Table3. Logistic regression analysis of baseline variables in subjects who did or did not exhibit additional attachment loss of 3mm or more at 1 or more sites over 2 years

Variables	Coefficients	S.E..	P value	Odds ratio	95% CI
Attachment level (0:<6 mm 1:≧6 mm)	3.28	0.578	***	2.288	1.395-3.753
Smoking habit (0:No 1:Yes)	2.64	1.869	**	3.741	1.404-9.960
Gender (0:Female 1:Male)	0.394	0.285	NS	1.107	0.667-1.834
Remaining teeth (0:≧20 1:<20)	-0.339	0.228	NS	0.919	0.565-1.494

Dependent variable: Additional attachment loss 0:Absent 1: Present
Subjects : N=389
Pseudo R^2 : 0.0641
LRchi2 : 27.86
Prob > chi2 : 0.0000
*** : P<0.001 ** : P<0.01 NS : Not significant

FcγRⅢb-NA1/NA2遺伝子多型からみた高齢者歯周炎抵抗性の解析

A．宛名：分担研究者　斉藤　毅　殿

B．指定課題名：平成 12 年度医療技術評価総合研究事業
「高齢者の口腔保健と全身的な健康状態の関係についての総合研究」

C．研究課題名：「FcγRIIIb-NA1/NA2 遺伝子多型からみた高齢者歯周炎抵抗性の解析」

D．研究協力者：杉田典子、小林哲夫、山本幸司、宮崎秀夫、吉江弘正
新潟大学歯学部予防歯科学講座

E．研究目的：

高齢者においてもほとんど歯周組織破壊を示さない歯周炎抵抗性の高い個体は、歯周病原性細菌に対する防御反応において歯周炎感受性の個体よりも有利な遺伝的素因を持っている可能性があると考えられる。生体防御の第一線を担う好中球は FcγR レセプターを介して IgG 免疫複合体を貪食する。FcγRIIIb は好中球に特異的に発言し２つのアレル NA1、NA2 を有する。我々はこれまでに FcγRIIIb-NA2 保有者に成人性歯周炎再発頻度が有意に高いこと、さらに FcγRIIIb-NA1 を発現する好中球は NA2 に比較して IgG1 および IgG3 を介した *Porphromonas gingivalis* 貪食能が有意に高いことを示した。本研究では FcγRIIIb-NA1/NA2 遺伝子多型が歯周炎抵抗性に関与するか否かを明らかにする目的で 70 歳の高齢者を対象に歯周組織破壊の程度と FcγRIIIb 遺伝子多型を解析した。

F．研究方法：

8020 データバンク調査に伴い新潟市に住む 70 歳、80 歳全員（6629 人）に全身及び口腔の健康状態に関する質問票を郵送した。研究への協力に合意した 763 人が採血・歯周診査を含む一連の検査を受けた。70 歳の対象のうち、559 人について全検査結果が得られた。その中から糖尿病を有さない 309 人を無作為に選び FcγRIIIb-NA1/NA2 遺伝子型を決定した（Background control）。その内で 20 歯以上を有する非喫煙者について Probing attachment level（PAL）4mm 以上の部位が全体に占める割合が 5%以下の人を Periodontitis-resistant（P-resistant）群（46 人）、同 20 %以上の人を Periodontitis 群（73 人）と定義し比較した。FcγRIIIb-NA1/NA2 遺伝子型は末梢血より DNA を抽出しアレル特異的 PCR にて決定した。

G．研究結果・考察：

FcγRIIIb-NA1/NA2 遺伝子型分布の比較において P-resistant 群と Presiodontitis 群間に有意差が認められた（$p<0.05$、χ^2検定）。NA1 保有者率及びアレル頻度は P-resistant 群が Periodontitis 群に比較し優位に高かった（$p<0.05$、χ^2検定）。血清 IgG1、IgG3 濃度について P-resistant 群と Periodontitis 群間、および各群における FcγRIIIb-NA1/NA2 遺伝子型冠で有意差は認められなかった（$p>0.05$、Mann-Whitney U 検定）。

