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Functional characteristics of periodontitis and peri-implantitis lesions in humans

Akademisk avhandling

som för avläggande av odontologie doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hörsal Arvid Carlsson, Academicum, Medicinaregatan 3, den 21 December 2023, klockan 9.00

av
Carlotta Dionigi

Fakultetsopponent:
Professor Giovanni E. Salvi
University of Bern, Switzerland

Avhandlingen baseras på följande delarbeten

I. Dionigi C., Larsson L., Carcuac O. & Berglundh T. *Cellular expression of DNA damage/repair and reactive oxygen/nitrogen species in human periodontitis and peri-implantitis lesions.* Journal of Clinical Periodontology 2020; 47 (12): 1466–1475.

II. Dionigi C., Larsson L., Difloe-Geisert J.C., Zitzmann N. & Berglundh T. *Cellular expression of epigenetic markers and oxidative stress in periodontitis lesions of smokers and non-smokers.* Journal of Periodontal Research 2022; 57 (5): 952–959.

III. Dionigi C., Nagy G., Ichioka Y., Derks J., Tomasi C., Larsson L., Primetzhofer D. & Berglundh T. *Titanium micro-particles in soft tissues around dental implants.* (In manuscript)

IV. Dionigi C., Larsson L. & Berglundh T. *Spatial transcriptomic assessments of gene expression profiles in human peri-implant lesions.* (In manuscript)

SAHLGRENSKA AKADEMIN
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Abstract

In the current series of studies functional characteristics of periodontitis and peri- implantitis lesions in humans were investigated. Cell markers for antimicrobial activity were used to evaluate differences between periodontitis and peri-implantitis lesions (**Study I**), while epigenetic and oxidative stress markers were used to compare periodontitis lesions in smokers and non-smokers (**Study II**). The occurrence and localization of titanium micro-particles were assessed in tissue samples obtained from dental implant sites with and without peri-implantitis and the influence of titanium particles on gene expression profiles was investigated in peri-implantitis lesions (**Study III)**. Gene expression profiles were analyzed in tissue samples obtained from dental implant sites with and without peri-implantitis by integrating spatial transcriptomics and RNA-sequencing data (**Study IV**).

It was demonstrated that:

- Peri-implantitis lesions were larger and presented with significantly larger densities of cells with antimicrobial activity than periodontitis lesions. In both lesions, cellular densities were higher in the inner zone, lateral to the pocket epithelium, than in the outer compartment of the lesion The non-infiltrated connective tissue in peri-implantitis specimens showed significantly higher densities of cells with antimicrobial activity than that in periodontitis specimens (**Study I**).
- Although periodontitis lesions did not differ in size between smokers and non-smokers, differences in cellular functions were observed. Periodontitis lesions in smokers presented with diminished antimicrobial activity and lower levels of epigenetic markers than lesions in non-smokers (**Study II**).
- Densities of titanium micro-particles in peri-implant tissues varied across patients but not between dental implant sites with and without peri-implantitis within the same individual. The titanium micro-particles were of similar size and morphology and mainly located in a 2-mm wide tissue zone close to the implant, in samples with and without peri-implantitis. Out of >36000 analyzed genes, only 14 were differentially expressed when comparing peri-implantitis specimens with high and low densities of titanium micro-particles (**Study III**).
- A clear association was observed between distinct gene clusters and specific compartments in peri-implant tissues. Peri-implantitis specimens showed overall higher levels of gene activity than specimens from reference implant sites. Several pathways specific for the activation of the host response towards bacterial insults were clearly dysregulated in peri-implantitis specimens (**Study IV**).

Keywords: periodontitis, peri-implantitis, biopsy, immunohistochemistry, oxidative stress, epigenetics, titanium micro-particles, proton-induced X-rays emission, RNA-sequencing, spatial transcriptomics.

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