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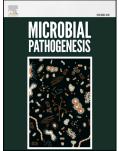
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Survival protein A is essential for virulence in Yersinia pestis

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Abstract

Plague is a highly pathogenic disease caused by the bacterium Yersinia pestis. There is currently no vaccine available for prophylaxis and antibiotic resistant strains have been isolated, thus there is a need for the development of new countermeasures to treat this disease. Survival protein A (SurA) is a chaperone that has been linked to virulence in several species of bacteria, including the close relative Yersinia pseudotuberculosis. In this study, we aimed to evaluate the role of SurA in virulence of the highly pathogenic Y. pestis by creating an unmarked surA deletion mutant. The Y. pestis Δ surA mutant was found to be more susceptible to membrane perturbing agents and was completely avirulent in a mouse infection model when delivered up to 2.1 x 10⁵ CFU by the subcutaneous route. This provides strong evidence that SurA would make a promising antimicrobial target.

Keywords: Yersinia pestis, mutant, virulence.

1. Introduction

Yersinia pestis, the causative agent of plague, is a highly pathogenic organism probably most famous for causing the Black Death in the 14th century [1]. Despite its fame as a historical disease, plague is considered as a re-emerging problem [2]. Antibiotics are used to treat the disease as there is no licenced vaccine currently available [3]. However, with the emergence of antibiotic resistance strains [4, 5], it is vital to develop new antimicrobials against novel targets in *Y. pestis*. One strategy is to target bacterial virulence factors, essentially disarming the bacteria to prevent disease [6]. *Y. pestis* is a facultative intracellular pathogen: it is thought to use macrophages to migrate to local lymph nodes where it switches to extracellular replication [7]. This requires a specific subset of virulence factors to allow it to survive and disseminate to various sites in the body (reviewed in [8]). One such potential virulence factor is Survival protein A (SurA), a chaperone involved in the biogenesis of outer membrane proteins (OMPs) [9, 10].

SurA was initially identified as important for stationary phase *survival* (*sur*) in *E. coli* [11] and later identified as having peptidy-prolyl isomerase (PPIase) activity, making it part of the

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