以上より FcγRIIIb-NA1 アレルは歯周炎抵抗性に関わるマーカーのひとつであるこ

とが示唆された。

H．結論：

8020データバンク調査に伴い新潟市に住む70歳、80歳の中で、研究への協力に合意した763人が採血・歯周診査を含む一連の検査を受けた。20歯以上を有する非喫煙者についてProbing attachment level(PAL)4mm以上の部位が全体に占める割合が5%以下の人をPeriodontitis-resistant (P-resistant)群(46人)、同20%以上の人をPeriodontitis群（73人）と定義し比較した。その結果、FcγRIIIb-NA1/NA2遺伝子型分布の比較においてP-resistant群とPresiodontitis群間に有意差が認められた（$p<0.05$、χ^2検定)。FcγRIIIb-NA1アレルは歯周炎抵抗性に関わるマーカーのひとつであることが示唆された。

I．研究発表論文：

投稿原稿

Increased Frequency of FcγRIIIb-NA1 Allele in Periodontitis-Resistant Subjects in Elderly Japanese Population

N. Sugita[1], T. Kobayashi[1], Y. Ando[2], A. Yoshihara[2], K.Yamamoto[1], J.G.J. van de Winkel[3,4], H. Miyazaki[2], and H. Yoshie[1]*

[1]Department of Periodontology, [2]Department of Preventive Dentistry, Faculty of Dentistry, Niigata University, Niigata, Japan; [3]Laboratory for Immunotherapy, Department of Immunology and [4]Genmab, University Medical Center Utrecht, The Netherlands.

*Corresponding author:

Prof. Dr. Hiromasa Yoshie,

Department of Periodontology, Faculty of Dentistry, Niigata University,

Gakko-cho 2-5274, Niigata 951-8514, Japan

Phone: (+81)25-227-2869

Fax: (+81)25-227-0808

E-mail: yoshie@dent.niigata-u.ac.jp

Short title: **FcγRIIIb Genotype in Periodontitis-Resistant Group**

Key words: **FcγRIIIb, Polymorphism, Periodontitis-Resisitant**

ABSTRACT

Elderly people showing minimum periodontal tissue destruction exist, which might be partly due to genetic advantages in host immune response against periodontopathic bacteria. The human IgG Fc receptor IIIb on neutrophils bears a NA1-NA2 polymorphism. The FcγRIIIb-NA1 displays a more efficient interaction with IgG1- and IgG3-opsonized bacteria, compared with the FcγRIIIb-NA2. We investigated a Japanese 70-year-old population (n=599) to determine whether the FcγRIIIb polymorphism was associated with resistance to periodontitis. Among subjects with ≥20 present teeth, periodontitis-resistant (n=46) and periodontitis-susceptible groups (n=73) were selected based on the percentage of sites with ≥4mm probing attachment loss in the entire dentition. The FcγRIIIb-NA1 allotype was over-represented in the periodontitis-resistant group, compared with the periodontitis-susceptible group (χ^2=4.89, p=0.03, Odd's ratio=1.87, 95%CI, 1.07 to 3.28). This suggests FcγRIIIb-NA1 may be associated with resistance to periodontitis.

INTRODUCTION

Periodontitis occurs at a high prevalence in adults and is the major cause of tooth loss (Brown *et al.*, 1989). Nevertheless, elderly people who show minimum periodontal tissue destruction certainly exist (Papapanou and Lindhe, 1992). The resistance to periodontitis might be explained by genetic components related to the immune host response against periodontopathic bacteria (Kornman *et al.*, 1997, Hart and Kornman, 1997).

Neutrophils play an important role in the control of periodontitis, and increased disease susceptibility is observed in patients with defective neutrophil production and/or function (Hart et al., 1994, Van Dyke et al., 1994, Kinane D, 1999). Neutrophils constitute approximately 90% of immunocompetent cells in gingival crevicular fluid. In addition, neutrophils are the first leukocytes that infiltrate inflammatory sites, and are also found in healthy gingival crevice (Sugita et al., 1993). Therefore, genetic polymorphisms that affect neutrophil effector function might be relevant for disease resistance.

