11β-Hydroxysteroid Dehydrogenases in Periodontal Disease

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Introduction

There is increasing evidence of 11β-hydroxysteroid dehydrogenase (11β-HSD) isoforms playing a pivotal role in the pathogenesis of various metabolic, systemic and inflammatory diseases such as diabetes mellitus or ischemic and coronary heart disease [1], [2]. Additionally, bone affecting diseases such as rheumatoid arthritis or osteoporosis correlate with altered 11β-HSD expression patterns and glucocorticoid (GC)-action as described earlier [1], [2]. Interestingly, the pathogenesis of periodontitis is indeed frequently accompanied by the aforementioned systemic inflammatory comorbidities [1] - [6].

The genomic response to inflammatory stimuli relies, besides on other mechanisms, on the activation of the glucocorticoid receptor (GR), which in turn represses or stimulates expression of diverse pro- and anti-inflammatory genes in order to regulate stress and inflammatory responses. To avoid or dampen unwanted systemic effects of GCs (e.g. cortisone, cortisol), this mechanism depends upon tissue-specific fine-tuning.
Thus, transformation of GCs is mediated by specialised enzymes, which convert steroid hormones from their inactive to their active forms and vice versa. A key role is played by the two isoforms of 11β-HSD which catalyse the interconversion of active cortisol and inactive cortisone. The interaction and expression of both 11β-HSD isoforms is highly dynamic in various types of tissues, as they individually equilibrate local and systemic GC-concentrations and hence control transcription patterns under different physiological conditions.

Objectives

For the first time, this pilot study examines human gingival tissue of periodontitis patients (n=7) and healthy controls (n=6) with the use of quantitative Real-Time PCR (qRT-PCR) in order to test whether tissue-specific dysregulation of 11β-HSD isoforms contributes to the progression of periodontal disease.

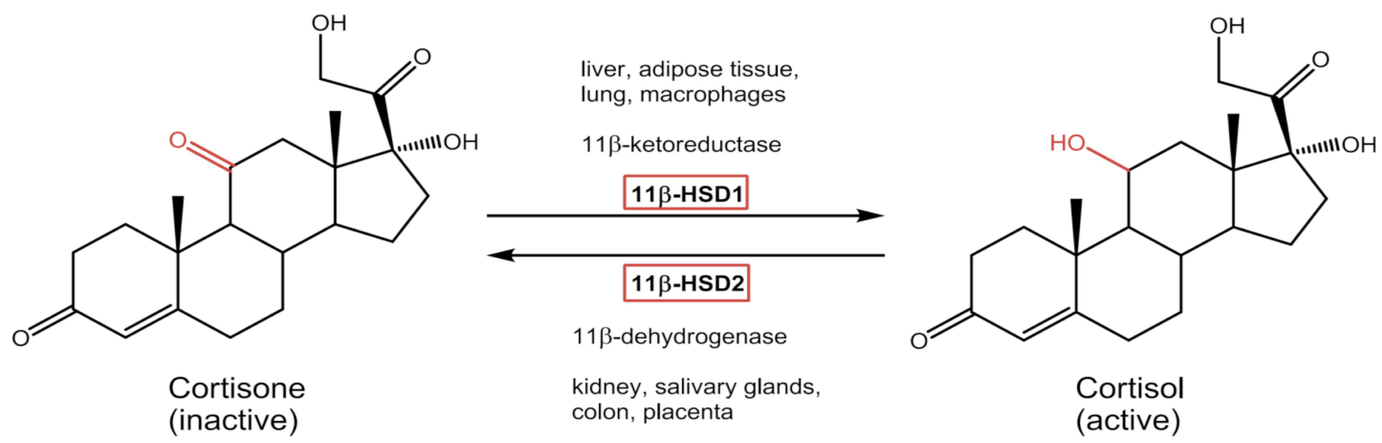

Figure 1: Physiological role of the two isoenzymes 11β – HSD type 1 and 2 [7]

Material & Methods

Gingival biopsies were collected by practitioners of the Department of Oral and Maxillofacial Surgery and the Clinic for Conservative Dentistry and Periodontology (University Medical School Schleswig-Holstein (UKSH), Campus Kiel, Germany).
Seven samples of gingival tissue were taken from patients diagnosed with advanced periodontitis. Six samples serving as a control were obtained during third molar surgery of otherwise healthy patients.
After isolation and prior to qRT-PCR analysis, RNA integrity was tested for each sample.
Mann-Whitney *U* tests were performed to determine differences between cases and healthy controls.

Results

Fig. 2 depicts gingival gene expression for both genes, HSD11b1 and HSD11b2, given as fold change values based on controls.
The calculated fold change values were 0.78 for 11β-HSD1 and 0.99 for 11β-HSD2.
The mRNA expression of HSD11b1 and HSD11b2 in periodontitis patients and healthy controls by delta cT values is provided in Figures 3a and 3b. Using Mann-Whitney *U* tests, no significant differences between cases and controls for neither 11β-HSD1 ($p = 0.7984$) nor 11β-HSD2 expression ($p \sim 1$) were detected.

