International Poster Journal IPJ of Dentistry and Oral Medicine

Int Poster J Dent Oral Med 2010, Vol 12 No 2, Poster 488

Interleukin-4 promoter polymorphisms in patients with aggressive or chronic periodontitis

Language: English

Authors:
PD Dr. med. dent. Stefan Reichert, Dr. med. dent. Jana Klapproth, Dr. med. dent. Uta Zimmermann, Prof. Dr. Hans-Günter Schaller, Dr. rer. nat. Susanne Schulz,
Martin-Luther-University Halle-Wittenberg, Dep. of Operative Dentistry and Periodontology, Halle (Saale), Germany
Dr. rer. nat. Helmut KG.Machulla,
Martin-Luther-University Halle-Wittenberg, Dep. Ghatt, Interbranch HLA Laborartory, Halle (Saale), Germany
Yvonne Reichert,
Private Dental Department, Halle (Saale), Germany
PD Dr. med. dent. Jamal M. Stein,
RWTH Aachen, Dep. of Operative Dentistry, Periodontology and Preventive Dentistry, Aachen, Germany
Dr. rer. nat. Christiane Gläser,
Martin-Luther-University Halle-Wittenberg, Institute of Human Genetics and Medical Biology, Halle (Saale), Germany

Date/Event/Venue:
November 4th-7th, 2009
Deutscher Zahnärztetag
München, Germany

Introduction

In periodontitis susceptibility individuals, disease progression involves a predominantly Th2-like immune response (1). IL-4 stimulates a Th2-type of immune response while inhibits Th1 cells (2,3). Moreover, IL-4 limits the persistence of macrophages in periodontitis lesions and down regulates CD14 receptor, one of the key receptors for lipopolysaccharides (4).

Objectives

Promoter polymorphisms of the interleukin-4 gene have been associated with altered IL-4 production (5-7). Thus, they could be indicative for periodontitis. Therefore, the aim of this study was to determine allele- genotype- and haplotype- frequencies of IL-4 SNPs at positions -1098T/G, -590C/T and -33C/T in patients with generalized aggressive (AP) or generalized chronic periodontitis (CP) in comparison to periodontitis free controls.Calculation of adjusted Odds ratios (OR) were carried out with respect to established cofactors for periodontitis such as age, gender, smoking, and plaque index.

Material and Methods

Study groups
121 patients with sever periodontitis (attachment loss >4mm in 80% of the teeth; CP: n=54, mean age 49,3 ±10.0 years; AP: n=67, mean age 41 ±9.9 years) and 81 individuals without periodontitis (Controls:mean age 46,9 ±10.7 years) were included.

Proof of IL-4 promoter polymorphisms
IL-4 SNPs were analyzed by PCR-SSP (CTS-Kit, Heidelberg, Germany). Distributions of single alleles, genotypes, and haplotypes were calculated by Chi^2-Test with Yates correction or Fisher's exact test. Risk factor analyses were carried out by logistic regression under consideration of established cofactors for periodontitis such as age, gender, smoking status, and plaque index.

Results

Allele frequencies
The mutant allele G at position -1098 was significantly increased among both patient groups. The mutant alleles -590 T und -33 T were more frequently proven only among patients with AP (Fig. 1)

Genotype frequencies
The mutant genotype -1098 TG was significantly increased among both patient groups (Fig. 2). Moreover, the mutant genotypes -590 CT and -33 CT were likewise significantly increased (linkage disequilibrium!) among patients with AP (Fig. 3 and 4).

Haplotype frequencies
Among both, patients with AP and CP the mutant haplotype -1098, -590, -33 GCC was significantly increased. Moreover, the haplotype -1098, -590, -33 TTT was significantly more proven only among patients with AP (Fig. 5).

Risik analysis with binary logistical regression
The haplotype -1098,-590,-33 GCC increased the adjusted OR for AP and CP. Mutations (C>T) at positions -590 and -33 were indicative only for AP (Fig. 6).

