



UMEÅ UNIVERSITY

Umeå University odontological dissertations no. 155

***Filifactor alocis* and its RTX protein FtxA**

Virulence, Diagnostic Potential, and in Synergy
with *Aggregatibacter actinomycetemcomitans*
in Periodontal Disease

Zeinab Razooqi

Academic dissertation

Which, with the due permission of the Vice-Chancellor of Umeå University for the examination for the Degree of Doctor of Medical Science, is presented for public defence in Hörsal B, plan 9, Tandläkarhögskolan, Norrlands Universitetssjukhus on Friday, 5 June, 2026 at 09:00.

The thesis will be defended in Swedish.

Faculty opponent:

Associate professor Daniel Jönsson, Lund University, Lund, Sweden

Organisation

Umeå University
Department of Odontology,
Faculty of Medicine, Umeå
University

Document type

Doctoral thesis

Date of publication

13 May 2026

Author

Zeinab Razooqi

Title

Filifactor alocis and its RTX protein FtxA: Virulence, Diagnostic Potential, and in Synergy with Aggregatibacter actinomycetemcomitans in Periodontal Disease

Abstract

Filifactor alocis is a Gram-positive anaerobic rod frequently detected in periodontal lesions. Interest in this species has increased following the discovery of *Filifactor alocis* toxin A (FtxA), a repeats-in-toxin (RTX) protein carried by approximately 50% of isolated strains. FtxA is the second RTX protein identified in oral bacteria, after the leukotoxin (LtxA) of *Aggregatibacter actinomycetemcomitans*. The co-occurrence of *F. alocis* and *A. actinomycetemcomitans* in diseased periodontal sites suggests possible synergistic interactions in pathogenesis, but the virulence properties and clinical relevance of FtxA have remained largely unknown.

This thesis aimed to investigate the clinical prevalence and diagnostic potential of *F. alocis* and *ftxA* in periodontal disease, explore interactions with *A. actinomycetemcomitans*, characterize the virulence-related properties of FtxA, and evaluate its effects on host immune responses.

Across three clinical studies, high levels of *F. alocis* and the presence of *ftxA* were associated with increased periodontal severity and disease progression. In a longitudinal Ghanaian adolescent cohort, carriage of *ftxA*-positive *F. alocis* was linked to higher bacterial loads and greater clinical attachment loss progression.

Disease progression was further enhanced when *F. alocis* co-occurred with non-JP2 genotype *A. actinomycetemcomitans*, whereas the JP2 genotype showed high virulence independently of *F. alocis*.

Site-specific analyses confirmed that higher loads of both species were associated with deeper periodontal pockets and greater progression, with the highest levels at sites positive for both JP2 genotype *A. actinomycetemcomitans* and *ftxA*-positive *F. alocis*.

In an independent Australian periodontitis cohort, high *F. alocis* levels and *ftxA* carriage were associated with more severe disease, including Grade C and Stage IV periodontitis.

Mechanistic studies in THP-1 cells showed that an *ftxA*-positive *F. alocis* strain, its extracellular vesicles, and recombinant FtxA were non-cytotoxic, but induced transcriptional and cytokine profiles consistent with immunosuppression. Inflammatory signaling, cytokine secretion, and apoptosis- and necroptosis-related pathways were reduced, whereas an *ftxA*-negative strain elicited a more pro-inflammatory response.

Together, these findings support a role for *F. alocis* and FtxA in periodontal disease progression and severity. Detection of high *F. alocis* levels and *ftxA* may have value as molecular risk markers, particularly in combination with *A. actinomycetemcomitans*. FtxA also emerges as a novel candidate virulence factor and potential therapeutic target in periodontitis.

Keywords: Filifactor alocis, FtxA, RTX protein, periodontitis, virulence factors Aggregatibacter actinomycetemcomitans, bacterial synergism, immune evasion, diagnostic markers, extracellular vesicles.

Language

English

ISBN

978-91-6850-056-0 (print)
978-91-6850-057-7 (pdf)

ISSN

0345-7532

Number of pages

111 + 4 delarbeten/papers