Characterisation of clinical Porphyromonas gingivalis isolates to determine the significance of DPPIV as a virulence factor

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Resistance to antibiotics is an increasing concern for the public health. A possible innovative therapy to overcome this problem and which is being widely investigated, is the inhibition of virulence factors.

Porphyromonas gingivalis is a member of the subgingival plaque microbiota and a key pathogen in the development of adult periodontitis. This Gram-negative, anaerobic bacterium produces proteolytic enzymes that cause tissue destruction and modulate the immune system. Dipeptidyl peptidase IV (DPPIV) is a serine protease that removes X-Pro or X-Ala dipeptides from the N-terminal end of polypeptide chains. It is involved in the degradation of the connective tissue and might be an interesting target for virulence inhibition.

This study aims to correlate DPPIV-activity with biofilm formation and in vivo pathogenicity of clinical P. gingivalis isolates to evaluate DPPIV as a target for virulence inhibition.

A method to fractionate and isolate DPPIV was optimized to determine the DPPIV-activity of five clinical isolates with a different capsular type (K1-K5)¹² and three reference strains (W50, W83 and ATCC 33277). Their capacity to form biofilms in a microtiter plate was quantified after staining with 0,01% crystal violet. In vivo pathogenicity was evaluated by daily assessment of the formation and location of skin lesions in BALB/c mice after dorsal, subcutaneous injection of a bacterial suspension.

As stated in literature DPPIV is membrane-associated and consequently the highest activities were found in the membrane fractions. The capsular types K4 and K5 showed the highest DPPIV-activity while K1, K2, K3 and the reference strains showed 10 to 100 times lower activities. Moreover, DPPIV-activity was associated with the formation of in vivo abscesses. Only for K4 and K5 significant abscesses were obtained. ATCC 33277 showed the best capacity to form biofilms, followed by K4 and K5. Capsule type 3 and the reference strain W50 also formed biofilms but to a lesser extent.

In conclusion, our results suggest that DPPIV might be an interesting therapeutic target to inhibit the pathogenicity of P. gingivalis. Further research should focus on the evaluation of DPPIV-inhibitors in P. gingivalis infection models.


Keywords virulence inhibition; P. gingivalis; dipeptidyl peptidase IV