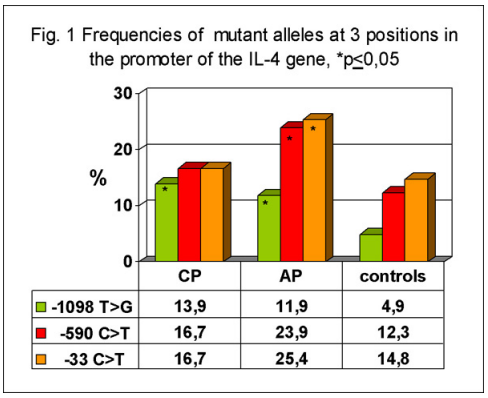


Fig. 1

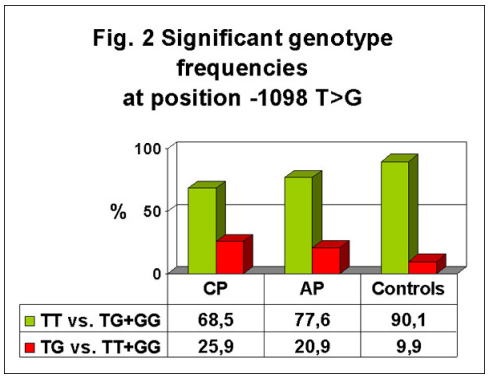


Fig. 2

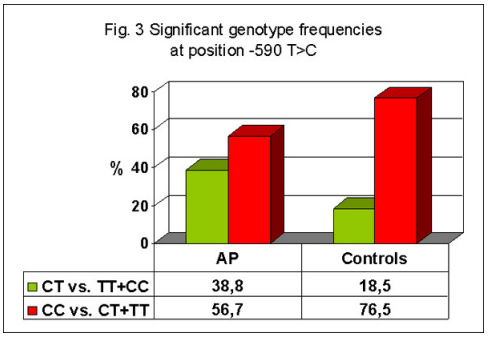


Fig. 3

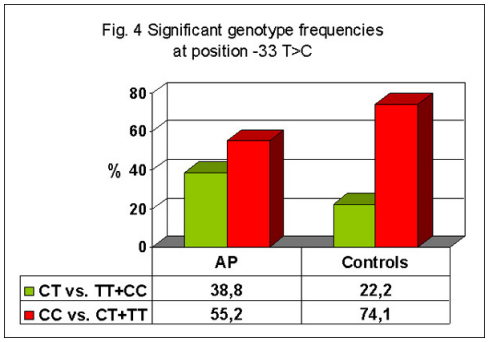


Fig. 4

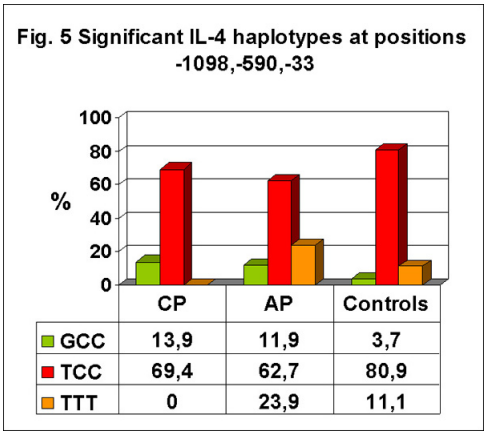


Fig. 5

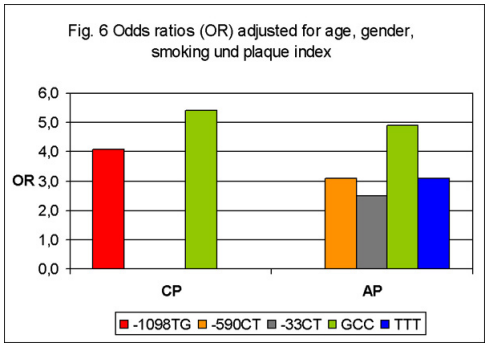


Fig. 6

Conclusions

Genotypes and haplotypes who expressed the mutant allele G at position -1098 were indicative for both, CP and AP. Polymorphisms (C>T) at positions -590 and -33 (high interleukin-4 producer genotypes) increased the Odds ratio for an AP. In a further study it would be useful to investigate the IL-4 production in association to IL-4 polymorphisms.