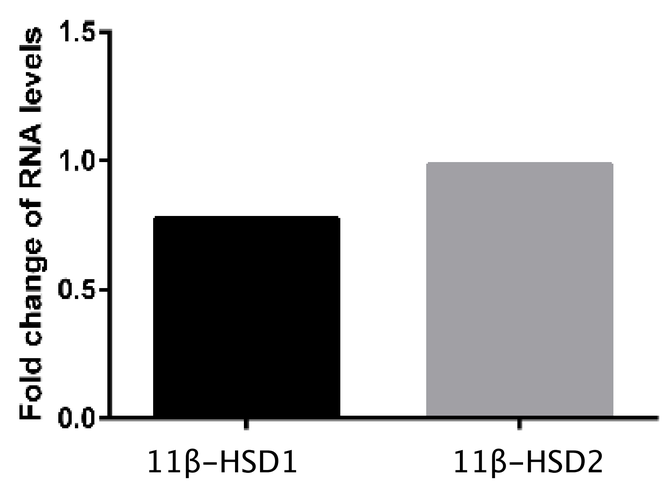

Figure 2: Fold change in gingival RNA expression
Gingival gene expression of HSDs was determined by qRT-PCR. Fold change values are based on controls. Closed columns: relative 11β-HSD1 expression. Shaded columns: relative 11β-HSD2 expression. Fold change values were 0.78 (11β-HSD1) and 0.99 (11β-HSD2).

Discussion & Conclusion

qRT-PCR analysis showed that the mRNA expression of neither 11β-HSD1 nor 11β-HSD2 is differentially regulated in periodontitis compared with healthy controls. It has to be added that this does not necessarily refer to the expression of the corresponding protein.
However, these results are congruent with the observations of 11β-HSD1 and 11β-HSD2 expression in rodents [8].
In future studies regulation patterns of 11β-HSD isoforms in the clinical picture of peri-implantitis remain to be investigated as these enzymes constitute promising pharmaceutical targets to ameliorate disease progression and medical conditions of the oral cavity.
Indeed, recent findings from our laboratory (data not shown) indicate upregulation of 11β-HSD1 in the gingival tissue of patients diagnosed with peri-implantitis.
Tissue remodelling and bone resorption are key mechanisms characterising the clinical picture of periodontitis. Therefore future studies might also evaluate the participation of other oxido-reductases involved in the regulation of these mechanisms.
In this context the metabolism of other inflammatory mediators such as prostaglandins, should be taken into consideration.

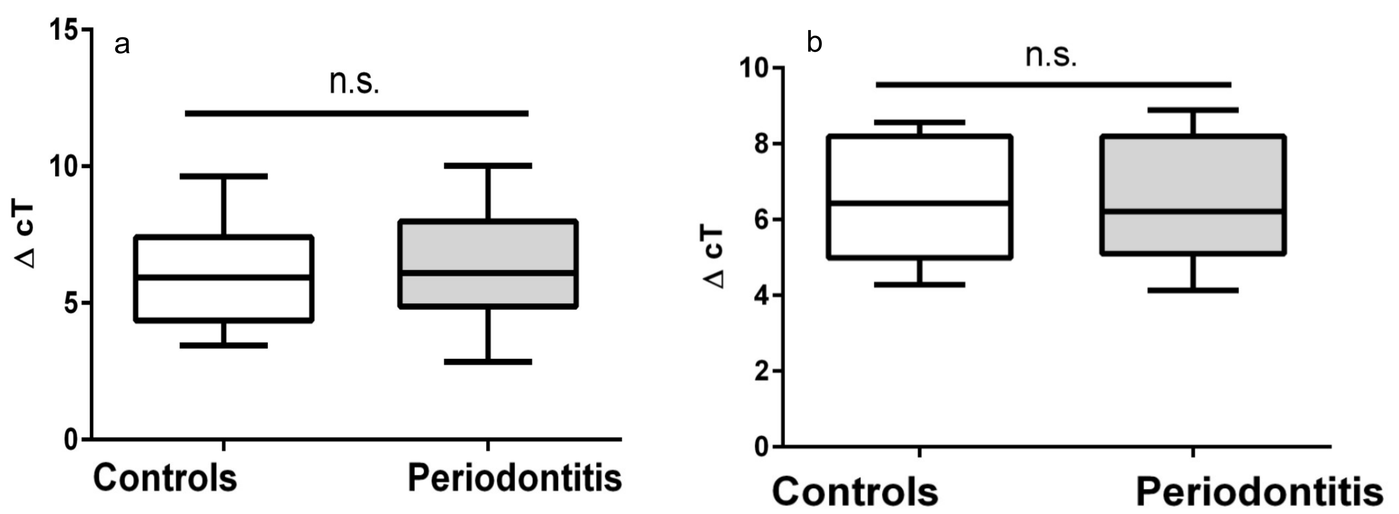

Figure 3a and 3b: Gingival mRNA expression in cases and controls
mRNA expression of HSD11b1 and HSD11b2 in periodontitis patients and healthy controls by delta cT values with beta actin (ACTB) serving as housekeeping gene. No significant changes in HSD11b1 ($p = 0.7984$) and HSD11b2 ($p = 0.7984$) expression were detected (Mann-Whitney *U*). Overall, thirteen samples were analysed (6 controls, 7 cases). n.s. = not significant.

summary

- With the use of qRT-PCR, this pilot study examined whether dysregulation of 11β-HSD isoforms contributes to the progression of periodontal disease.
- Our expression analysis did not show any significant alterations in 11β-HSD1 or 11β-HSD2 expression in periodontitis patients compared to healthy controls.
- These observations are congruent with the observations of 11β-HSD1 and 11β-HSD2 in rodents [8].
- However, recent findings from our laboratory (data not shown) indicate upregulation of 11β-HSD1 in gingival tissue of peri-implantitis patients.

References

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