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(54) Titre : MARQUEURS BIALLELES DERIVES DE REGIONS GENOMIQUES PORTEUSES DE GENES
INTERVENANT DANS LE METABOLISME DE L'ACIDE ARACHIDONIQUE
(54) Title: BIALLELIC MARKERS DERIVED FROM GENOMIC REGIONS CARRYING GENES INVOLVED IN
ARACHIDONIC ACID METABOLISM

(57) **Abrégé/Abstract:**

The invention provides polynucleotides including biallelic markers derived from genes involved in arachidonic acid metabolism and from genomic regions flanking those genes. Primers hybridizing to regions flanking these biallelic markers are also provided. This invention also provides polynucleotides and methods suitable for genotyping a nucleic acid containing sample for one or more biallelic markers of the invention. Further, the invention provides methods to detect a statistical correlation between a biallelic marker allele and a phenotype and/or between a biallelic marker haplotype and a phenotype.



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(21) International Application Number: PCT/IB00/00184 (22) International Filing Date: 11 February 2000 (11.02.00) (30) Priority Data: 60/119,917 12 February 1999 (12.02.99) US 09/275,267 23 March 1999 (23.03.99) US 60/133,200 7 May 1999 (07.05.99) US (71) Applicant (for all designated States except US): GENSET [FR/FR]; Intellectual Property Dept., 24, rue Royale, F-75008 Paris (FR). (72) Inventors; and (75) Inventors/Applicants (for US only): BLUMENFELD, Marta [FR/FR]; 5, rue Tagore, F-75013 Paris (FR). BOUGUEL- ERET, Lydie [FR/FR]; 108, avenue Victor Hugo, F-92170 Vanves (FR). CHUMAKOV, Ilya [FR/FR]; 196, rue des Chevreuillees, F-77000 Vaux-le-Penil (FR). (74) Common Representative: GENSET; Intellectual Property Dept., 24, rue Royale, F-75008 Paris (FR).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: BIALLELIC MARKERS DERIVED FROM GENOMIC REGIONS CARRYING GENES INVOLVED IN ARACHIDONIC ACID METABOLISM		
(57) Abstract The invention provides polynucleotides including biallelic markers derived from genes involved in arachidonic acid metabolism and from genomic regions flanking those genes. Primers hybridizing to regions flanking these biallelic markers are also provided. This invention also provides polynucleotides and methods suitable for genotyping a nucleic acid containing sample for one or more biallelic markers of the invention. Further, the invention provides methods to detect a statistical correlation between a biallelic marker allele and a phenotype and/or between a biallelic marker haplotype and a phenotype.		

WHAT IS CLAIMED IS:

1. An isolated polynucleotide comprising a contiguous span of at least 12 nucleotides of a sequence selected from the group consisting of the sequences described in Figure 3 and the complements thereof.
2. A polynucleotide according to claim 1, wherein said span includes an eicosanoid-related biallelic marker in said sequence.
3. An isolated polynucleotide comprising a contiguous span of at least 12 nucleotides of a sequence selected from the group consisting of the sequences described in Figure 4 and the complements thereof, wherein said span includes an eicosanoid-related biallelic marker in said sequence with the alternative allele present at said biallelic marker.
4. An isolated polynucleotide consisting essentially of a contiguous span of 8 to 50 nucleotides of a sequence selected from the group consisting of the sequences described in Figure 4 and the complements thereof, wherein said span includes an eicosanoid-related biallelic marker in said sequence with the original allele present at said biallelic marker.
5. An isolated polynucleotide consisting essentially of a contiguous span of 8 to 50 nucleotides of a sequence selected from the group consisting of the sequences described in Figure 5 and the complements thereof, wherein said span includes an eicosanoid-related biallelic marker in said sequence.
6. A polynucleotide according to any one of claims 2 to 5, wherein said contiguous span is 18 to 35 nucleotides in length and said biallelic marker is within 4 nucleotides of the center of said polynucleotide.
7. A polynucleotide according to claim 6, wherein said polynucleotide consists of said contiguous span and said contiguous span is 25 nucleotides in length and said biallelic marker is at the center of said polynucleotide.
8. A polynucleotide according to claim 1, wherein the 3' end of said contiguous span is present at the 3' end of said polynucleotide.

9. A polynucleotide according to any one of claims 2 to 5, wherein the 3' end of said contiguous span is located at the 3' end of said polynucleotide and said biallelic marker is present at the 3' end of said polynucleotide.
- 5
10. A polynucleotide according to claim 8, wherein the 3' end of said polynucleotide is located within 20 nucleotides upstream of an eicosanoid-related biallelic marker in said sequence.
11. An isolated polynucleotide consisting essentially of a contiguous span of 8 to 50 nucleotides in
10 a sequence selected from the group consisting of the sequences described in Figure 4, the sequences described in Figure 5, and the complements thereof, wherein the 3' end of said contiguous span is located at the 3' end of said polynucleotide, and wherein the 3' end of said polynucleotide is located within 20 nucleotides upstream of an eicosanoid-related biallelic marker in said sequence.
- 15 12. A polynucleotide according to either claim 10 or 11, wherein the 3' end of said polynucleotide is located 1 nucleotide upstream of an eicosanoid-related biallelic marker in said sequence.
13. A polynucleotide according to claim 1, wherein said polynucleotide consists essentially of a sequence selected from the sequences described in Figure 7.
- 20
14. An isolated polynucleotide comprising a contiguous span of at least 12 nucleotides of a sequence selected from the sequences described in Figure 6.
15. A polynucleotide consisting essentially of a sequence selected from the sequences described in
25 Figure 8.
16. A polynucleotide consisting essentially of a sequence selected from the sequences described in Figure 9.
- 30 17. A polynucleotide according to any one of claims 1, 3, 4, 5, 11, 14, 15 and 16 wherein said contiguous span comprises at least 15 contiguous nucleotides in said sequence.
18. A polynucleotide according to any one of claims 1, 3, 4, 5, 11, 14, 15 and 16 wherein said contiguous span comprises at least 20 contiguous nucleotides in said sequence.

19. A polynucleotide according to any one of claims 1, 3, 4, 5, 11, 14, 15 and 16 wherein said contiguous span comprises at least 25 contiguous nucleotides in said sequence.
- 5 20. A polynucleotide according to any one of claims 1, 3, 4, 5, 11, 14, 15 and 16 attached to a solid support.
21. An array of polynucleotides comprising at least one polynucleotide according to claim 20.
- 10 22. An array according to claim 21, wherein said array is addressable.
23. A polynucleotide according to any one of claims 1, 3, 4, 5, 11, 14, 15 and 16, further comprising a label.
- 15 24. A method of genotyping comprising determining the identity of a nucleotide at an eicosanoid-related biallelic marker or 12-LO-related biallelic marker in a biological sample.
25. A method according to claim 24, wherein said eicosanoid-related biallelic marker or 12-LO-related biallelic marker is selected from the biallelic markers described in Figure 2, preferably the
- 20 biallelic markers found in SEQ ID Nos. 1-418, 425-489, 491-530, 532-539, and 541-652; or more preferably SEQ ID Nos. 26-418, 425-489, 491-530, 532-539, 541-646, and 651-652.
26. A method according to claim 24, wherein said biological sample is derived from a single subject.
- 25
27. A method according to claim 26, wherein the identity of the nucleotides at said biallelic marker is determined for both copies of said biallelic marker present in said subject's genome.
28. A method according claim 24, wherein said biological sample is derived from multiple subjects.
- 30
29. A method according to claim 24, further comprising amplifying a portion of said sequence comprising the biallelic marker prior to said determining step.
30. A method according to claim 29, wherein said amplifying is performed by PCR.

31. A method according to claim 24, wherein said determining is performed by a hybridization assay.
- 5 32. A method according to claim 24, wherein said determining is performed by a sequencing assay.
33. A method according to claim 24, wherein said determining is performed by a microsequencing assay.
- 10 34. A method according to claim 24, wherein said determining is performed by an enzyme-based mismatch detection assay.
35. A method of determining the frequency in a population of an allele of an eicosanoid-related biallelic marker or 12-LO-related biallelic marker, comprising:
- 15 a) genotyping individuals from said population for said biallelic marker according to the method of claim 24; and
- b) determining the proportional representation of said biallelic marker in said population.
- 20 36. A method according to claim 24, wherein said eicosanoid-related biallelic marker or 12-LO-related biallelic marker is selected from the biallelic markers described in Figure 2, preferably the biallelic markers found in SEQ ID Nos. 1-418, 425-489, 491-530, 532-539, and 541-652; or more preferably SEQ ID Nos. 26-418, 425-489, 491-530, 532-539, 541-646, and 651-652.
- 25 37. A method according to claim 35, wherein said genotyping of step a) is performed on each individual of said population.
38. A method according to claim 35, wherein said genotyping is performed on a single biological sample derived from said population.
- 30 39. A method of detecting an association between an allele and a phenotype, comprising the steps of:

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a) determining the frequency of at least one eicosanoid-related biallelic marker allele or 12-LO-related biallelic marker allele in a affected population according to the method of claim 35;

b) determining the frequency of said eicosanoid-related biallelic marker allele or 12-LO-related biallelic marker allele in a control population according to the method of claim 35; and

c) determining whether a statistically significant association exists between said allele and said phenotype.

