

WHAT IS CLAIMED IS

1. A method of determining whether a patient is predisposed to having severe periodontal disease and/or having high risk of progression of periodontal disease, comprising the steps of:

- (i) genotyping a biological sample obtained from the patient for genetic polymorphism pattern comprising IL 1B (rs16944), IL 1B (rs1143623) IL 1B (rs4848306), and IL 1B (rs1143633);
- (ii) comparing said genetic polymorphism pattern to a reference composite genotype pattern, wherein the similarity of said genetic polymorphism pattern to said reference pattern indicate said patient's predisposition to having severe periodontal disease and/or having high risk of progression of periodontal disease,

wherein said reference composite genotype pattern is selected from the group consisting of

- a. one copy of IL1B (rs16944; C/T) allele 1 (C), one copy of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C) , and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- b. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- c. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
- d. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C) , and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- e. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
- f. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C) , and two copies of IL1B (rs1143633; G/A) allele 1 (G);

- g. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
- h. two copies of IL1B (rs16944; C/T) allele 2 (T), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C) , and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- i. two copies of IL1B (rs16944; C/T) allele 2 (T), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
- j. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G); and
- k. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), one copy of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- l. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), one copy of IL1B (rs4848306; C/T) allele 2 (T) and one copy of allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G); and
- m. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 2 (C), two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G).

2. The method of claim 1, wherein said biological sample is saliva, buccal cells, blood, tissue samples or urine.

3. The method of claim 1 for determining whether said patient is predisposed to having severe periodontal disease.

4. The method of claim 1 for determining said patient's risk of progression of periodontal disease.

5. The method of any one of claim 1 to 4, wherein said patient is Caucasian, African, Chinese or other ethnicities.
6. A testing kit for determining whether a patient is predisposed to having severe periodontal disease and/or having high risk of progression of periodontal disease, comprising:
- (i) one or more primers for determining the number of copies of allele 1 and allele 2 of each of the IL1B single-nucleotide polymorphisms (SNPs) comprising IL1B (rs16944; C/T), IL1B (rs1143623; G/C), IL1B (rs4848306; C/T) , and IL1B (rs1143633);
 - (ii) a control sample as a reference, and
 - (iii) an instruction, wherein said instruction classifies said patient as having high risk of progression of periodontal disease when said patient has a composite genotype selected from the group consisting of
 - a. one copy of IL1B (rs16944; C/T) allele 1 (C), one copy of IL1B (rs1143623; G/C) allele 1 (G); two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
 - b. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C) , and two copies of IL1B (rs1143633; G/A) allele 1 (G);
 - c. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
 - d. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G) two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
 - e. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
 - f. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G) two copies of IL1B (rs4848306; C/T) allele 1 (C) , and two copies of IL1B (rs1143633; G/A) allele 1 (G);

- g. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
- h. two copies of IL1B (rs16944; C/T) allele 2 (T), two copies of IL1B (rs1143623; G/C) allele 1 (G) two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- i. two copies of IL1B (rs16944; C/T) allele 2 (T), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
- j. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- k. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), one copy of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- l. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), one copy of IL1B (rs4848306; C/T) allele 2 (T) and one copy of allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G); and
- m. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 2 (C), two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G).

7. The testing kit of claim 6, wherein said patient is Caucasian, African, Chinese or of other ethnicities.

8. A method of determining whether a patient has a high risk of progression of periodontal disease, comprising the steps of:

- (i) selecting a patient presenting a sign of a periodontal disorder;
- (ii) isolating a nucleic acid sample from a biological sample obtained from said patient;

- (iii) contacting the nucleic acid sample with one or more primers that specifically hybridise 5' and 3' of at least one allele of an ILB locus haplotype comprising single nucleotide polymorphism (SNP) IL IB (rs16944; C/T), IL IB (rs 1143623; G/C), IL IB (rs4848306; C/T), and IL IB (rs1143633);
- (iv) detecting the number of copies of allele 1 and allele 2 of each of said SNPs IL IB (rs16944; C/T), IL IB (rs 1143623; G/C), IL IB (rs4848306; C/T), and IL IB (rs1143633);
- (v) assigning a composite genotype to the patient based upon the alleles detected in step (iv); and
- (vi) classifying said patient into a periodontal disease risk progression group based on analysis of said alleles of said SNPs detected in step (iv), wherein a patient with a composite genotype selected from the group consisting of:
 - a. one copy of IL1B (rs16944; C/T) allele 1 (C), one copy of IL1B (rs1143623; G/C) allele 1 (G); two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
 - b. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C)), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
 - c. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
 - d. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (g) two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
 - e. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
 - f. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
 - g. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);

- h. two copies of IL1B (rs16944; C/T) allele 2 (T), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- i. two copies of IL1B (rs16944; C/T) allele 2 (T), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 1 (C), and one or two copies of IL1B (rs1143633; G/A) allele 2 (A);
- j. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- k. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), one copy of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G);
- l. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), one copy of IL1B (rs4848306; C/T) allele 2 (T) and one copy of allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G); and
- m. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 2 (C), two copies of IL1B (rs4848306; C/T) allele 1 (C), and two copies of IL1B (rs1143633; G/A) allele 1 (G);

is classified as being at a high risk of progression of periodontal disease.

