF research.

Future directions. The future of ASF vaccine development lies in integrating advanced genomic, immunological, and computational tools. CRISPR-Cas9 and other gene-editing technologies can facilitate the precise attenuation of ASFV, enhancing the safety and efficacy of live vaccines. Research into host-virus interactions will uncover new targets for subunit and DNA vaccines, enabling the design of immunogens that elicit stronger protective responses (Turlewicz-Podbielska et al 2021).

Additionally, innovations in vaccine delivery, such as nanoparticle-based platforms and oral formulations, will enhance accessibility and uptake in both domestic and wild pig populations. Developing a comprehensive DIVA strategy and leveraging global collaboration will be crucial to the successful deployment of ASF vaccines (Urbano & Ferreira 2022).

Conclusions. While significant strides have been made in ASF vaccine development, the journey remains challenging due to the virus's complexity and the constraints of current technologies. Continued research, innovation, and collaboration are essential to overcome these barriers and deliver effective solutions to mitigate the global threat posed by ASF.

Conflict of interest. The authors declare that there is no conflict of interest.

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