Literature

1. Seymour GJ, Gemmell E, Reinhardt RA, Eastcott J, Taubman MA. Immunopathogenesis of chronic inflammatory periodontal disease: cellular and molecular mechanisms. J Periodontal Res1993;28:478-486.
2. Yamazaki K, Nakajima T, Hara K. Immunopathogenesis of chronic inflammatory periodontal diseases: Cellular and molecular mechanisms. Clin Exp Immunol 1995;99:384-391.
3. Gemmell E, Marshall RI, Seymour GJ. Cytokines and prostaglandins in immune homeostasis and tissue destruction in periodontal disease. Periodontol 2000 1997;14:112-143.
4. Shapira L, van Dyke TE, Hart TC. A localized absence of interleukin-4 triggers periodontal disease activity: a novel hypothesis. Med Hypotheses 1992;39:319-322.
5. Rosenwasser LJ, Klemm DJ, Dresback JK, Inamura H, Mascali JJ, Klinnert M, Borish L. Promoter polymorphisms in the chromosome 5 gene cluster in asthma and atopy. Clin Exp Allergy 1995;25 Suppl 2:74-78.
6. Rosenwasser LJ, Borish L. Genetics of atopy and asthma: the rationale behind promoter-based candidate gene studies (IL-4 and IL-10). Am J Respir Crit Care Med 1997;156:152-155.
7. Nakashima H, Miyake K, Inoue Y, Shimizu S, Akahoshi M, Tanaka Y, Otsuka T, Harada M. Association between IL-4 genotype and IL-4 production in the Japanese population. Genes Immun 2002;3:107-109.

Abbreviations

AP = aggressive periodontitis
CP = chronic periodontitis
IL = interleukin
Th = T helper cells
PCR-SSP = polymerase chain reaction with sequence specific primers

This Poster was submitted by PD Dr. med. dent. Stefan Reichert.

Correspondence address:
PD Dr. med. dent. Stefan Reichert
Martin-Luther-University Halle-Wittenberg
Dep. für Zahnerhaltungskunde und Parodontologie
Große Steinstrasse 19
06108 Halle (Saale), Germany

Poster Faksimile:

P 15
Periodontology

Interleukin-4 promoter polymorphisms in patients with aggressive or chronic periodontitis

S Reichert[1], HKG Machulla[2], J Klapproth[1], U Zimmermann[1], Y Reichert[3], J Stein[4], CH Gläser[5], HG Schaller[1], S Schulz[1]
[1]Department of Operative Dentistry and Periodontology, Martin-Luther-University Halle-Wittenberg
[2]Interbranch HLA Laboratory, Department GHATT, Martin-Luther-University Halle-Wittenberg
[3]private dental department Halle (Saale)
[4]Department of Operative Dentistry, Periodontology and Preventive Dentistry, RWTH Aachen
[5]Institute of Human Genetics and Medical Biology, Martin-Luther-University Halle-Wittenberg

INTRODUCTION

IL-4 stimulates a Th2-type of immune response while inhibits Th1 cells. For example, IL-4 limits the persistence of macrophages in periodontitis lesions and down regulates CD14 receptor, one of the key receptors for lipopolysaccharides. Promoter polymorphisms of the interleukin-4 gene have been associated with altered IL-4 production. Thus, they could be indicative for periodontitis.

AIMS

- Determination of allele- genotype- and haplotype-frequencies of IL-4 SNPs at positions -1098T/G, -590C/T and -33C/T in patients with generalized aggressive (AP) or generalized chronic periodontitis (CP)
- Calculation of adjusted Odds ratios (OR) with respect to the cofactors age, gender, smoking, and plaque index.

MATERIAL UND METHODS

Study groups

121 patients with sever periodontitis (attachment loss ≥4mm in 80% of the teeth; CP: n=54, age 49,3 years; AP: n=67, age 41 years) and 81 individuals without periodontitis (Controls: age 46,9 years) were included.

