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Interleukin-4RA 1902 A/G polymorphism in relation to aggressive and chronic periodontitis

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Bonn

Introduction

Both, IL-4 and IL-13 (Fig. 1) can bind on the α-chain of the IL4 receptor (1). The IL-4 RA1902 A/G (rs 1801275) polymorphism lead to an amino acid exchange at position 551 (Q551T) (2) of the intracellular component of the Rα chain and was found associated with a more Th2 type of immune response (3). Since the IL-4 RA 1902 A/G polymorphism influence IL-4 and IL-13 signalling and given the fact that both cytokines are important in the pathogenesis of periodontitis at all it would be interesting to evaluate whether the 1902 IL-4RA SNP is also associated with periodontitis or indicative for an infection with periodontopathogens.

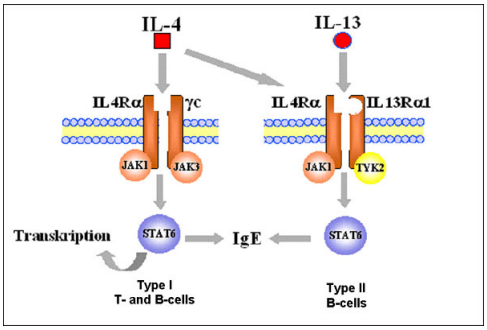

Fig. 1: IL-4 receptor complex (with friendly authorization Philip Deindl, Dissertation, Berlin 2005)

Objectives

Our hypothesis is that the IL-4RA polymorphism could be a putative risk indicator for periodontitis or an infection with periodontopathogens. Following three aims were pursued in this study:

1. Determination of allele and genotype frequencies of the IL-4RA -1902 A/G polymorphism in patients with periodontitis in comparison to periodontitis-free controls
2. Association of the IL-4RA polymorphism to the subgingival occurrence of five periodontopathic bacteria
3. Calculation of adjusted Odds ratios (OR) with respect to the cofactors age, gender, smoking, pocket depth and plaque index.

Material and Methods

Study groups
121 patients with severe periodontitis (attachment loss >4mm in 80% of the teeth); CP: n=53, mean age 48,9±9,8 years, females 59,2%; AP: n=67, mean age 41±9,9 years, females 65,7%) and 81 individuals without periodontitis (Controls: mean age 46,9±10,7 years, females 53,1%) were included.

Proof of 5 periodontopathic bacteria
Microbial samples were taken from the deepest pocket of each quadrant by an insertion of a sterile paper point for 20 seconds. The analyses for A. actinomycetemcomitans, P. gingivals, P. intermedia. T. forsythia, and T. denticola were carried out using the micro-Ident® test (Hain Lifescience, Nehren, Germany).

Proof of IL-4 promoter polymorphism and statistical analysis
The IL-4RA 1902 A/G SNP was analyzed by PCR-SSP (CTS-Kit, Heidelberg, Germany). Distributions of single alleles and genotypes were calculated by Chi²-Test with Yates correction or Fisher's exact test. Risk factor analyses were carried out by logistic regression with respect of established cofactors for periodontitis such as age, gender, smoking status, pocket depth and plaque index.

Results

Allele frequencies
The frequency of the mutant allele G was significantly increased among patients with CP and the total (AP+CP) patient group (Fig. 2)

Genotype frequencies
Genotypes with the mutant allele G (AG+GG) occurred significantly more frequently among patients with CP and the total (CP+AP) patient group (Fig. 3) compared with controls.

Relation to five periodontopathic bacteria
Among both, the total study cohort and the control group T. forsythia occurred more frequently in individuals who expressed the mutant genotypes AG+GG (Fig. 4)

Risk analysis with binary logistic regression
Carriers who expressed genotypes with the allele G (AG+GG) have an increased adjusted odds ratio for CP (OR=2,97 95%CI 1,4-6,5) and severe periodontitis (AP+CP)(OR=2,15 95%CI 1,2-4,0). Fur-thermore, among the control group the mutant genotypes AG+GG were associated with a an increased adjusted odds ratio for an infection with T. forsythia (OR=5,87 95%CI 1,4-24,7).