Leukocyte receptors for the constant (or Fc-) part of immunoglobulins create an important link between humoral and cellular arms of the immune response, which are considered essential for host defense against bacteria. Of human IgG receptors (FcγR), three receptor subclasses have been shown functionally polymorphic (FcγRIIa-131R-H, FcγRIIIa-158V-F, FcγRIIIb-NA1-NA2) (Van de Winkel and Capel, 1993). FcγRIIIb is a neutrophil-specific receptor and has two alleles, NA1 and NA2. FcγRIIIb-NA1 neutrophils exhibit higher binding and phagocytic capacities of IgG1- and IgG3-opsonized bacteria than FcγRIIIb-NA2 neutrophils (Salmon *et al.*, 1990, Bredius *et al.*, 1994).

In our previous study, a significant over-representation of the FcγRIIIb-NA2 allotype was found in patients with recurrence of adult periodontitis compared with those without recurrence (Kobayashi *et al.*, 1997).

The definition of periodontitis-resistant individual is safer in elderly population than in younger one, since elderly subjects have most certainly already expressed their propensity towards periodontal attachment loss.

To determine whether the FcγRIIIb-NA1-NA2 polymorphism is associated with resistance to periodontitis, we compared FcγRIIIb-NA1-NA2 genotype distribution between

periodontitis-resistant and periodontitis-susceptible groups in a Japanese 70-year-old population.

MATERIALS AND METHODS

Subjects and clinical assessments

In 1998, we sent questionnaires to all 6629 residents of 70 or 80 years old in Niigata City (Japan) regarding their medical and dental health conditions in an oral health survey of elderly population by the Ministry of Health and Welfare of Japan.

Among them, 599 of 70 years old came to undergo the medical and dental examinations (screened population) with the signed informed consents to the protocol that was reviewed and approved by the Ethics Committee of Faculty of Dentistry, Niigata University. Clinical evaluations were performed on the following items (i) number of present teeth, (ii) probing pocket depth (PPD), (iii) probing attachment level (PAL), by four dentists who had been trained and the standardization of probing. PPD and PAL were assessed by Williams probe at six sites per tooth and recorded to the nearest millimeter.

From the screened population, 309 subjects with neither diabetes mellitus nor blood sugar ≥140mg/dl were randomly selected and determined FcγRIIIb-NA1/NA2 genotype (subjects included in the study).

Among the subjects included in the study, the periodontitis-resistant group was defined as having ≤5% of sites with a loss of ≥4mm in PAL in the entire dentition, whereas the periodontitis-susceptible group done as having ≥20% sites with a loss of ≥4mm in PAL. Both groups only included non-smokers with more than 20 teeth present.

The FcγRIIIb genotype of 87 healthy controls of 23-29 years old were published before (Kobayashi *et al.*, 1997) and used in this study for comparison with those of the subjects included in the study, and periodontitis-resistant subjects (healthy control group).

Determination of FcγRIIIb-NA1/NA2 genotype

Genomic DNA was isolated from peripheral blood (Easy-DNA kit; Invitrogen, San Diego, CA) and genotyped for FcγRIIIb-NA1-NA2 by allele-specific polymerase chain reaction as previously described (de Haas *et al.*, 1995, Kobayashi *et al.*, 1997).

Determination of serum IgG1 and IgG3 levels

Serum IgG1 and IgG3 concentrations were determined by one-step sandwich enzyme-linked immunosorbent assay (human IgG subclass profile ELISA kit; Zymed, San Francisco,

CA). The optical density of each well was read at 450nm (Multiscan Bichromatic; Labsystem, Helsinki, Finland) and analyzed with computer software GENESIS-LITE (Labsystem).

Statistical analysis

Mann-Whitney *U* test was used to compare the clinical parameters between the periodontitis-resistant and periodontitis-susceptible groups. The χ^2 or Fisher's exact probability test was used to compare the FcγRIIIb genotype distributions between the periodontitis-resistant and periodontitis-susceptible groups, between the periodontitis-resistant and healthy control groups, between the subjects included in the study and healthy control groups (3X2 contingency tables). The same tests were used to assess the role of FcγRIIIb-NA1 allele as a resistant marker for periodontitis in 2X2 contingency tables; the periodontitis-resistant *versus* periodontitis-susceptible groups, FcγRIIIb-NA1 carrier (subjects with at least one FcγRIIIb-NA1 allele) *versus* non-carrier; the periodontitis-resistant *versus* periodontitis-susceptible groups, and the absolute numbers of FcγRIIIb-NA1-NA2 alleles. Serum IgG1 and IgG3 levels were compared between the periodontitis-resistant and periodontitis-susceptible groups, and among FcγRIIIb genotypes in each group, by Mann-Whitney *U* test and Kruskal-Wallis test, respectively. Significance was set at 5%.