9. The method of claim 8 wherein said risk of progression of periodontal disease is risk of progression to severe periodontal disease.

10. The method of claim 8 or 9, further comprising after step (ii) and before step (iii) amplifying a target DNA region comprising an IL1B gene from said nucleic acid sample.

11. The method of claim 8, wherein said biological sample is saliva, buccal cells, blood, tissue samples or urine.

12. The method of any one of claims 8 to 11, wherein said patient is Caucasian, African, Chinese or other ethnicities.

13. A testing kit for determining whether a patient has high risk of progression of periodontal disease, comprising:

- (i) one or more primers for determining the number of copies of allele 1 and allele 2 of each of the IL1B single nucleotide polymorphisms (SNPs) comprising IL IB (rs16944; C/T), IL IB (rs1143623; G/C) IL IB (rs4848306; C/T), and IL IB (rs1143633);
- (ii) a control sample as a reference; and
- (iii) instructions for carrying out the method of claim 8, or 9.

WHAT IS CLAIMED IS

1. A method of determining whether a patient is predisposed to having severe periodontal disease and/or having high risk of progression of periodontal disease, comprising the steps of:
 - (i) genotyping a biological sample obtained from the patient for genetic polymorphism pattern comprising IL 1B (rs16944), IL 1B (rs1143623) IL 1B (rs4848306), and IL 1B (rs1143633);
 - (ii) comparing said genetic polymorphism pattern to a reference composite genotype pattern, wherein the similarity of said genetic polymorphism pattern to said reference pattern indicate said patient's predisposition to having severe periodontal disease and/or having high risk of progression of periodontal disease, wherein said reference composite genotype pattern is selected from the group consisting of
 - a. one copy of IL1B (rs16944; C/T) allele 1 (C), one copy of IL1B (rs1143623; G/C) allele 1 (G), and two copies of IL1B (rs4848306; C/T) allele 1 (C);
 - b. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 1 (G), and two copies of IL1B (rs4848306; C/T) allele 1 (C);
 - c. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), and two copies of IL1B (rs4848306; C/T) allele 1 (C);
 - d. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), and two copies of IL1B (rs4848306; C/T) allele 1 (C);
 - e. two copies of IL1B (rs16944; C/T) allele 2 (T), two copies of IL1B (rs1143623; G/C) allele 1 (G), and two copies of IL1B (rs4848306; C/T) allele 1 (C);
 - f. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G); and
 - g. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), one copy of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G).
2. The method of claim 1, wherein said biological sample is saliva, buccal cells, blood, tissue samples or urine.

3. The method of claim 1 for determining whether said patient is predisposed to having severe periodontal disease.
4. The method of claim 1 for determining said patient's risk of progression of periodontal disease.
5. The method of claim 1, wherein said patient is Caucasian, African, Chinese or other ethnicities.
6. A testing kit for determining whether a patient is predisposed to having severe periodontal disease and/or having high risk of progression of periodontal disease, comprising:
 - (i) one or more primers for determining the number of copies of allele 1 and allele 2 of each of the IL1B single-nucleotide polymorphisms (SNPs) comprising IL1B (rs16944; C/T), IL1B (rs1143623; G/C), and IL1B (rs4848306; C/T);
 - (ii) a control sample as a reference, and
 - (iii) an instruction, wherein said instruction classifies said patient as having high risk of progression of periodontal disease when said patient has a composite genotype selected from the group consisting of
 - a. one copy of IL1B (rs16944; C/T) allele 1 (C), one copy of IL1B (rs1143623; G/C) allele 1 (G); and two copies of IL1B (rs4848306; C/T) allele 1 (C);
 - b. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 1 (G), and two copies of IL1B (rs4848306; C/T) allele 1 (C);
 - c. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G) and two copies of IL1B (rs4848306; C/T) allele 1 (C);
 - d. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G) and two copies of IL1B (rs4848306; C/T) allele 1 (C); and
 - e. two copies of IL1B (rs16944; C/T) allele 2 (T), two copies of IL1B (rs1143623; G/C) allele 1 (G) and two copies of IL1B (rs4848306; C/T) allele 1 (C).

