Editorial Epigenetics: A Missing Link Between Periodontitis and Peri-implantitis?

Current or past history of periodontal disease is a potential risk factor for the initiation and progression of peri-implantitis.[1–8] Peri-implantitis can display bursts of activity associated with the release of cytokines and/or chemokines that evoke an inflammatory cascade, leading to destruction of bone and soft tissues surrounding the implant. A primary etiologic factor, as in periodontitis, is the microbial biofilm. Mounting evidence also supports a potential complex of factors driving pathologic mechanisms around oral implants, such as surface characteristics of the implant material, occlusion, and excess cement.

Microbiologic data suggest that after full-mouth extraction, there is a substantial reduction of the putative periodontal microbial load.[9,10] In contrast, edentulous individuals possessing multiple implants—often as a consequence of severe periodontal disease—display higher rates of peri-implantitis.[11,12] Indeed, peri-implantitis lesions are more than twice as large and contain significantly greater proportions, numbers, and densities of CD138-, CD68-, and MPO-positive cells than periodontitis lesions.[13] Nevertheless, these striking features of the lesions are in disagreement with the expression of Th17-related cytokines in mucositis sites, which seem to be similar around periodontal and peri-implant alveolar bone defects.[14] These differing lines of evidence suggest more information is required to understand the pathologic mechanisms—both parallels and contrasts—between peri-implantitis and periodontitis.

Epigenetics, different from genetics, is a stably heritable phenotype resulting from changes in a chromosome without alternations in the DNA sequence.[15] Three major epigenetic mechanisms (DNA methylation, histone modifications, and microRNAs) have been shown to influence DNA expression via chromatin remodeling, which modifies gene expression.[16,17] While it seems that in the field of periodontology histone modification and DNA methylation mostly entail the expression level of cytokines, chemokines, and toll-like receptors of the oral epithelia, microRNAs have been shown to be more involved in the expression of osteogenic and osteoclast-related genes.[18,19] Major disease risk factors, such as smoking and diabetes, alter epigenetics by down-regulating the gene expression of bone matrix proteins.[20] Epidrugs have been successfully implemented in the treatment of alveolar bone loss in an experimental periodontitis murine model.[21] Accordingly, it could be speculated that epigenetic changes during periodontitis in patients possessing implants may tilt the balance of susceptibility in the pathway from mucositis to peri-implantitis by suppressing specific transcription factors for osteogenesis or by activating certain transcription factors for osteoclastogenesis.

Emerging data are being accumulated that recognize that specific materials, including titanium, may evoke differing responses of biomaterial surfaces on cells derived from the periodontium that are modulated due to material surface energy, composition, or topography.[22] Epigenetic modifications might be sustained in periodontal tissues even subsequent to nonsurgical periodontal therapy. As such, these epigenetically altered tissues subsequent to tooth extraction may differ from those not exposed to epigenetic cues

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such as histone deacetylation or DNA hypermethlyation.[23,24] This connection could be the missing link between periodontitis and peri-implantitis and could serve as a rationale for why patients with a history of periodontal disease, even with enhanced oral hygiene measures, should have more intense monitoring. This theory needs to be tested, given the very limited information available on epigenetic mechanisms and the initiation and progression of peri-implantitis. Future investigations may help shed light on this field of epigenetics in relation to oral disease to advance a better understanding of pathogenesis of periodontitis and peri-implantitis.

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