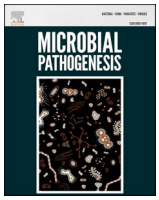
Microbial Pathogenesis 164 (2022) 105435

Contents lists available at ScienceDirect

Microbial Pathogenesis

journal homepage: www.elsevier.com/locate/micpath



# Expression of virulence factor genes in co-infections with *Trueperella pyogenes* isolates and other bacterial pathogens; an in vivo study

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ARTICLE INFO

*Keywords:*
Actinomycetes
Virulence factors
Gene expression
Combined infections

ABSTRACT

*Trueperella pyogenes* is an opportunistic bacterial pathogen causing several infectious diseases, including metritis, mastitis and abscesses in domestic animals such as dairy cattle. Several virulence proteins are released by *T. pyogenes* strains contributing to the pathogenic and causing disease potential of this pathogen. So far, many aspects of *T. pyogenes* pathogenesis are unknown. In this study, expression levels of *plo*, *fimA*, *nanH* and *cbpA* genes encoding pyolysin, fimbriae, neuraminidase and collagen-binding protein, respectively in *T. pyogenes* isolated from totally 15 metritis, mastitis and cutaneous abscesses convenience samples in response to co-culture with other pathogens including *E. coli*, *St. dysgalactiae*, *S. aureus*, *F. necrophorum* and *L. plantarum* strains in mice study model have been investigated. We found that expression levels of *plo*, *fimA*, *nanH* and *cbpA* genes in *T. pyogenes* isolates in response to co-culture with *F. necrophorum* and *E. coli* were significantly increased; however, no significant changes was seen in the level of expression of these genes in the isolates in response to co-culture with *St. dysgalactiae* and *S. aureus*. Notably, expression of all virulence factor genes was suppressed in *T. pyogenes* in response to co-culture with *L. plantarum*. We observed that *L. plantarum* might be used to prevent infectious diseases caused by *T. pyogenes*.

## 1. Introduction

*Trueperella pyogenes*, formerly *Arcanobacterium pyogenes*, is a common inhabitant of skin and mucus membrane of respiratory and urinary tracts, as well as the gut microbiota of pigs and cattle [1]. These bacteria are opportunistic in nature causing mainly metritis, mastitis, abortion, abscesses, pneumonia and urine infections in different domestic and wild animals [2]. Reduced meat and milk production, reproductive failure and elimination of infected cattle from the herds are economic effects of *T. pyogenes* infections [3]. *T. pyogenes* has been seen co-infecting the host cells with other bacterial infectious agents such as *Escherichia coli*, *Streptococcus dysgalactiae* and *Fusobacterium* spp.; which could be improves pathogenesis and antimicrobial resistance of *T. pyogenes* isolates [4].

A set of virulence factors of *T. pyogenes* have been characterized. Pyolysin O (PLO, only hemolysin of *T. pyogenes*) protein is a cholesterol-dependent exotoxin considered the main virulence and protective factor of this pathogen encoded by *plo* gene and been detected in all pathogenic *T. pyogenes* isolates. PLO has shown cytotoxic effect on polymorphonuclear neutrophils, erythrocytes, macrophages, endometrial stromal and epithelial cells; and mammalian red blood cells [5]. Four fimbrial proteins are related to adhesion, colonization and pathogenesis of this gram-positive pathogen, including *fimA*, *fimC*, *fimE* and *fimG* [6]. Neuraminidases, another virulence factor, promote adhesion of *T. pyogenes* to the receptors of cryptic host and mucosal epithelial cells, with an enzymatic role in the catabolism of sialic acid encode with *nanH* and *nanP* genes. These compounds are produced by both gram-positive and gram-negative pathogens, promote colonization, lead to reducing mucus viscosity and weakening the immune response as a protective virulence factor [7]. Collagen binding protein (which encoded by *cpbA*) an extracellular protein released by *T. pyogenes* mediated adherence and colonization of bacteria to collagen-rich tissue such as animal skin and udder [8].

The opportunistic nature of *T. pyogenes* has been related to different virulence factors, required to establish the acute disease, particularly in immunocompromised patients. Pathogenesis mechanisms of *T. pyogenes*

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https://doi.org/10.1016/j.micpath.2022.105435
Received 11 August 2021; Received in revised form 25 January 2022; Accepted 30 January 2022
Available online 1 February 2022