10 40. A method of estimating the frequency of a haplotype for a set of biallelic markers in a population, comprising:

a) genotyping each individual in said population for at least one eicosanoid-related biallelic marker or 12-LO-related biallelic marker according to claim 24;

15 b) genotyping each individual in said population for a second biallelic marker by determining the identity of the nucleotides at said second biallelic marker for both copies of said second biallelic marker present in the genome; and

c) applying a haplotype determination method to the identities of the nucleotides determined in steps a) and b) to obtain an estimate of said frequency.

20 41. A method according to claim 40, wherein said haplotype determination method is selected from the group consisting of asymmetric PCR amplification, double PCR amplification of specific alleles, the Clark method, or an expectation maximization algorithm.

25 42. A method according to claim 40, wherein said eicosanoid-related biallelic marker or 12-LO-related biallelic marker is selected from the biallelic markers described in Figure 2, preferably the biallelic markers found in SEQ ID Nos. 1-418, 425-489, 491-530, 532-539, and 541-652; or more preferably SEQ ID Nos. 26-418, 425-489, 491-530, 532-539, 541-646, and 651-652.

30 43. A method of detecting an association between a haplotype and a phenotype, comprising the steps of:

a) estimating the frequency of at least one haplotype in a affected population according to the method of claim 40;

b) estimating the frequency of said haplotype in a control population according to the method of claim 40; and

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c) determining whether a statistically significant association exists between said haplotype and said phenotype.

44. A method according to either claim 39 or 43, wherein said control population is a trait negative
5 population.

45 A method according to either claim 39 or 43, wherein said case control population is a random population.

10 46. A method according to claim 39, wherein each of said genotyping of steps a) and b) is performed on a single pooled biological sample derived from each of said populations.

47. A method according to claim 39, wherein said genotyping of steps a) and b) is performed separately on biological samples derived from each individual in said populations.

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48. A method according to either claim 39 or 43, wherein said phenotype is a disease involving arachidonic acid metabolism.

49. A method according to either claim 39 or 43, wherein said phenotype is a response to an agent
20 acting on arachidonic acid metabolism.

50. A method according to either claim 39 or 43, wherein said phenotype is a side effect to an agent acting on arachidonic acid metabolism.

25 51. A method according to claim 39, wherein the identity of the nucleotides at all of the biallelic markers described in Figure 2 is determined in steps a) and b).

52. A computer readable medium having stored thereon a sequence selected from the group consisting of a nucleic acid code comprising a contiguous span of at least 12 nucleotides of a sequence
30 described in Figure 3, Figure 4, Figure 6 and the complements thereof; wherein said contiguous span of a sequence described in Figure 4 comprises an eicosanoid-related biallelic marker with the alternative allele present at said biallelic marker.

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53. A computer system comprising a processor and a data storage device wherein said data storage device has stored thereon a sequence selected from the group consisting of a nucleic acid code comprising a contiguous span of at least 12 nucleotides of a sequence described in Figure 3, Figure 4, Figure 6 and the complements thereof; wherein said contiguous span of a sequence described in Figure 4 comprises an eicosanoid-related biallelic marker with the alternative allele present at said biallelic marker.
54. The computer system of Claim 53 further comprising a sequence comparer and a data storage device having reference sequences stored thereon.
55. The computer system of Claim 54 wherein said sequence comparer comprises a computer program which indicates polymorphisms.
56. A method for comparing a first sequence to a reference sequence, comprising the steps of:
- a) reading said first sequence and said reference sequence through use of a computer program which compares sequences; and
 - b) determining differences between said first sequence and said reference sequence with said computer program; wherein said first sequence is selected from the group consisting of a nucleic acid comprising a contiguous span of at least 12 nucleotides of a sequence described in Figure 3, Figure 4, Figure 6 and the complements thereof; wherein said contiguous span of a sequence described in Figure 4 comprises an eicosanoid-related biallelic marker with the alternative allele present at said biallelic marker.
57. The method of Claim 56, wherein said step b) comprises identifying polymorphisms.
58. A method of administering a drug or treatment comprising:
- a) obtaining a nucleic acid sample from an individual;
 - b) determining the identity of the polymorphic base of at least one eicosanoid-related biallelic marker or 12-LO-related biallelic marker according to the method of claim 29 which is associated with a positive response to said drug or treatment, or at least one eicosanoid-related marker or 12-LO-related biallelic marker or which is associated with a negative response to said drug or treatment; and
 - c) administering said drug or treatment to said individual if said nucleic acid sample contains at least one biallelic marker associated with a positive response to said drug or

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treatment, or if said nucleic acid sample lacks at least one biallelic marker associated with a negative response to said drug or treatment.

59. A method of selecting an individual for inclusion in a clinical trial of a drug or treatment

5 comprising:

a) obtaining a nucleic acid sample from an individual;

b) determining the identity of the polymorphic base of at least one eicosanoid-related biallelic marker or 12-LO-related biallelic marker according to the method of claim 29 which is associated with a positive response to said drug or treatment, or at least one biallelic marker associated with a negative response to said drug or treatment in said nucleic acid sample; and

c) including said individual in said clinical trial if said nucleic acid sample contains at least one biallelic marker which is associated with a positive response to said drug or treatment, or if said nucleic acid sample lacks at least one biallelic marker associated with a negative response to said drug or treatment.

60. A method according to claims 58 or 59, wherein said administering step comprises administering said drug or treatment to said individual if said nucleic acid sample contains at least one biallelic marker associated with a positive response to said drug treatment, and said nucleic acid sample lacks at least one biallelic marker associated with a negative response to said drug or treatment.

61. The method according to either claim 58 or 59, wherein said eicosanoid-related marker or 12-LO-related biallelic marker is selected from the group consisting of the biallelic markers described in Figure 2, preferably the biallelic markers found in SEQ ID Nos. 1-418, 425-489, 491-530, 532-539, and 541-652; or more preferably SEQ ID Nos. 26-418, 425-489, 491-530, 532-539, 541-646, and 651-652.

62. A diagnostic kit comprising a polynucleotide according to any one of claims 2, 3, 4, 5, 10, 11, 13, 14, 15, and 16.

63. The use of a polynucleotide in a hybridization assay for determining the identity of a nucleotide at an eicosanoid-related biallelic marker or 12-LO-related biallelic marker.

64. The use of a polynucleotide in a sequencing assay for determining the identity of a nucleotide at an eicosanoid-related biallelic marker or 12-LO-related biallelic marker.

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65. The use of a polynucleotide in an allele specific amplification assay for determining the identity of an eicosanoid-related biallelic marker or 12-LO-related biallelic marker.
66. The use of a polynucleotide in amplifying a segment of nucleotides comprising an eicosanoid-
5 related biallelic marker.
67. An isolated, purified, or recombinant polynucleotide comprising a contiguous span of at least 12 nucleotides of SEQ ID No 651, wherein said contiguous span comprises at least 1 one of the following nucleotide positions of SEQ ID No 651: 1 to 2584, 4425 to 5551, 5634 to 5757, 5881 to
10 5995, 6100 to 6348, 6510 to 7378, 7523 to 8644, 8855 to 12253, 12341 to 12853, 13024 to 13307, 13430 to 16566, 16668 to 16774, 16946 to 17062, 17555 to 20674; and the complements thereof.
68. An isolated, purified, or recombinant polynucleotide comprising a contiguous span of at least 12 nucleotides of SEQ ID No 651 and the complements thereof; wherein said contiguous span
15 comprises at least one nucleotide positions selected from the group consisting of: a C at position 3355, a G at position 3488, a G at position 3489, and a G at position 3708 of SEQ ID No 651.
69. An isolated, purified, or recombinant polynucleotide comprising a contiguous span of at least 12 nucleotides of SEQ ID No 651 and the complements thereof; wherein said contiguous span
20 comprises a least one nucleotide positions selected from the group consisting of: a T at position 2323, a C at position 2341, an A at position 2623, an A at position 2832, a C at position 2844, an A at position 2934, an A at position 2947, a G at position 3802, a G at position 4062, a C at position 4088, a T at position 4109, a T at position 4170, an A at position 6019, a C at position 6375, a C at position 6429, an A at position 6467, a G at position 6484, an A at position 8658, a G at position 8703, an A at position
25 8777, a G at position 8785, a G at position 13341, an A at position 16836, an A at position 16854, and a T at position 17355 of SEQ ID No 651.
70. An isolated, purified, or recombinant polynucleotide comprising a contiguous span of at least 12 nucleotides of SEQ ID No 652, wherein said contiguous span comprises a T at position 1205 of SEQ
30 ID No 652 or nucleotide positions 2151 to 2157 of SEQ ID No 652; and the complements thereof.
71. An isolated, purified, or recombinant polynucleotide comprising a contiguous span of at least 12 nucleotides of SEQ ID No 652 and the complements thereof; wherein said contiguous span comprises a least one nucleotide position selected from the group consisting of: G at position 366, an A

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at position 605, a C at position 712, a T at position 766, an A at position 804, a G at position 821, an A at position 1004, a G at position 1049, an A at position 1123, a G at position 1131, a G at position 1491, an A at position 1742, an A at position 1760, an A at position 1941, and a T at position 2144 of SEQ ID No 652.