RESULTS

As shown in Table 1, periodontitis-resistant subjects exhibited fewer signs of periodontitis and more numbers of present teeth than periodontitis-susceptible subjects ($p<0.01$).

We found a significant difference in the FcγRIIIb genotype distribution between the periodontitis-resistant and periodontitis-susceptible groups (Fig. 1, Fisher's exact probability=0.02), and between the periodontitis-resistant and healthy control groups (Fisher's exact probability=0.03). FcγRIIIb genotype distribution did not differ between the subjects included in the study and healthy control groups ($\chi^2=1.52$, $p=0.47$). One subject included in the study was found to have no FcγRIIIb-NA1-NA2 gene.

We then assessed the relevance of FcγRIIIb-NA1 allele to resistance to periodontitis. There were significant over-representations of the NA1 carrier (Fisher's exact probability=0.02) and the FcγRIIIb-NA1 allele ($\chi^2=4.89$, $p=0.03$, Odd's ratio=1.87, 95%CI, 1.07 to 3.28) in the periodontitis-resistant group compared with the periodontitis-susceptible group (Table 2).

Serum IgG1 and IgG3 levels were neither significantly different between the periodontitis-resistant and periodontitis-susceptible group in each FcγRIIIb-NA1-NA2 genotype group, nor among the FcγRIIIb genotypes in each group (Table 3).

DISCUSSION

Efficient clearance of periodontopathic bacteria by neutrophils via IgG1 and IgG3-FcγRIIIb interactions may be crucial for the prevention of periodontitis. This hypothesis is supported by the following observations. FcγRIIIb is the predominant FcγR on neutrophils, which are present of high numbers in gingival crevicular fluid and subjacent to the apical part of the pocket epithelium (Sugita *et al.*, 1993, Yuan *et al.*, 1999). Serum samples from patients with periodontitis and gingivitis contain significant levels of IgG1 and IgG3 specific for periodontopathic bacteria (Ogawa *et al.*, 1990). In inflamed human gingiva and crevicular fluid, IgG1 represents the predominant subclass (Kinane, *et al.*, 1997). Previous studies showed the genetically determined polymorphism of FcγRIIIb, NA1 and NA2, to be associated with recurrence of adult periodontitis (Odd's ratio 4.3, 95% CI, 1.19 to 16.24), risk of early-onset periodontitis (Odd's ratio 2.0, 95% CI, 1.2-3.6) (Kobayashi *et al.*, 1997, 2000). This has been linked to a lower activity of FcγRIIIb-NA2 in neutrophil phagocytosis/induction of oxidative burst upon interaction with IgG1- and IgG3-opsonized *Porphyromonas gingivalis*. Phagocytic capacities of IgG1- and IgG3-opsonized *Porphyromonas gingivalis* by FcγRIIIb-NA1/NA1 neutrophils were 1.5-1.8 times higher compared with those of FcγRIIIb-NA2/NA2 neutrophils (Kobayashi *et al.*, 2000).

These findings suggested the FcγRIIIb-NA1-NA2 polymorphism to contribute to inter-individual differences in resistance to periodontitis. In the present study, we found a significant association between the FcγRIIIb-NA1 allele and periodontitis-resistance in elderly Japanese subjects. This is the first report suggesting a role for an FcγR allele as a resistance marker for periodontitis.

Recent study with the American Caucasian population documented FcγRIIIb-NA1-NA2 genotype not to be associated with susceptibility to adult periodontitis individually (van Shie *et al.*, 1998), suggesting several factors to underlie the discrepancy. In population association studies, differences in allele distributions among different ethnic populations affect significance of these alleles, as well as variance in definition for cases and controls (Gambaro *et al.*, 2000). Nevertheless, FcγRIIIb, of which functions and roles in periodontitis have demonstrated

previously, are expected to be reliable as a candidate genetic factor for resistance to periodontitis in Japanese.

