IL-22?expressing CD4+AhR+ T lymphocytes are associated with RANKL-mediated alveolar bone resorption during experimental periodontitis

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Background and Objective: Over the past few years, the importance of interleukin-22 (IL-22) and T-helper (Th)22 lymphocytes in the pathogenesis of periodontitis has become apparent; however, there are still aspects that are not addressed yet. Cells expressing IL-22 and aryl hydrocarbon receptor (AhR), transcription factor master switch gene implicated in the differentiation and function of Th22 lymphocytes, have been detected in periodontal tissues of periodontitis-affected patients. In addition, IL-22 has been associated with osteoclast differentiation and their bone resorptive activity in vitro. However, the destructive potential of IL-22?expressing AhR+ Th22 lymphocytes over periodontal tissues during periodontitis has not been demonstrated in vivo yet. Therefore, this study aimed to analyze whether IL-22?expressing CD4+AhR+ T lymphocytes detected in periodontal lesions are associated with alveolar bone resorption during experimental periodontitis. Material and Methods: Using a murine model of periodontitis, the expression levels of IL-22 and AhR, as well as the Th1-, Th2-, Th17- and T regulatory-associated cytokines, were analyzed in periodontal lesions using qPCR. The detection of CD4+IL-22+AhR+ T lymphocytes was analyzed in periodontal lesions

and cervical lymph nodes that drain these periodontal lesions using flow cytometry. In addition, the expression of the osteoclastogenic mediator called receptor activator of nuclear factor-?B ligand (RANKL) was analyzed by qPCR, western blot, and immunohistochemistry. Finally, alveolar bone resorption was analyzed using micro-computed tomography and scanning electron microscopy, and the bone resorption levels were correlated with IL-22 and RANKL expression. Results: Higher levels of IL-22, AhR, and RANKL, as well as IL-1?, IL-6, IL-12, IL-17, IL-23, and TNF-?, were expressed in periodontal lesions of infected mice compared with periodontal tissues of sham-infected and non-infected controls. Similarly, high RANKL immunoreaction was observed in periodontal tissues of infected mice; however, few or absent RANKL immunoreaction was observed in controls. This association between RANKL and periodontal infection was ratified by western blot. Furthermore, a higher detection of CD4+IL-22+AhR+ T lymphocytes was found in periodontal lesions and cervical lymph nodes that drain these periodontal lesions in infected mice compared with non-infected controls. Finally, the increased IL-22 and RANKL expression showed positive correlation between them and with the augmented alveolar bone resorption observed in experimental periodontal lesions. Conclusion: This study demonstrates the increase of IL-22?expressing CD4+AhR+ T lymphocytes in periodontitis-affected tissues and shows a positive correlation between IL-22, RANKL expression, and alveolar bone resorption.

alveolar bone resorption

interleukin-22

periodontitis

RANKL

Th22 lymphocytes

aromatic hydrocarbon receptor

interleukin derivative

interleukin-22

osteoclast differentiation factor

alveolar bone loss

animal

human

metabolism

micro-computed tomography

mouse

osteolysis

periodontitis

Alveolar Bone Loss

Animals

Bone Resorption

Humans

Interleukins

Mice

Periodontitis

RANK Ligand

Receptors, Aryl Hydrocarbon

X-Ray Microtomography