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72. An isolated, purified, or recombinant polynucleotide consisting of, or consisting essentially of a contiguous span of 8 to 50 nucleotides of either one of SEQ ID Nos: 651, 652 or the complements thereof, wherein said span includes a 12-LO-related biallelic marker in said sequence.

10 73. A polynucleotide according to claim 72, wherein said 12-LO-related biallelic marker is selected from the group consisting of the biallelic markers described in Table I.

74. A polynucleotide according to claim 72, wherein said 12-LO-related biallelic marker is selected from the group consisting of biallelic markers: 12-197-244, 12-208-35, 12-226-167, 12-206-366, 10-
15 346-141, 10-347-111, 10-347-165, 10-347-203, 10-347-220, 10-349-97, 10-349-224, 10-341-116, 12-196-119, 12-214-129, 12-216-421, 12-219-230, and 12-223-207.

75. An isolated, purified, or recombinant polynucleotide which encodes a polypeptide comprising a contiguous span of at least 6 amino acids of SEQ ID No 653, wherein said contiguous span comprises at
20 least one amino acid position selected from the group consisting of: an His residue et amino acid position 189, an His residue at amino acid position 225, a Cys residue at amino acid position 243, an Arg residue at amino acid position 261, an Asn residue at amino acid position 322, an Arg residue at amino acid position 337, a Asn residue at amino acid position 362, an Asn at amino acid position 568 and a Lys residue at amino acid position 574.

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76. An isolated, purified, or recombinant polynucleotide which encodes a polypeptide comprising a contiguous span of at least 6 amino acids of SEQ ID No. 654, wherein said contiguous span comprises at least one of amino acid positions 110-131 of SEQ ID No 654.

30 77. A recombinant vector comprising a polynucleotide according to any one of claims 67 to 76.

78. A host cell comprising a recombinant vector according to claim 77.

79. A non-human host animal or mammal comprising a recombinant vector according to claim 77.

80. A mammalian host cell comprising a 12-LO gene disrupted by homologous recombination with a knock out vector comprising a polynucleotide according to any one of claims 67 to 76.
- 5 81. A non-human host mammal comprising a 12-LO gene disrupted by homologous recombination with a knock out vector comprising a polynucleotide according to any one of claims 67 to 76.
82. A diagnostic kit comprising a polynucleotide according to any one of claims 67 to
- 10 83. An isolated, purified, or recombinant polypeptide comprising a contiguous span of at least 6 amino acids of SEQ ID No 653, wherein said contiguous span comprises at least one amino acid position selected from the group consisting of: an His residue et amino acid position 189, an His residue at amino acid position 225, a Cys residue at amino acid position 243, an Arg residue at amino acid position 261, an Asn residue at amino acid position 322, an Arg residue at amino acid position
- 15 337, a Asn residue at amino acid position 362, an Asn at amino acid position 568 and a Lys residue at amino acid position 574.
84. An isolated or purified antibody composition capable of selectively binding to an epitope-containing fragment of a polypeptide according to claim 83, wherein said epitope comprises at least one
- 20 amino acid position selected from the group consisting of: an His residue et amino acid position 189, an His residue at amino acid position 225, a Cys residue at amino acid position 243, an Arg residue at amino acid position 261, an Asn residue at amino acid position 322, an Arg residue at amino acid position 337, a Asn residue at amino acid position 362, an Asn at amino acid position 568 and a Lys residue at amino acid position 574.
- 25
85. An isolated, purified, or recombinant polypeptide comprising a contiguous span of at least 6 amino acids of SEQ ID No. 654, wherein said contiguous span comprises at least one of amino acid positions 110-131 of SEQ ID No 654.
- 30 86. An isolated or purified antibody composition capable of selectively binding to an epitope-containing fragment of a polypeptide according to claim 85, wherein said epitope comprises at least one of amino acid positions 110-131 of SEQ ID No 654.