Other polymorphisms than FcγRIIIb-NA1-NA2 have been recently shown to be risk factors for periodontitis as well. Composite IL-1A and IL-1B genotypes were important components influencing severity of adult periodontitis (severe *versus* mild periodontitis: Odd's ratio 18.9, 95% CI, 1.04 to 343) in non-smoker Caucasians (Kornman et al, 1997). FcγRIIIa 158V-F polymorphism was also associated with recurrence of periodontitis (Odd's ratio 5.06, 95% CI, 1.01 to 25.4) (Sugita *et al.*, 1999). Genetic polymorphisms of fMLP and vitamin D receptors have been shown to be associated with early-onset periodontitis (Gwinn *et al.*, 1999, Hennig *et al.*, 1999). There is a possibility that certain alleles of these genes might be associated with resistance to periodontitis. Further studies in the periodontitis-resistant subjects selected by identical criteria would also confirm the reliability of these genes as risk factors of the disease.

"Periodontitis-resistant" subjects have earlier been defined in various ways (Papapanou and Lindhe, 1992, Payne *et al.*, 1993, Heasman *et al.*, 1998). In this study, we chose to restrict the age of subjects to 70 years to better allow a precise definition of and comparison between the periodontitis-resistant and periodontitis-susceptible groups. Subjects with teeth number less than 20 were excluded, because causes (and time) of teeth loss were not clear. Smokers and diabetes patients, known to be high-risk subjects for periodontitis, were also not included (Genco, 1996).

We also re-classified periodontitis-resistant and periodontitis-susceptible subjects using only PAL of interproximal sites, considering the existence of periodontitis-resistant subjects with a great deal of facial recession. This change of database moved no subject from periodontitis-susceptible group to periodontitis-resistant group.

FcγRIIIb-NA1-NA2 genotype distribution in the subjects included in the study was similar to that of the healthy control group and another Japanese population (Hatta *et al.*, 1999) (χ^2 test, $p>0.05$), which supported the subjects included in the study to have minimum sampling bias concerning the FcγRIIIb-NA1-NA2 genotype distribution.

Comparable levels of serum IgG1 and IgG3 between the periodontitis-resistant and periodontitis-susceptible groups, and among FcγRIIIb-NA1-NA2 genotypes suggested that the

relationship between FcγRIIIb genotype and resistance to periodontitis could not be attributed to differences in serum levels of IgG1 and IgG3 in the patient groups.

In summary, our results support the FcγRIIIb-NA1-NA2 polymorphism may be associated with periodontitis-resistance in Japanese subjects. Further studies should be undertaken to confirm these observations in different ethnic backgrounds. Identification of genetic markers for disease resistance will be important for the development of new strategies for diagnosis, prevention and therapy of periodontitis.

ACKNOWLEDGMENTS

The authors are indebted to Dr. Nobuhiro Hanada, Department of Oral Science, National Institutes of Infectious Diseases, Tokyo, Japan, for kindly providing serum samples, Drs. Hiroshi Ogawa, Naoko Saito, Toshinobu Hirotomi, and Takayuki Yamaga, Department of Preventive Dentistry, for dental and periodontal clinical examinations, and Dr. Akira Miyazaki, Department of Periodontology, Faculty of Dentistry, Niigata University, for preparation of blood samples.

This work was supported by a grant-in-aid from the Ministry of Health and Welfare of Japan (H10-Iryo-001), a Grant for Development of Advanced Medical Technology and No.10470457, 10307053, 11307051 from the Ministry of Education, Science, Sports and Culture of Japan, and the Fund for Scientific Promotion of Tanaka Industries Co. Ltd., Niigata, Japan.

REFERENCES

Bredius RGM, Fijen CAP, de Haas M, Kuijper EJ, Weening RS, van de Winkel JGJ, *et al.* (1994). Role of neutrophil FcγRIIa (CD32) and FcγRIIIb (CD16) polymorphic forms in phagocytosis of human IgG1- and IgG3-opsonized bacteria and erythrocytes. *Immunology* 83:624-630.