Proof of IL-4 promoter polymorphisms

IL-4 SNPs were analyzed by PCR-SSP (CTS-Kit, Heidelberg, Germany). Distributions of single alleles, genotypes, and haplotypes were calculated by Chi²-Test with Yates correction or Fisher's exact test. Risk factor analyses were carried out by logistic regression under consideration of established cofactors for periodontitis such as age, gender, smoking status, and plaque index.

RESULTS

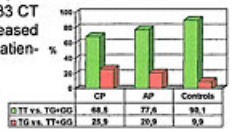
Allele frequencies

The mutant allele G at position -1098 was significantly increased among both patient groups. The mutant alleles -590 T und -33 T were more frequently proven only among patients with AP (Fig. 1)

Genotype frequencies

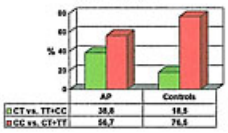
The mutant genotype -1098 TG was significantly increased among both patient groups (Fig. 2). Moreover, the mutant genotypes -590 CT and -33 CT were likewise significantly increased (linkage disequilibrium!) among patients with AP (Fig. 3 and 4).

Abb. 2 Significant genotype frequencies at position -1098 T>G



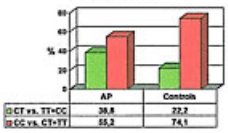
	CP	AP	Controls
TT vs. TG+GG	48,5	77,6	90,1
TG vs. TT+GG	25,9	20,9	9,9

Fig. 3 Significant genotype frequencies at position -590 T>C



	AP	Controls
CT vs. TT+CC	38,8	18,5
CC vs. CT+TT	56,7	76,5

Fig. 4 Significant genotype frequencies at position -33 T>C

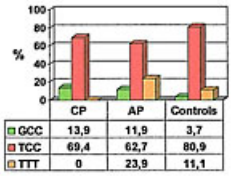


	AP	Controls
CT vs. TT+CC	38,8	22,2
CC vs. CT+TT	55,2	74,1

Haplotype frequencies

Among both, patients with AP and CP the mutant haplotype -1098, -590, -33 GCC was significantly increased. -1098, -590, -33 **TTT** was significantly more proven only among patients with AP (Fig. 5)

Fig. 5 Significant IL-4 haplotypes at positions -1098,-590,-33

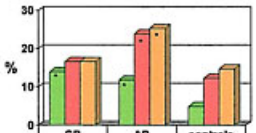


	CP	AP	Controls
GCC	13,9	11,9	3,7
TCC	69,4	62,7	80,9
TTT	0	23,9	11,1

Risik analysis with binary logistical regression

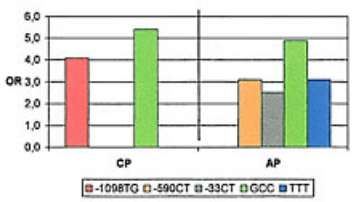
The haplotype -1098,-590,-33 GCC increased the adjusted OR for AP and CP. Mutations at positions -590 and -33 were indicative only for AP (Fig. 6).

Fig. 1 Frequencies of mutant alleles at 3 positions in the promoter of the IL-4 gene, *p≤0,05



	CP	AP	controls
-1098 T>G	13,9	11,9	4,9
-590 C>T	16,7	23,9	12,3
-33 C>T	16,7	25,4	14,8

Fig. 6 Odds ratios (OR) adjusted for age, gender, smoking und plaque index



CONCLUSIONS

Genotypes and haplotypes who expressed the mutant allele G at position -1098 were indicative for both, CP and AP. Polymorphisms at positions -590 and -33 (high interleukin-4 producer genotypes) increased the Odds ratio for an AP. In a further study it would be useful to investigate the IL-4 serum levels in association to IL-4 polymorphisms.

stefan.reichert@medizin.uni-halle.de, DEUTSCHER ZAHNÄRZTETAG, Munich 2009