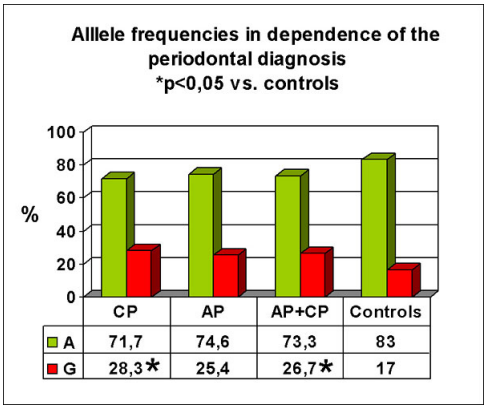

Fig. 2: Allele frequencies in dependence of the periodontal diagnosis *p<0.05

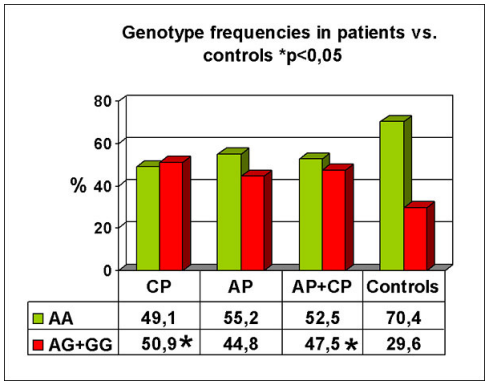

Fig. 3: Genotype frequencies in patients vs. controls *p<0.05

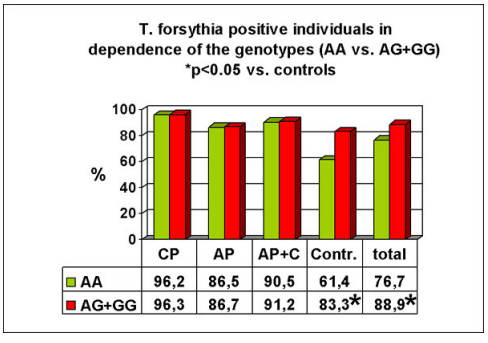

Fig. 4: T. forsythia positive individuals in dependence of the genotypes AA vs. AG+GG. *p<0.05

Conclusions

The IL-4RA 1902 A/G polymorphism is indicative for severe chronic periodontitis and a putative risk indicator for severe periodontitis in general. Moreover, genotypes with the mutant allele G predispose individuals for a subgingival infection with T. forsythia.

Literature

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2. G. K. Hershey, M. F. Friedrich, L. A. Esswein, Thomas M.L. and T. A. Chatila, The association of atopy with a gain-of-function mutation in the alpha subunit of the interleukin-4 receptor, N Engl J Med 337 (24) (1997), pp.1720-1725.
3. J. Youn, S. H. Hwang, C. S. Cho, J. K. Min, W. U. Kim, S. H. Park et al., Association of the interleukin-4 receptor alpha variant Q576R with Th1/Th2 imbalance in connective tissue disease, Immunogenetics 51 (8-9) (2000), pp. 743-746.

Abbreviations

AP: aggressive periodontitis
CP: chronic periodontitis
IL: interleukin
IL-4RA: interleukin 4 receptor alpha

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Poster Faksimile:

P 19
Periodontology

Interleukin-4RA 1902 A/G polymorphism in relation to aggressive and chronic periodontitis

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INTRODUCTION

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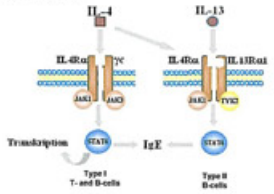

Fig. 1 IL-4 receptor complex (with friendly authorization Philip Deindl, Dissertation, Berlin 2005)

AIMS

- Determination of allele and genotype frequencies of the IL-4RA -1902 A/G polymorphism in patients in comparison to controls
- Association of the IL-4RA polymorphism to the subgingival proof of five periodontopathic bacteria
- Calculation of adjusted Odds ratios (OR) with respect to the cofactors age, gender, smoking, pocket depth and plaque index.

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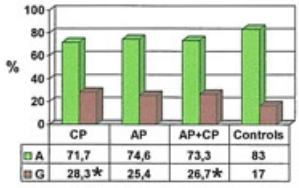
RESULTS

Allele frequencies

The frequency of the mutant allele G was significantly increased among patients with CP and the total (AP+CP) patient group (Fig. 2)

Fig. 2 Allele frequencies in dependence of the periodontal diagnosis
***p<0,05 vs. controls**

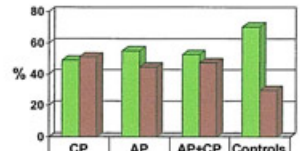


	CP	AP	AP+CP	Controls
A	71,7	74,6	73,3	83
G	28,3*	25,4	26,7*	17

Genotype frequencies

Genotypes with the mutant allele G (AG+GG) occurred significantly more frequently among patients with CP and the total (CP+AP) patient group (Fig. 3) compared with controls.

Fig. 3 Genotype frequencies in patients vs. controls *p<0,05

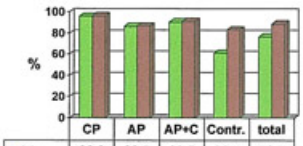


	CP	AP	AP+CP	Controls
AA	49,1	55,2	52,5	70,4
AG+GG	50,9*	44,8	47,5*	29,6

Relation to five periodontopathic bacteria

Among both, the total study cohort and the control group *T. forsythia* occurred more frequently in individuals who expressed the mutant genotypes AG+GG (Fig. 4)

Fig. 4 T. forsythia positive individuals in dependence of the genotypes (AA vs. AG+GG)
***p<0.05 vs. controls**



	CP	AP	AP+C	Contr.	total
AA	96,2	86,5	90,5	61,4	76,7
AG+GG	96,3	86,7	91,2	83,3*	88,9*

Risk analysis with binary logistic regression

Carriers who expressed genotypes with the allele G **(AG+GG)** have an increased adjusted odds ratio for **CP (OR=2,97 95%CI 1,4-6,5)** and severe periodontitis **(AP+CP)(OR=2,15 95%CI 1,2-4,0).** Furthermore, among the control group the mutant genotypes **AG+GG** were associated with a an increased adjusted odds ratio for an infection with ***T. forsythia* (OR=5,87 95%CI 1,4-24,7).**

CONCLUSIONS

The IL-4RA 1902 A/G polymorphism is indicative for severe chronic periodontitis and a putative risk indicator for severe periodontitis in general. Moreover, genotypes with the mutant allele G predispose individuals for a subgingival infection with *T. forsythia*.

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