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Fig.1A

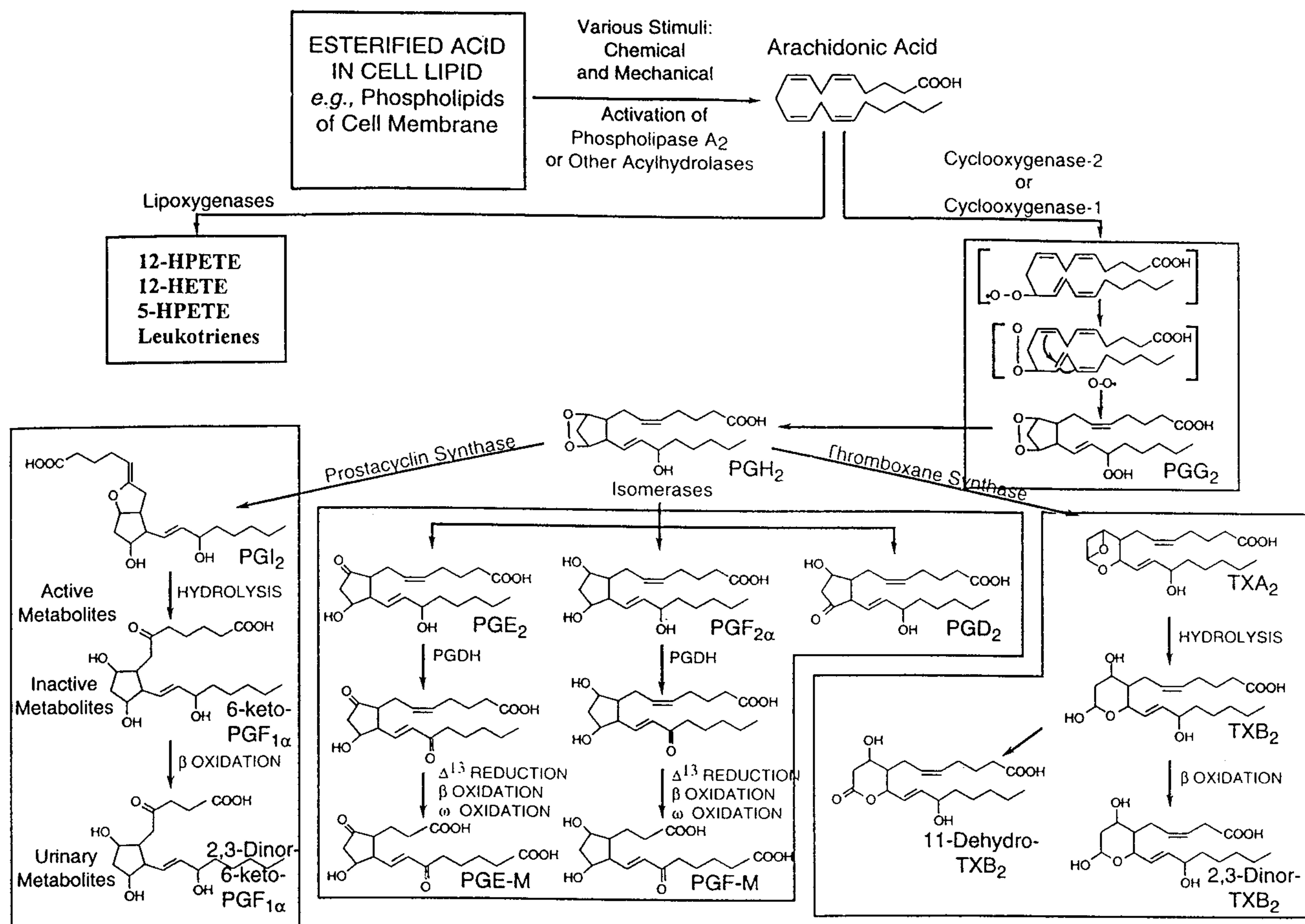


Fig.1B

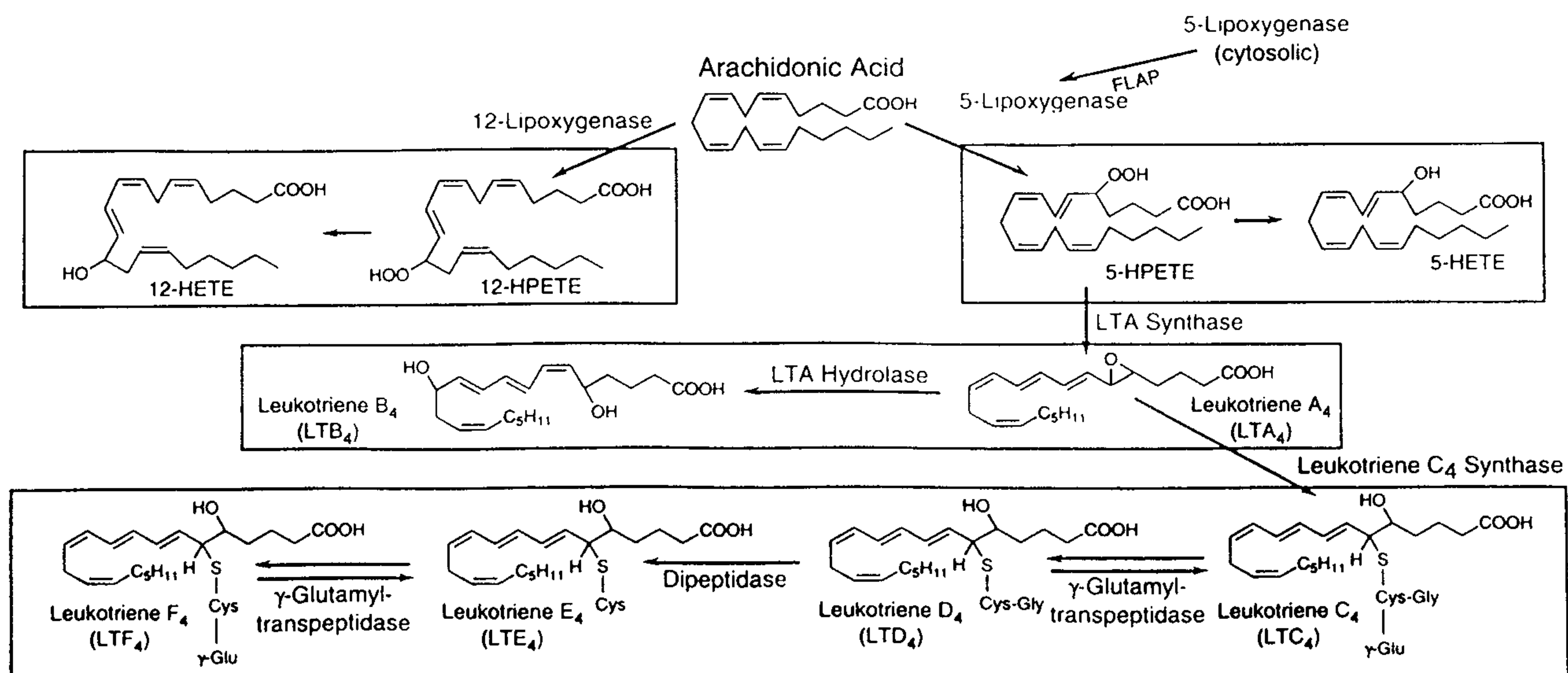


FIG.2A

GENE	BIALLELIC MARKER ID	SEQ ID NO.	BIALLELIC MARKER POSITION IN SEQ ID NO.	VALIDATION MICRO- SEQUENCING	GENOTYPING LEAST COMMON ALLELE FREQUENCY %	
FLAP	10-253-118	1	478	N		
FLAP	10-253-298	2	478	Y	G	4.57
FLAP	10-253-315	3	478	N		
FLAP	10-499-155	4	478	N		
FLAP	10-520-256	5	478	N	T	40.8
FLAP	10-500-258	6	478	N		
FLAP	10-500-410	7	478	N		
FLAP	10-503-159	8	478	N		
FLAP	10-504-172	9	478	N		
FLAP	10-504-243	10	478	N		
FLAP	10-204-326	11	478	Y	A	6.63
FLAP	10-32-357	12	478	Y	A	33.5
FLAP	10-33-175	13	478	Y	T	2.30
FLAP	10-33-211	14	478	N		
FLAP	10-33-234	15	478	Y	A	44.0
FLAP	10-33-270	16	478	Y	G/G	
FLAP	10-33-327	17	478	Y	C	24.5
FLAP	10-34-290	18	478	N		
FLAP	10-35-358	19	478	Y	C	31.3
FLAP	10-35-390	20	478	Y	T	23.0
FLAP	10-36-164	21	478	Y	G/G	
FLAP	10-498-192	22	478	N		
FLAP	12-628-306	23	478	Y	T	10.3
FLAP	12-628-311	24	478	N		
FLAP	12-629-241	25	478	Y	C	28.3
12-LO	12-206-366	26	478	Y	C	38.2
12-LO	10-343-339	27	478	N		
12-LO	10-347-74	28	478	N		
12-LO	10-347-111	29	478	N	G/G	
12-LO	10-347-165	30	478	N	C/C	
12-LO	10-347-203	31	478	Y	G	41.6
12-LO	10-347-220	32	478	Y	A	40.5
12-LO	10-347-271	33	478	N		
12-LO	10-347-348	34	478	N		
12-LO	10-348-391	35	478	N		
12-LO	10-349-47	36	478	N		
12-LO	10-349-97	37	478	Y	G	39.6
12-LO	10-349-142	38	478	N	C/C	
12-LO	10-349-224	39	478	Y	T	39.6
12-LO	10-349-368	40	478	N		
12-LO	10-339-32	41	478	N		
12-LO	10-341-116	42	478	Y	A	10.8
12-LO	10-341-319	43	478	N		
12-LO	12-196-119	44	119	Y	C	29.1
12-LO	12-197-244	45	243	Y	C	32.8
12-LO	12-198-128	46	128	N		
12-LO	12-206-81	47	478	N		
12-LO	12-208-35	48	35	Y	A	42.3
12-LO	12-214-129	49	129	Y	C	38.7
12-LO	12-214-151	50	151	N		
12-LO	12-214-360	51	358	N		
12-LO	12-215-467	52	466	N		

FIG.2B

12-LO	12-216-421	53	418	Y	A	36.0
12-LO	12-219-230	54	229	Y	G	32.1
12-LO	12-219-256	55	255	N		
12-LO	12-220-48	56	478	N		
12-LO	12-221-302	57	302	N		
12-LO	12-223-179	58	179	N		
12-LO	12-223-207	59	207	Y	C	38.4
12-LO	12-225-541	60	540	Y	C	37.4
12-LO	12-226-167	61	166	Y	G	41.2
12-LO	12-226-458	62	455	N		
12-LO	12-229-332	63	332	N		
12-LO	12-229-351	64	351	N		
12-LO	12-230-364	65	364	N		
12-LO	12-231-100	66	99	N		
12-LO	12-231-148	67	147	N		
12-LO	12-231-266	68	265	N		
cPLA ₂	10-231-23	69	500	Y	A	8.79
cPLA ₂	10-233-386	70	501	Y	G	28.3
cPLA ₂	10-238-328	71	501	Y	T	17.9
cPLA ₂	10-239-368	72	501	N		
cPLA ₂	10-223-30	73	501	Y	G	22.5
cPLA ₂	10-223-72	74	501	N		
cPLA ₂	10-223-130	75	501	N		
cPLA ₂	10-223-262	76	501	N		
cPLA ₂	10-223-392	77	501	N		
cPLA ₂	10-224-341	78	501	N		
cPLA ₂	10-227-282	79	501	Y	G	3.93
ANX1	10-240-241	80	501	N		
ANX1	10-249-185	81	501	N		
ANX1	10-251-128	82	501	N		
ANX1	10-252-209	83	501	N		
ANX1	12-387-32	84	501	Y	G	33.9
ANX1	10-242-316	85	500	N		
ANX1	10-245-412	86	501	N		
ANX1	12-378-171	87	501	N		
ANX1	12-378-228	88	501	N		
ANX1	12-378-450	89	501	N		
ANX1	12-379-65	90	501	N		
ANX1	12-382-204	91	501	Y	G	50.0
ANX1	12-383-117	92	501	N		
ANX1	12-383-170	93	501	N		
ANX1	12-383-268	94	501	N		
ANX1	12-384-336	95	501	N		
ANX1	12-384-451	96	501	N		
ANX1	12-385-123	97	258	N		
ANX1	12-385-427	98	501	N		
ANX1	12-386-155	99	443	Y	G	8.15
ANX1	12-386-24	100	313	N		
ANX1	12-387-177	101	501	Y	T	33.5
ANX1	12-389-431	102	501	N		
ANX1	12-391-366	103	501	N		
ANX1	12-394-85	104	501	N		
ANX1	12-395-382	105	385	N		
ANX1	12-400-217	106	501	Y	G	27.2
ANX1	12-400-280	107	501	N		
ANX1	12-401-378	108	380	N		

