

# Rab27a-mediated exosome secretion facilitates classical swine fever virus release and immune evasion

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**ABSTRACT** Classical swine fever is a highly contagious disease caused by the classical swine fever virus (CSFV), a member of the *Flaviviridae* family. Exosomes are extracellular vesicles that mediate intercellular communication by transferring membrane components and nucleic acids between cells. They play a role in the progression of various infectious diseases and help viruses evade immune responses. However, the impact of CSFV on exosome secretion and whether exosomes facilitate CSFV's evasion of the host immune response remains unclear. In this study, we first demonstrated that CSFV infection upregulates Rab27a, a small GTPase that regulates exosome secretion by mediating the trafficking and fusion of multivesicular bodies with the plasma membrane. By overexpressing and silencing Rab27a, we assessed its involvement in CSFV replication and release. We also demonstrated an interaction between the CSFV E0 and E2 proteins and Rab27a. Our findings show that Rab27a facilitates the release of exosomes, which, in turn, enhances CSFV spread. These results suggest that CSFV infection upregulates Rab27a, promoting the exosome-mediated release pathway, thereby contributing to viral spread and immune evasion.

**IMPORTANCE** Classical swine fever, caused by the classical swine fever virus (CSFV) from the *Flaviviridae* family, is highly contagious. Exosomes, extracellular vesicles that transfer membrane components and nucleic acids, play a role in viral progression and immune evasion. This study shows that CSFV infection upregulates Rab27a, and the CSFV E0 and E2 proteins interact with Rab27a. By manipulating Rab27a expression, we found that Rab27a facilitates exosome release, which enhances CSFV spread. These findings suggest that CSFV exploits Rab27a to promote exosome-mediated release, aiding viral spread and immune evasion.

**KEYWORDS** classical swine fever virus (CSFV), exosome, Rab27a, immune evasion, release

Classical swine fever (CSF) is an acute, highly contagious viral disease affecting pigs, caused by the classical swine fever virus (CSFV). This disease poses a significant threat to the global swine industry. Control strategies for CSF typically involve mandatory vaccination combined with the culling of infected animals. However, despite stringent vaccination measures, CSFV continues to re-emerge in multiple outbreaks (1). CSFV is a single-stranded positive-sense RNA virus, and its genome is divided into three major regions: the uncapped 5' untranslated region (containing an internal ribosome entry site), the open reading frame (ORF), and the 3' untranslated region (which lacks a polyA tail) (2). The ORF encodes a polyprotein that is cleaved into four structural proteins (C, Erns, E1, and E2) and eight non-structural proteins (Npro, p7, NS2, NS3, NS4A, NS4B, NS5A, and NS5B) (3).

Rab GTPases are a conserved family of proteins critical for regulating vesicular transport in eukaryotic cells (4). Research has shown that the activation or inhibition

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