7. The testing kit of claim 6, further comprising one or more primers for detecting the number of copies of allele 1 and allele 2 of IL 1B (rs1143633) and wherein said instruction classifies said patient as having high risk of progression of periodontal disease when said patient has a composite genotype selected from the group consisting of

f. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G); and

g. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), one copy of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G).

8. The testing kit of claim 6, wherein said patient is Caucasian, African, Chinese or of other ethnicities.

9. A method of determining whether a patient has a high risk of progression of periodontal disease, comprising the steps of:

- (i) selecting a patient presenting a sign of a periodontal disorder;
- (ii) isolating a nucleic acid sample from a biological sample obtained from said patient;
- (iii) contacting the nucleic acid sample with one or more primers that specifically hybridise 5' and 3' of at least one allele of an ILB locus haplotype comprising single nucleotide polymorphism (SNP) IL 1B (rs16944; C/T), IL 1B (rs 1143623; G/C) and IL 1B (rs4848306; C/T);
- (iv) detecting the number of copies of allele 1 and allele 2 of each of said SNPs IL 1B (rs16944; C/T), IL 1B (rs 1143623; G/C) and IL 1B (rs4848306; C/T);
- (v) assigning a composite genotype to the patient based upon the alleles detected in step (iv); and
- (vi) classifying said patient into a periodontal disease risk progression group based on analysis of said alleles of said SNPs detected in step (iv), wherein a patient with a composite genotype selected from the group consisting of:
 - a. one copy of IL1B (rs16944; C/T) allele 1 (C), one copy of IL1B (rs1143623; G/C) allele 1 (G); and two copies of IL1B (rs4848306; C/T) allele 1 (C);

- b. two copies of IL1B (rs16944; C/T) allele 2 (T), one copy of IL1B (rs1143623; G/C) allele 1 (G), and two copies of IL1B (rs4848306; C/T) allele 1 (C);
- c. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G) and two copies of IL1B (rs4848306; C/T) allele 1 (C);
- d. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G) and two copies of IL1B (rs4848306; C/T) allele 1 (C); and
- e. two copies of IL1B (rs16944; C/T) allele 2 (T), two copies of IL1B (rs1143623; G/C) allele 1 (G) and two copies of IL1B (rs4848306; C/T) allele 1 (C)

is classified as being at a high risk of progression of periodontal disease.

10. The method of claim 9 wherein said risk of progression of periodontal disease is risk of progression to severe periodontal disease.

11. The method of claim 9 or 10, wherein said method further comprises detecting the number of copies of allele 1 and allele 2 of IL1B (rs1143633; G/A).

12. The method of claim 11, wherein step (vi) further comprises classifying said patient into a periodontal disease progression risk group based on analysis of said alleles of said SNPs detected in step (iv) wherein a patient with a composite genotype selected from the group consisting of:

- f. two copies of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), two copies of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G); and
- g. one copy of IL1B (rs16944; C/T) allele 1 (C), two copies of IL1B (rs1143623; G/C) allele 1 (G), one copy of IL1B (rs4848306; C/T) allele 2 (T), and two copies of IL1B (rs1143633; G/A) allele 1 (G)

is classified as being at high risk of progression of periodontal disease.

13. The method of claim 9 or 10 wherein in step (vi), the patient is classified as being at a low risk of progression of periodontal disease when the patient's assigned genotype is none of a

— g.

14. The method of any one of claims 9 to 13, further comprising after step (ii) and before step (iii) amplifying a target DNA region comprising an IL1B gene from said nucleic acid sample.

15. The method of claim 9, wherein said biological sample is saliva, buccal cells, blood, tissue samples or urine.

16. The method of any one of claims 9 to 15, wherein said patient is Caucasian, African, Chinese or other ethnicities.

17. A testing kit for determining whether a patient has high risk of progression of periodontal disease, comprising:

- (i) one or more primers for determining the number of copies of allele 1 and allele 2 of each of the IL1B single nucleotide polymorphisms (SNPs) comprising IL 1B (rs16944; C/T), IL 1B (rs1143623; G/C) and IL 1B (rs4848306; C/T);
- (ii) a control sample as a reference; and
- (iii) instructions for carrying out the method of claim 9, 10, 11, 12 or 13.

18. The test kit of claim 17 further comprising one or more primers for detecting the number of copies of allele 1 and allele 2 of IL1B (rs1143633; G/A).