FIG.2C

ANX1	12-402-126	109	323	N		
ANX1	12-404-265	110	317	N		
ANX1	12-406-52	111	501	N		
ANX1	12-406-409	112	501	N		
ANX1	12-407-217	113	501	N		
ANX1	12-407-399	114	501	N		
ANX1	12-408-355	115	501	Y	G	2.69
ANX1	12-409-221	116	229	N		
ANX1	12-410-301	117	486	N		
ANX2	10-395-101	118	501	N		
ANX2	10-395-124	119	501	N		
ANX2	10-395-155	120	501	N		
ANX2	10-395-294	121	501	N		
ANX2	10-396-100	122	501	N		
ANX2	10-397-201	123	501	N		
ANX2	10-399-178	124	501	N		
ANX2	10-400-369	125	501	N		
ANX2	10-392-20	126	497	N		
ANX2	10-392-103	127	501	N		
ANX2	10-392-324	128	501	N		
ANX2	10-393-27	129	501	N		
ANX2	10-393-324	130	501	N		
ANX2	12-727-237	131	501	N		
ANX2	12-728-224	132	501	N		
ANX2	12-730-142	133	501	N		
ANX2	12-730-193	134	501	N		
ANX2	12-731-60	135	501	N		
ANX2	12-731-119	136	501	N		
ANX2	12-731-137	137	501	N		
ANX2	12-731-146	138	501	N		
ANX2	12-731-398	139	501	N		
ANX2	12-732-113	140	501	N		
ANX2	12-732-164	141	501	N		
ANX2	12-732-165	142	501	Y	C	27.4
ANX2	12-732-445	143	501	N		
ANX2	12-734-201	144	501	N		
ANX2	12-735-42	145	501	N		
ANX2	12-736-363	146	501	N		
ANX2	12-737-69	147	501	Y	A	36.8
ANX2	12-737-296	148	501	N		
ANX2	12-738-429	149	501	Y	T	35.5
ANX2	12-740-112	150	501	Y	G	37.6
ANX2	12-740-118	151	501	N		
ANX2	12-741-265	152	501	N		
ANX2	12-741-327	153	501	N		
ANX2	12-741-376	154	501	N		
ANX2	12-745-30	155	501	N		
ANX2	12-745-75	156	501	N		
ANX2	12-745-343	157	501	N		
ANX2	12-745-350	158	501	N		
ANX2	12-746-320	159	501	N		
ANX2	12-747-181	160	501	N		
ANX2	12-747-302	161	501	N		
ANX2	12-749-240	162	501	N		
ANX2	12-749-255	163	501	N		
ANX2	12-752-37	164	508	N		

FIG.2D

ANX2	12-752-85	165	501	N		
ANX2	12-752-196	166	501	N		
ANX2	12-752-484	167	501	N		
ANX2	12-753-139	168	501	N		
ANX2	12-753-376	169	501	N		
ANX2	12-754-172	170	501	N		
ANX2	12-754-218	171	501	N		
ANX2	12-754-328	172	501	N		
ANX2	12-754-396	173	501	N		
ANX2	12-755-280	174	501	N		
ANX2	12-757-384	175	501	N		
ANX2	12-758-257	176	501	N		
ANX2	12-758-374	177	501	N		
ANX2	12-758-424	178	501	N		
ANX2	12-761-23	179	541	N		
ANX2	12-761-178	180	501	N		
ANX2	12-764-329	181	501	N		
ANX2	12-764-377	182	501	N		
ANX2	12-765-168	183	501	N		
ANX2	12-765-504	184	501	N		
ANX3	10-372-279	185	501	N		
ANX3	10-375-136	186	501	N		
ANX3	10-376-281	187	501	N		
ANX3	10-369-392	188	501	N		
ANX3	10-371-257	189	501	N		
ANX3	12-513-389	190	501	N		
ANX3	12-513-494	191	501	N		
ANX3	12-515-394	192	501	N		
ANX3	12-516-97	193	501	Y	T	37.2
ANX3	12-520-287	194	501	N		
ANX3	12-520-323	195	501	Y	A	21.5
ANX3	12-523-179	196	501	Y	A	29.9
ANX3	12-523-270	197	501	N		
ANX3	12-527-367	198	501	Y	T	18.9
ANX3	12-529-376	199	501	N		
ANX3	12-529-489	200	501	N		
ANX3	12-530-134	201	501	Y	T	39.3
ANX3	12-530-393	202	501	N		
ANX3	12-531-173	203	501	Y	C	37.6
ANX3	12-539-441	204	501	N		
ANX3	12-543-78	205	501	N		
ANX3	12-543-79	206	501	N		
ANX3	12-546-235	207	501	N		
ANX3	12-549-287	208	501	N		
ANX3	12-550-287	209	501	N		
ANX3	12-552-175	210	501	N		
ANX3	12-554-330	211	501	N		
ANX3	12-556-312	212	501	N		
ANX3	12-556-443	213	501	N		
ANX3	12-558-205	214	501	N		
ANX3	12-558-238	215	501	N		
ANX3	12-558-305	216	501	N		
ANX3	12-769-39	217	501	N		
ANX3	12-769-430	218	501	N		
ANX3	12-770-73	219	501	N		
ANX3	12-772-200	220	501	N		

FIG.2E

ANX3	12-772-254	221	501	N		
CAL1	10-87-73	222	72	N		
CAL1	10-87-74	223	73	N		
CAL1	10-87-80	224	79	N		
CAL1	10-87-140	225	138	N		
CAL1	10-88-81	226	81	Y	C	44.7
CAL1	10-89-41	227	41	N		
CAL1	10-90-35	228	35	Y	A	1.14
CAL1	10-91-274	229	274	N		
CAL1	10-93-133	230	133	N		
CAL1	10-94-197	231	197	Y	G/G	
CAL1	10-94-198	232	198	N		
CAL1	10-166-362	233	362	N		
CAL2	10-207-386	234	387	Y	C/C	
CAL2	10-207-409	235	409	Y	G	9.04
CAL2	10-118-307	236	307	Y	A	0.27
CAL2	10-173-247	237	247	N		
CAL2	10-173-294	238	294	Y	G	2.87
CAL2	10-173-347	239	347	Y	C/C	
CAL3	10-103-104	240	104	N		
CAL3	10-103-323	241	323	Y	T	22.3
CAL3	10-103-402	242	403	N		
CAL3	10-106-98	243	98	N		
CAL3	10-106-288	244	288	Y		
CAL3	10-106-378	245	380	Y		
CAL3	10-168-160	246	160	Y	T	42.1
CAL3	10-168-206	247	206	Y		
CAL3	10-168-284	248	283	N		
CAL3	10-169-318	249	317	N		
CALPA1	12-86-79	250	501	Y	C	37.4
CALPA1	12-88-393	251	501	N		
CALPA1	12-89-369	252	501	Y	G	36.3
CALPA1	12-89-91	253	501	N		
CALPA1	12-94-210	254	501	N		
CALPA1	12-94-516	255	521	N		
CALPA1	12-96-64	256	501	Y	T	8.52
CALPA1	12-97-83	257	501	N		
CALPA1	12-99-296	258	501	Y	T	6.45
CALPA1	12-100-266	259	501	Y	G	32.2
CALPA1	12-811-174	260	501	N		
CALPA1	12-815-94	261	501	N		
CALPA1	12-815-383	262	501	N		
CALPA1	12-815-384	263	500	N		
CALPA1	12-815-391	264	501	N		
CALPA1	12-817-214	265	501	N		
CALPA1	12-817-355	266	501	N		
CALPA1	12-819-437	267	501	N		
CALPA1	12-821-62	268	501	N		
CALPA1	12-821-483	269	501	N		
CALPA1	12-825-173	270	501	N		
CALPA1	12-826-312	271	501	N		
CALPA1	12-831-59	272	501	N		
CALPA1	12-833-264	273	501	N		
CALPA1	12-833-279	274	501	N		
CALPA1	12-833-280	275	502	N		
CALPA1	12-833-373	276	501	N		

FIG.2F

CALPA1	12-834-183	277	483	N		
CALPA1	12-835-54	278	501	N		
CALPA1	12-836-134	279	501	N		
CALPA1	12-836-237	280	500	N		
CALPA1	12-836-238	281	476	N		
CALPA1	12-836-257	282	498	N		
CALPA1	12-836-275	283	501	N		
CALPA1	12-838-179	284	501	N		
CALPA1	12-839-397	285	501	N		
CALPA1	12-840-47	286	501	N		
CALPA1	12-840-77	287	501	N		
CALPA1	12-841-445	288	445	N		
CALPA1	12-842-215	289	501	N		
CALPA1	12-842-447	290	499	N		
CALPA1	12-844-167	291	501	N		
CALPA1	12-845-364	292	501	N		
CALPA1	12-846-209	293	501	N		
CALPA1	12-847-123	294	501	N		
CALPA1	12-849-242	295	501	N		
CYP2J2	10-336-58	296	501	N		
CYP2J2	10-336-137	297	501	N		
CYP2J2	10-336-232	298	501	N		
CYP2J2	12-102-104	299	379	N		
CYP2J2	12-102-111	300	386	N		
CYP2J2	12-102-275	301	501	N		
CYP2J2	12-103-202	302	501	Y	C	14.3
CYP2J2	12-103-214	303	501	N		
CYP2J2	12-104-351	304	501	Y	T	27.4
CYP2J2	12-105-435	305	439	N		
CYP2J2	12-109-149	306	278	Y	A	8.51
CYP2J2	12-109-197	307	326	N		
CYP2J2	12-109-209	308	338	N		
CYP2J2	12-109-284	309	413	N		
CYP2J2	12-113-276	310	501	Y	G	31.2
CYP2J2	12-115-57	311	501	Y	G	8.87
CYP2J2	12-119-26	312	501	Y	G	29.8
COX1	12-347-308	313	501	N		
COX1	12-354-334	314	501	Y	C/C	
COX1	12-357-140	315	501	Y	C	7.14
COX1	12-361-320	316	501	Y	G	18.3
COX1	12-361-388	317	501	Y	A	18.5
COX1	12-365-251	318	501	Y	C	18.8
COX1	12-374-261	319	501	Y	T	21.3
COX1	10-308-116	320	501	N		
COX1	10-311-274	321	501	N		
COX1	10-314-76	322	501	N		
COX1	10-306-265	323	501	N		
COX2	10-52-386	324	386	N		
COX2	10-62-240	325	240	Y	C	12.23
COX2	10-65-276	326	276	Y		
COX2	10-67-42	327	42	N		
COX2	10-67-340	328	341	Y		
COX2	10-55-265	329	264	Y	C	40.9
COX2	10-57-278	330	278	Y		
COX2	10-59-176	331	176	Y		
COX2	10-60-114	332	114	N		