Brown LJ, Oliver RC, Loe H (1989). Periodontal disease in the US in 1981: prevalence, severity, extent, and role in tooth mortality. *J Periodontol* 60:363-370.

De Haas M, Kleijer M, van Zwieten R, Roos D, von dem Borne AEGK (1995). Neutrophil FcγRIIIb deficiency, nature and clinical consequences: a study of 21 individuals from 14 families. *Blood* 86:2403-2413.

Gambaro G, Anglani F, D'Angelo A (2000). Association studies of genetic polymorphisms and complex disease. *Lancet* 355:308-311.

Genco RJ (1996). Current view of risk factors for periodontal diseases. *J Periodontol* 67:1041-1049.

Gwinn MR, Sharma A, De Nardin E (1999). Single nucleotide polymorphisms of the N-formyl peptide receptor in localized juvenile periodontitis. *J Periodontol* 70:1194-1201.

Hart TC, Shapira L, Van Dyke TE (1994). Neutrophil defects as risk factors for periodontal diseases. *J Periodontol* 65:521-529.

Hart TC, Kornman KS. (1997). Genetic factors in the pathogenesis of periodontitis. *Periodontology 2000* 14:202-215.

Hatta Y, Tsuchiya N, Ohashi J, Matsushita M, Fujiwara K, Hagiwara K, *et al.* (1999). Association of Fcγ receptor IIIB, but not of Fcγ receptor IIA and IIIA, polymorphisms with systemic lupus erythematosus in Japanese. *Genes and Immunity* 1:53-60.

Heasman PA, Lauffart BL, Preshaw PM (1998). Crevicular fluid prostaglandin E_2 levels in periodontitis-resistant and periodontitis-susceptible adults. *J Clin Periodontol* 25:1003-1007.

Hennig BJW, Parkhill JM, Chapple ILC, Heasman PA, Taylor JJ (1999). Association of a vitamine D receptor gene polymorphism with localized early-onset periodontal diseases. *J Periodontol* 70:1032-1038.

Kinane DF, Takahashi K, Mooney J (1997). Crevicular fluid and serum IgG subclasses and corresponding mRNA expressing plasma cells in periodontitis lesions. *J Periodont Res* 32: 176-178.

Kinane DF (1999). Blood and lymphoreticular disorders. *Periodontology 2000* 21:84-93.

Kobayashi T, Westerdaal NAC, Miyazaki A, van der Pol W-L, Suzuki T, Yoshie H, *et al.* (1997). Relevance of immunoglobulin G Fc receptor polymorphism to recurrence of adult periodontitis in Japanese patients. *Infect Immun* 65:3556-3560.

Kobayashi T, van der Pol W-L, Sugita N, Westerdaal NAC, Yoshie H, Horigome T, *et al.* (2000). Relevance of IgG receptor IIIb (CD16) polymorphism to handling of *Porphyromonas gingivalis*: Implications for the pathogenesis of adult periodontitis. *J Periodont Res* 35:65-73.

Kobayashi T, Sugita N, van der Pol W-L, Nunokawa Y, Westerdaal NAC, Yamamoto K, *et al.* (2000). The Fcγ receptor genotype as a risk factor for generalized early-onset periodontitis in Japanese patients. *J Periodontol* 71:1425-1432.

Kornman KS, Crane A, Wang H-Y, di Giovine FS, Newman MG, Pirk FW, *et al.* (1997). The interleukin-1 genotype as a severity factor in adult periodontal disease. *J Clin Periodontol* 24:72-77.

Ogawa T, Kusumoto Y, Hamada S, McGhee JR, Kiyono H (1990). *Bacteroides gingivalis*-specific serum IgG and IgA subclass antibodies in periodontal diseases. *Clin Exp Immunol* 82:318-325.

Papapanou PN, Lindhe J (1992). Preservation of probing attachment and alveolar bone levels in 2 random population samples. *J Clin Periodontol* 19:583-588.

Payne JB, Peluso Jr JF, Nichols FC (1993). Longitudinal evaluation of peripheral blood monocyte secretory function in periodontitis-resistant and periodontitis-susceptible patients. *Archs oral Biol* 38:309-317.

