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Enzymatic Pathways of Intracellular Survival, Replication and Phagosomal Escape of *Francisella spp.*: A Review

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Abstract

Francisella tularensis is an important microbial agent which causes the severe infection of tularemia. The intracellular life cycle of this bacterium is supported by a vast range of protective guards such as enzymes. Although several enzymes are recognized in different subspecies of the bacterium, acid phosphatase and superoxide dismutase are seen in all bacterial subspecies. On the other hand, the most important enzymatic system relating to host cells is NADPH oxidase. For this reason, the clear aim of this mini-review is to discuss about the intracellular life cycle of *Francisella* tularensis and important enzymatic machineries in association to bacterium and its host cells. As a result, all of the biological systems including bacterial (prokaryotic) and host (eukaryotic) cells are protected by their enzymatic machineries. There are a wide range of enzymes within organisms. But, NADPH oxidase (in host cells), acid phosphatase and superoxide dismutase (in all of *Francisella tularensis* subspecies) were the main enzymes in this discussion. In conclusion, detection and identification of the enzymatic machineries and their activities enables us to find out appropriate mechanisms for definite therapeutic methods.

Keywords: *Francisella* tularensis, Phagocyte, Enzyme

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Introduction

The genus of *Francisella* involves Gram negative, non-motile, and facultative intracellular pathogenic bacteria. It may cause different types of zoonotic infection of tularemia including glandular, oculoglandular, ulceroglandular, oropharyngeal (gastrointestinal), respiratory (pneumonic), and typhoidal demonstrations [1-4].

Francisella genus includes two species of *Francisella* tularensis (*F. tularensis*) and F.philomiragia. Besides, *F. tularensis* involves four subspecies (*spp.)* of tularensis (type A), novicida, holarctica (type B) and mediasiatica. However, the classification of *F. tularensis* ssp. novicida and F.novicida is variable in different sources [2-6].

Transmission of tularemia is achieved via direct contact with insect vectors, infected animals, ingesting contaminated food or water, and inhalation of aerosolized bacteria [7-10].

The harshness of tularemia is directly associated with the bacterial cell number, the way of bacterial entrance, and the bacterial species and subspecies. The most severe form of tularemia is caused by *F. tularensis* subspecies (*spp*.) *tularensis*. With ignorance of bacterial entrance, the lethal dosage of *F. tularensis* ssp. tularensis is about 10 cells and the rate of mortality in untreated situation is up to 35%. Thus, this subspecies is recognized as an important case regarding to bioterrorism concern. The centers for infectious diseases control and prevention (CDC) have classified the life threatening bacterium of *F. tularensis* spp. *tularensis* in category A [2,3,6,9,11,12].

In accordance with previous studies, the intracellular life cycle of *Francisella* within a host cell begins by entrance into the phagocytes and continues via bioactivities and replication. The host cells consist of alveolar and dendritic cells, fibroblasts, hepatocytes, macrophages and polymorphonuclear leukocytes (neutrophils) [2,13-16].

The process of intracellular replication is known as an important factor regarding to *F. tularensis* pathogenicity. The formation of pseudopod loops in macrophages reveals the entrance of *F. tularensis* into the cell. The bacterial entrance is followed by