FIG.2G

PGDS	10-27-176	333	176	Y	A	5.32
PGDS	10-28-242	334	242	Y		
PGDS	10-30-349	335	350	Y	A/A	
PGDS	10-181-42	336	42	Y	C	30.2
PGDS	10-181-372	337	374	Y	C	26.3
PGDS	10-183-260	338	259	N		
PG15OH	10-475-163	339	501	N		
PG15OH	12-884-203	340	501	Y	T	29.7
PG15OH	10-479-266	341	501	N		
PG15OH	10-479-350	342	501	N		
PG15OH	10-479-394	343	501	N		
PG15OH	10-482-145	344	501	N		
PG15OH	12-854-64	345	501	N		
PG15OH	12-854-472	346	501	N		
PG15OH	12-855-194	347	501	N		
PG15OH	12-855-288	348	501	N		
PG15OH	12-855-423	349	501	N		
PG15OH	12-857-25	350	476	N		
PG15OH	12-858-346	351	501	Y	T	37.2
PG15OH	12-858-443	352	501	N		
PG15OH	12-860-388	353	501	N		
PG15OH	12-861-270	354	501	N		
PG15OH	12-862-349	355	501	N		
PG15OH	12-862-365	356	501	N		
PG15OH	12-862-452	357	501	N		
PG15OH	12-866-423	358	501	Y	C	46.2
PG15OH	12-867-47	359	501	N		
PG15OH	12-868-181	360	501	N		
PG15OH	12-868-198	361	501	N		
PG15OH	12-868-282	362	501	N		
PG15OH	12-869-128	363	501	N		
PG15OH	12-870-491	364	501	N		
PG15OH	12-872-52	365	501	N		
PG15OH	12-872-293	366	501	N		
PG15OH	12-873-185	367	501	N		
PG15OH	12-873-319	368	501	N		
PG15OH	12-875-248	369	501	Y	G	28.8
PG15OH	12-876-265	370	501	N		
PG15OH	12-876-280	371	501	N		
PG15OH	12-876-454	372	501	N		
PG15OH	12-877-59	373	501	N		
PG15OH	12-877-69	374	501	N		
PG15OH	12-877-79	375	501	N		
PG15OH	12-878-153	376	501	N		
PG15OH	12-878-419	377	501	N		
PG15OH	12-879-67	378	501	N		
PG15OH	12-879-439	379	501	N		
PG15OH	12-881-210	380	501	N		
PG15OH	12-881-389	381	501	N		
PG15OH	12-883-273	382	501	N		
PG15OH	12-885-196	383	501	N		
PG15OH	12-885-333	384	501	N		
PG15OH	12-885-407	385	501	N		
PG15OH	12-885-410	386	501	N		
PG15OH	12-886-195	387	501	Y	A	21.1
PG15OH	12-886-348	388	501	N		

FIG.2H

PG15OH	12-887-201	389	501	N		
PG15OH	12-887-467	390	501	N		
PG15OH	12-888-98	391	501	N		
PG15OH	12-888-203	392	501	Y	G	38.3
PG15OH	12-888-315	393	501	N		
PG15OH	12-889-518	394	479	N		
PG15OH	12-894-266	395	501	N		
PG15OH	12-895-391	396	501	Y	C	34.6
PG15OH	12-896-140	397	501	N		
PG15OH	12-897-115	398	501	N		
PG15OH	12-897-225	399	501	N		
PG15OH	12-898-49	400	528	N		
CYP8	12-164-119	401	501	Y	C	11.8
CYP8	12-168-84	402	501	Y	T	20.1
CYP8	12-168-365	403	501	N		
CYP8	12-170-299	404	501	Y	T	6.52
CYP8	12-171-360	405	501	Y	T	8.70
CYP8	12-173-59	406	501	Y	G	26.0
CYP8	12-175-214	407	501	Y	A	10.1
CYP8	12-177-183	408	501	Y	G	25.4
CYP8	12-177-366	409	501	N		
TAX2	10-128-45	410	45	Y	T/T	
TAX2	10-128-63	411	63	N		
TAX2	10-123-177	412	177	N		
TAX2	10-123-402	413	402	N		
TAX2	10-120-137	414	136	Y	A	1.60
TAX2	10-120-141	415	140	Y	A	3.09
TAX2	10-179-39	416	39	N		
TAX2	10-180-65	417	65	Y	C	44.7
TAX2	10-179-257	418	257	Y		
15-LOA	10-43-124	419	123	N		
15-LOA	10-43-134	420	133	N		
15-LOA	10-43-193	421	192	N		
15-LOA	10-43-195	422	194	N		
15-LOA	10-43-233	423	232	N		
15-LOA	10-43-138	424	137	Y		
15-LOA	10-46-372	425	369	Y	T	2.43
15-LOA	10-46-36	426	35	N		
15-LOA	10-47-103	427	102	Y		
15-LOA	10-47-125	428	124	Y	T	5.68
15-LOA	10-48-184	429	183	Y	T	28.0
15-LOA	10-48-381	430	382	Y	T	31.4
15-LOA	10-49-33	431	33	Y	T	14.3
15-LOA	10-39-148	432	150	Y	G	14.5
15-LOA	10-40-222	433	222	Y	A	47.6
15-LOA	10-40-252	434	250	N		
15-LOA	10-42-354	435	354	Y		
15-LOA	10-154-42	436	42	N		
15-LOA	10-154-156	437	156	Y	T	24.2
15-LOA	10-154-226	438	226	N		
15-LOB	12-776-259	439	501	N		
5-LO	10-384-109	440	501	N		
5-LO	12-296-388	441	501	Y	G	37.6
5-LO	10-388-379	442	501	N		
5-LO	10-389-116	443	501	N		
5-LO	10-389-349	444	501	N		

FIG.2I

5-LO	10-391-94	445	501	N		
5-LO	12-277-147	446	501	Y	T	44.9
5-LO	12-278-413	447	501	Y	A	33.9
5-LO	12-288-190	448	501	N		
5-LO	12-289-35	449	501	N		
5-LO	12-296-119	450	501	N		
5-LO	12-297-291	451	501	N		
5-LO	12-298-105	452	501	N		
5-LO	12-300-126	453	501	N		
5-LO	12-300-410	454	501	N		
5-LO	12-301-379	455	501	N		
5-LO	12-302-264	456	501	N		
5-LO	12-309-405	457	501	N		
5-LO	12-310-105	458	501	N		
5-LO	12-314-453	459	501	Y	A	18.8
5-LO	12-316-292	460	501	Y	C	40.8
LTA4H	10-281-314	461	501	N		
LTA4H	10-268-381	462	501	N		
LTA4H	12-54-297	463	501	Y	C	9.34
LTA4H	10-276-407	464	501	N		
LTA4H	12-44-50	465	501	Y	A	25.9
LTA4H	12-44-67	466	501	N		
LTA4H	12-45-145	467	501	N		
LTA4H	12-45-166	468	501	N		
LTA4H	12-45-305	469	501	N		
LTA4H	12-46-92	470	501	Y	G	31.9
LTA4H	12-47-132	471	501	Y	C	4.84
LTA4H	12-47-61	472	501	N		
LTA4H	12-48-100	473	501	N		
LTA4H	12-48-323	474	501	N		
LTA4H	12-48-369	475	501	N		
LTA4H	12-48-37	476	501	N		
LTA4H	12-49-131	477	501	Y	A	40.1
LTA4H	12-49-53	478	501	N		
LTA4H	12-49-64	479	501	N		
LTA4H	12-51-234	480	501	Y	A	43.3
LTA4H	12-51-253	481	501	N		
LTA4H	12-51-370	482	501	N		
LTA4H	12-52-400	483	501	N		
LTA4H	12-57-192	484	501	Y	T	41.2
LTA4H	12-57-221	485	501	Y	T	4.40
LTA4H	12-57-510	486	501	N		
LTB4H2	10-1-139	487	139	Y	G	36.3
LTB4H2	10-1-212	488	212	Y	T	16.3
LTB4H2	10-1-241	489	241	Y	A	5.84
LTB4H2	10-9-143	490	143	Y		
LTB4H2	10-9-185	491	185	Y	T/T	
LTB4H2	10-9-264	492	264	Y		
LTB4H2	10-11-22	493	22	N		
LTB4H2	10-13-152	494	152	Y	T	20.8
LTB4H2	10-13-256	495	256	Y		
LTB4H2	10-13-282	496	282	Y	C	25.0
LTB4H2	10-15-281	497	281	N		
LTB4H2	10-17-142	498	142	Y	C/C	
LTB4H2	10-18-302	499	302	N		
LTB4H2	10-23-331	500	331	N		

