

FORSKNINGSRAPPORT - ABSTRACTS 2019

S100A12 expression is altered in gingival tissue and circulatory monocytes in periodontitis

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Introduction: S100A12 is a calcium-binding protein secreted mainly by myeloid cells, which acts as an alarmin to induce a pro-inflammatory innate immune response. It has been linked to several chronic inflammatory diseases, however its role in periodontitis is largely unknown.

Aim: This study evaluated S100A12 expression dynamics in a co-culture oral tissue model, as well as in peripheral monocytes, gingival tissue and saliva from patients having periodontitis.

Methods: A three-dimensional multi-cellular oral tissue model was set up with and without monocytes and inflammatory stimuli. S100A12 expression was assessed in gingival tissue, as well as circulating monocytes from periodontitis patients and healthy controls. Three-hundred and fifty individuals were enrolled and clinically examined, and stimulated saliva was collected for the assessment of S100A12 levels.

Results: In a co-culture oral tissue model, monocyte differentiation resulted in increased S100A12 secretion over time, which further increased with inflammatory stimuli. S100A12 expression was higher in gingival tissue from periodontitis patients where monocyte-derived cells exhibited an increased expression of S100A12 compared to control tissue. Peripheral monocytes from periodontitis patients had higher S100A12 expression than monocytes from controls, a difference particularly observed in the intermediate and non-classical monocyte subsets. Further, monocytes from periodontitis patients displayed an increased secretion of S100A12 compared with monocytes from controls. In line with that, patients with periodontitis stages III and IV displayed significantly higher levels of S100A12 in saliva compared to non-periodontitis patients, and the levels correlated to clinical periodontal parameters.

Conclusions: S100A12 is increased in inflamed tissue, potentially as a result of enhanced production by monocyte-derived cells. This study implicates the involvement of S100A12 in the pathogenesis of periodontitis, and both gingival tissue and circulatory monocytes are altered in periodontitis. S100A12 levels in saliva reflect the severe stages of periodontitis.