Salmon JE, Edberg JC, Kimberly RP (1990). Fcγ receptor III on human neutrophils. Allelic variants have functionally distinct capacities. *J Clin Invest* 85:1287-1295.

Sugita N, Suzuki T, Yoshie H, Yoshida N, Adachi M, Hara K (1993). Differential expression of CR3, FcεRII and FcγRIII on polymorphonuclear leukocytes in gingival crevicular fluid. *J Periodont Res* 28:363-372.

Sugita N, Yamamoto K, Kobayashi T, van der Pol W-L, Horigome T, Yoshie H, *et al.* (1999). Relevance of FcγRIIIa-158V-F polymorphism to recurrence of adult periodontitis in Japanese patients. *Clin Exp Immunol* 117:350-354.

Yuan Z-N, Schreurs O, Gjermo P, Helgeland K, Schenck K (1999). Topical distribution of FcγRI, FcγRII and FcγRIII in inflamed human gingiva. *J Clin Periodontol* 26:441-447.

Van de Winkel JGJ, Capel PJA (1993). Human IgG Fc receptor heterogeneity: molecular aspects and clinical implications. *Immunol Today* 14:215-221.

Van Dyke TE, Vaikuntam J (1994). Neutrophil function and dysfunction in periodontal disease. *Curr Opin Periodontol* 19-27

Van Schie RC, Grossi SG, Dunford RG, Wilson ME, Genco RJ (1998). Fcγ receptor polymorphisms are associated with periodontitis. *J Dent Res* 77:648 (abstract).

Table 1. Biographical and periodontal characteristics of each subject group.

Parameters[a]	Screened population (n=599)	Subjects included in the study[b] (n=309)	Periodontitis-resistant group[c] (n=46)	Periodontitis-susceptible group[c] (n=73)
Male/Female	306/293	157/152	11/35	41/32
Smokers (%)	18.7	19.7	None	None
Subjects under medical treatment for diabetes (%)	5.0	None	None	None
Subjects with blood sugar≥140mg/dl (%)	7.0	None	None	None
Edentulous subjects (%)	7.5	12.9	None	None
Number of present teeth (mean±SE)	17.4±0.4	18.3±0.6	26.4±0.4[d]	24.6±0.3
Subjects with ≥20 present teeth (%)	49.6	68.9	All	All
Probing pocket depth, PPD mm (mean±SE)	2.03±0.03	2.00±0.04	1.61±0.04[e]	2.19±0.07
Probing attachment level, PAL mm (mean±SE)	3.10±0.05	3.04±0.08	1.85±0.03[e]	3.45±0.08
Percent of sites (mean±SE):				
PPD ≤3mm	89.6±0.6	90.4±1.0	98.7±0.2[e]	87.3±1.5
PPD 4-5mm	8.7±0.5	7.9±0.7	1.3±0.2[e]	10.7±1.2
PPD ≥6mm	1.6±0.2	1.7±0.4	0.1±0.03[d]	1.5±0.4
PAL ≤3mm	68.3±1.1	70.1±1.7	97.8±0.2[e]	57.3±2.4
PAL 4-5mm	23.9±0.8	22.3±1.2	2.1±0.2[e]	34.9±1.6
PAL ≥6mm	7.8±0.6	7.7±1.1	0.1±0.05[e]	7.7±1.2

[a] All clinical parameters contained third molars.

[b] Subjects included in the study were selected from screened population independently of periodontal conditions.

[c] Periodontitis-resistant and periodontitis-susceptible groups were selected from subjects included in the study with ≥20 teeth, as follows:

Periodontitis-resistant group was defined as subjects having ≤5% of sites with loss of ≥4mm in PAL in the entire dentition.

Periodontitis-susceptible group was defined as subjects having ≥20% sites with loss of ≥4mm in PAL in the entire dentition.

[d] Difference between the periodontitis-resistant and periodontitis-susceptible group is statistically significant ($p<0.01$; Mann-Whitney U test).

[e] Difference between the periodontitis-resistant and periodontitis-susceptible group is statistically significant ($p<0.0001$; Mann-Whitney U test).