FIG.2J

LTB4H2	10-25-152	501	152	Y		
LTB4H2	10-25-258	502	258	N		
LTB4H2	10-3-103	503	103	Y	T	47.7
LTB4H2	10-3-144	504	144	Y		
LTB4H2	10-3-275	505	275	Y		
LTB4H2	10-5-227	506	227	Y	A	28.1
LTB4H2	10-7-155	507	155	Y	T	30.4
LTB4H2	10-7-383	508	381	N		
LTB4H2	10-7-98	509	98	N		
LTB412OH	12-561-270	510	501	Y	T	35.2
LTB412OH	12-563-87	511	501	Y	C	28.0
LTB412OH	12-564-64	512	501	Y	T	36.0
LTB412OH	12-564-214	513	501	N		
LTB412OH	12-568-207	514	501	N		
LTB412OH	12-568-365	515	501	N		
LTB412OH	12-568-367	516	501	N		
LTB412OH	12-571-337	517	501	Y	G	17.9
LTB412OH	12-573-378	518	501	Y	A	6.91
LTB412OH	10-294-256	519	501	N		
LTB412OH	10-294-304	520	501	N		
LTB412OH	10-295-201	521	501	N		
LTB412OH	10-296-80	522	501	N		
LTB412OH	10-296-373	523	501	N		
LTB412OH	10-298-122	524	501	N		
LTB412OH	10-298-158	525	501	N		
LTB412OH	10-300-49	526	501	N		
LTB412OH	10-300-185	527	501	N		
LTB4H3	10-10-328	528	327	Y	A	12.5
LTB4H3	10-12-52	529	52	N		
LTB4H3	10-14-46	530	46	Y	T	39.3
LTB4H3	10-19-358	531	357	Y		
LTB4H3	10-20-111	532	110	Y	A	15.8
LTB4H3	10-20-274	533	273	Y	A/A	
LTB4H3	10-24-90	534	90	Y	C	19.2
LTB4H3	10-24-204	535	204	Y	A	25.0
LTB4H3	10-24-221	536	221	N		
LTB4H3	10-24-234	537	234	Y	A	36.1
LTB4H3	10-24-288	538	288	N		
LTB4H3	10-24-311	539	311	N		
LTB4H3	10-26-289	540	289	N		
LTB4H3	10-8-39	541	39	Y		
LTB4H3	10-8-120	542	120	N		
LTB4H3	10-8-154	543	154	N		
LTB4H3	10-8-101	544	101	Y		
LTB4H3	10-8-86	545	86	Y		
LTB4H3	10-8-92	546	92	N		
LTB4H3	10-8-94	547	94	N		
LTB4R	12-61-472	548	501	N		
LTB4R	12-63-402	549	416	N		
LTB4R	12-63-74	550	88	N		
LTB4R	12-64-271	551	287	Y	C	28.6
LTB4R	12-65-98	552	439	N		
LTB4R	12-70-147	553	501	Y	C	11.5
LTB4R	12-70-397	554	501	Y	T	39.7
LTB4R	12-71-320	555	501	Y	A	4.49
LTB4R	12-73-150	556	501	N		

FIG.2K

LTB4R	12-73-49	557	501	Y	A	43.3
LTB4R	12-73-56	558	501	N		
LTB4R	12-74-38	559	501	Y	C	44.1
LTB4R	12-76-238	560	501	Y	T	20.6
LTB4R	12-77-217	561	501	N		
LTB4R	12-77-478	562	501	Y	A	4.40
LTB4R	12-80-114	563	501	N		
LTB4R	12-80-233	564	501	Y	C	4.55
LTB4R	12-82-250	565	250	N		
LTC4	10-176-85	566	85	Y	T	0.54
LTC4	10-176-51	567	51	N		
LTC4	10-176-207	568	207	N		
LTC4	10-176-397	569	397	Y	A	1.63
LTC4	10-177-219	570	219	Y	C	29.0
12-LO	12-214-85	571	85	N		
12-LO	12-215-272	572	271	N		
12-LO	12-221-163	573	163	N		
12-LO	12-225-82	574	82	N		
cPLA ₂	10-234-179	575	214	Y	Deletion AA	32.6
cPLA ₂	10-235-272	576	491	N		
ANX1	10-251-342	577	498	N		
ANX2	10-395-367	578	497	N		
ANX2	12-730-58	579	498	N		
ANX2	12-735-208	580	412	Y	Deletion	21.5
ANX2	12-739-22	581	498	Y	Insertion G	23.4
ANX3	12-540-363	582	498	N		
ANX3	12-550-206	583	497	N		
CAL2	12-207-410	584	409	N		
CAL3	10-171-254	585	255	N		
CALPA1	12-94-110	586	498	Y	Deletion AATT	32.5
CALPA1	12-834-290	587	498	N		
COX2	10-55-115	588	114	Y	Deletion TTATA	3.01
PG15OH	12-857-122	589	498	N		
PG15OH	12-872-175	590	498	N		
PG15OH	12-882-40	591	498	N		
PG15OH	12-888-234	592	498	N		
5-LO	12-278-353	593	499	N		
5-LO	12-283-386	594	498	N		
LTA4H	12-44-181	595	458	N		
ANX3	10-370-132	596	501	N		
ANX3	10-370-254	597	501	N		
15PGDHB	10-485-256	598	501	N		
15PGDHB	10-485-257	599	501	N		
15PGDHB	10-474-320	600	501	N		
5LO	10-387-371	601	501	N		
LTB412OH	12-570-239	602	501	N		
LTB412OH	12-570-344	603	501	N		
LTB412OH	12-570-393	604	501	N		
LTB412OH	12-570-421	605	501	N		
LTB412OH	12-570-62	606	501	N		
LTB4H3	10-4-144	607	141	N		
LTB4H3	10-4-161	608	158	N		

FIG.2L

LTB4H3	10-4-270	609	267	N		
LTB4H3	10-4-340	610	337	N		
LTB4H3	10-4-369	611	366	N		
LTB4H3	10-4-420	612	417	N		
LTB4H2	10-13-396	613	396	N		
12-LO	10-509-284	614	501	N		
12-LO	10-509-295	615	501	N		
12-LO	10-339-124	616	501	N		
12-LO	10-340-112	617	501	N		
12-LO	10-340-130	618	501	N		
12-LO	10-340-238	619	501	N		
12-LO	10-342-301	620	501	N		
12-LO	10-342-373	621	501	N		
12-LO	10-343-231	622	501	N		
12-LO	10-343-278	623	501	N		
12-LO	10-346-141	624	501	N	G/G	
12-LO	10-346-23	625	500	N		
12-LO	10-346-263	626	501	N		
12-LO	10-346-305	627	501	N		
12-LO	10-349-216	628	501	N		
12-LO	10-350-332	629	501	N		
12-LO	10-350-72	630	501	N		
12-LO	10-507-170	631	501	N		
12-LO	10-507-321	632	501	N		
12-LO	10-507-353	633	501	N		
12-LO	10-507-364	634	501	N		
12-LO	10-507-405	635	501	N		
12-LO	10-508-191	636	501	N		
12-LO	10-508-245	637	501	N		
12-LO	10-510-173	638	501	N		
12-LO	10-511-337	639	501	N		
12-LO	10-512-36	640	501	Y	C	39.4
12-LO	10-511-62	641	501	N		
12-LO	10-512-318	642	501	N		
12-LO	10-513-250	643	501	N		
12-LO	10-513-262	644	501	N		
12-LO	10-513-352	645	501	N		
12-LO	10-513-365	646	501	N		
FLAP	10-517-100	647	501	N		
FLAP	10-518-125	648	501	N		
FLAP	10-518-194	649	501	N		
FLAP	10-522-71	650	501	N		

FIG.3A

SEQ ID NO.	BIALLELIC MARKER ID	1 ST ALLELE	2 ND ALLELE	POSITION RANGE OF PREFERRED SEQUENCE
1	10-253-118	A	G	[1-955]
2	10-253-298	G	C	[1-840]
3	10-253-315	C	T	[1-823]
4	10-499-155	A	G	[1-556],[898-955]
5	10-520-256	C	T	[1-384],[726-955]
6	10-500-258	G	T	[1-311],[653-955]
7	10-500-410	A	G	[1-160],[502-955]
8	10-503-159	G	T	[143-160],[388-408],[447-955]
9	10-504-172	A	T	[1-85],[124-792]
10	10-504-243	A	C	[1-15],[54-722]
19	10-35-358	G	C	[555-842]
23	12-628-306	G	A	[1-868],[904-955]
24	12-628-311	T	C	[1-873],[909-955]
25	12-629-241	G	C	[1-17],[247-658],[705-787],[882-955]
27	10-343-339	G	T	[487-506],[733-904]
28	10-347-74	A	G	[1-134],[240-487],[784-956]
35	10-348-391	A	G	[351-552],[682-776]
40	10-349-368	C	T	[416-525]
44	12-196-119	C	T	[1-469]
45	12-197-244	C	T	[153-206]
48	12-208-35	A	T	[1-346],[453-507]
52	12-215-467	G	T	[1-161],[254-499]
53	12-216-421	A	G	[1-486]
54	12-219-230	A	G	[1-485]
55	12-219-256	C	T	[1-485]
56	12-220-48	G	A	[1-577],[883-956]
57	12-221-302	A	C	[1-64],[265-286]
58	12-223-179	A	G	[1-468]
59	12-223-207	C	T	[1-468]
60	12-225-541	C	T	[1-60],[368-598]
61	12-226-167	G	C	[1-255],[344-508]
62	12-226-458	C	T	[1-255],[344-508]
63	12-229-332	G	C	[1-456]
64	12-229-351	G	C	[1-456]
65	12-230-364	C	T	[1-420]
66	12-231-100	C	T	[1-490]
67	12-231-148	C	T	[1-490]
68	12-231-266	C	T	[1-490]
71	10-238-328	C	T	[1-254],[483-728]
72	10-239-368	C	T	[1-144],[373-618]
73	10-223-30	G	C	[1-653],[729-1001]
74	10-223-72	A	G	[1-612],[688-1001]
75	10-223-130	A	T	[1-555],[631-1001]
76	10-223-262	A	G	[1-424],[500-1001]
77	10-223-392	A	G	[1-294],[370-1001]
78	10-224-341	C	T	[137-176],[428-563],[920-1001]
82	10-251-128	A	G	[202-240],[373-415],[464-518],[581-777]
84	12-387-32	A	G	[1-396],[464-1001]
85	10-242-316	G	C	[1-350],[418-1000]
86	10-245-412	A	G	[367-701]
87	12-378-171	T	C	[1-731]
88	12-378-228	G	A	[1-788]
89	12-378-450	T	A	[1-1001]
90	12-379-65	A	G	[1-1001]
91	12-382-204	A	G	[1-1001]

FIG.3B

92	12-383-117	A	G	[1-37],[246-317],[383-1001]
93	12-383-170	A	G	[193-264],[330-1001]
94	12-383-268	G	T	[95-166],[232-1001]
98	12-385-427	G	T	[257-826]
99	12-386-155	G	T	[272-682],[823-943]
100	12-386-24	C	T	[272-682]
101	12-387-177	C	T	[1-251],[319-1001]
102	12-389-431	C	T	[1-386],[470-583],[644-996]
103	12-391-366	C	T	[293-1001]
104	12-394-85	A	C	[1-103],[184-266],[345-1001]
105	12-395-382	A	G	[1-885]
108	12-401-378	A	G	[1-880]
109	12-402-126	C	T	[99-823]
110	12-404-265	A	G	[1-261],[314-501],[715-733],[782-817]
111	12-406-52	C	T	136-952],[984-1001]
112	12-406-409	A	G	[1-595],[627-1001]
113	12-407-217	G	C	[247-673]
114	12-407-399	A	T	[1-491],[955-1001]
115	12-408-355	G	C	[80-907]
116	12-409-221	A	C	[1-500]
117	12-410-301	C	T	[111-986]
118	10-395-101	A	G	[1-529],[633-1001]
119	10-395-124	A	G	[1-539],[611-1001]
120	10-395-155	A	T	[1-509],[581-1001]
121	10-395-294	C	T	[1-371],[443-858]
122	10-396-100	A	G	[1-506],[635-776],[952-1001]
124	10-399-178	A	G	[1-142],[178-514],[632-1001]
125	10-400-369	A	T	[1-285],[385-513],[555-844],[878-941]
126	10-392-20	A	G	[75-203],[245-534],[568-631],[746-849],[898-997]
127	10-392-103	A	G	[1-552],[663-770],[819-1001]
128	10-392-324	G	C	[1-331],[442-549],[598-891],[977-1001]
129	10-393-27	G	C	[1-76],[187-294],[343-636],[722-1001]
130	10-393-324	A	G	[1-340],[423-1001]
131	12-727-237	A	G	[513-1001]
132	12-728-224	A	G	[352-507],[661-772],[862-1001]
133	12-730-142	A	G	[1-1001]
134	12-730-193	A	G	[1-1001]
135	12-731-60	C	T	[97-665],[711-729],[898-1001]
136	12-731-119	C	T	[1-606],[652-670],[839-1001]
137	12-731-137	G	T	[1-588],[634-652],[821-1001]
138	12-731-146	A	C	[1-579],[625-643],[812-1001]
139	12-731-398	C	T	[1-327],[373-391],[560-743],[823-1001]
140	12-732-113	A	G	[58-1001]
141	12-732-164	A	G	[1-1001]
142	12-732-165	G	C	[1-1001]
143	12-732-445	C	T	[1-935],[975-1001]
144	12-734-201	T	C	[161-1001]
145	12-735-42	G	A	[1-343],[374-566],[656-682],[731-961]
146	12-736-363	G	A	[1-1001]
147	12-737-69	T	C	[1-739]
148	12-737-296	G	A	[1-960]
149	12-738-429	G	A	[1-205],[411-1001]
150	12-740-112	A	G	[1-26],[144-616],[743-1001]
151	12-740-118	C	T	[1-20],[138-610],[737-1001]
152	12-741-265	G	A	[1-1001]
153	12-741-327	T	A	[1-1001]
154	12-741-376	G	A	[1-1001]

FIG.3C

155	12-745-30	G	A	[1-1001]
156	12-745-75	T	C	[1-1001]
157	12-745-343	T	G	[1-1001]
158	12-745-350	C	A	[1-1001]
159	12-746-320	C	T	[1-1001]
160	12-747-181	C	T	[1-1001]
161	12-747-302	C	T	[1-1001]
164	12-752-37	G	A	[1-1003]
165	12-752-85	C	G	[1-1001]
166	12-752-196	T	C	[1-62],[108-1001]
167	12-752-484	T	C	[396-1001]
168	12-753-139	C	T	[1-1001]
169	12-753-376	C	T	[1-778],[855-1001]
170	12-754-172	C	T	[1-1001]
171	12-754-218	C	T	[1-1001]
172	12-754-328	G	C	[1-1001]
173	12-754-396	G	T	[1-1001]
174	12-755-280	G	C	[1-1001]
176	12-758-257	A	C	[1-1001]
177	12-758-374	A	C	[1-1001]
178	12-758-424	A	G	[1-1001]
179	12-761-23	G	A	[1-177],[253-701]
180	12-761-178	G	A	[1-292],[368-1001]
181	12-764-329	G	A	[1-1001]
182	12-764-377	G	A	[1-1001]
183	12-765-168	G	A	[1-906]
184	12-765-504	T	C	[1-1002]
190	12-513-389	C	T	[1-1001]
191	12-513-494	G	C	[1-999]
192	12-515-394	A	T	[77-950]
193	12-516-97	C	T	[1-744],[798-1001]
194	12-520-287	A	T	[179-468],[506-885]
195	12-520-323	A	G	[143-432],[470-849]
196	12-523-179	G	A	[1-291],[344-1001]
197	12-523-270	G	A	[1-382],[435-1001]
198	12-527-367	T	A	[1-496],[595-1001]
199	12-529-376	T	C	[279-1001]
200	12-529-489	T	C	[1-37],[391-1001]
201	12-530-134	A	T	[1-94],[166-224],[316-803]
202	12-530-393	C	T	[57-544],[766-1001]
203	12-531-173	C	T	[1-231],[414-735],[789-1001]
204	12-539-441	C	T	[1-1001]
205	12-543-78	G	A	[1-836]
206	12-543-79	C	G	[1-837]
207	12-546-235	C	T	[1-403],[492-1001]
208	12-549-287	T	C	[149-494]
209	12-550-287	A	G	[304-1001]
210	12-552-175	G	A	[1-750],[831-883]
211	12-554-330	G	T	[1-1001]
212	12-556-312	A	C	[1-1001]
213	12-556-443	C	T	[1-1001]
214	12-558-205	C	G	[1-1001]
215	12-558-238	T	C	[1-1001]
216	12-558-305	T	A	[1-1001]
217	12-769-39	G	T	[1-292],[593-624],[690-1001]
218	12-769-430	C	T	[202-233],[299-633]
219	12-770-73	G	A	[1-716]

FIG.3D

220	12-772-200	G	A	[1-732],[788-1001]
221	12-772-254	T	C	[1-786],[842-1001]
233	10-166-362	A	C	
250	12-86-79	G	A	[70-653],[748-1001]
252	12-89-369	G	C	[1-51],[102-1001]
253	12-89-91	A	G	[1-329],[380-1000]
254	12-94-210	C	T	[573-588]
255	12-94-516	A	T	[287-302]
256	12-96-64	C	A	[1-630],[936-1001]
257	12-97-83	A	C	[1-20],[543-649],[719-916],[964-1001]
258	12-99-296	G	A	[1-210],[305-522],[904-1001]
259	12-100-266	T	C	[504-545],[927-949]
260	12-811-174	T	C	[1-945]
261	12-815-94	A	G	[1-1001]
262	12-815-383	A	G	[1-1001]
263	12-815-384	G	C	[1-1001]
264	12-815-391	C	T	[1-1001]
268	12-821-62	T	G	[1-294],[376-437],[621-887]
269	12-821-483	T	G	[1-48],[460-510],[664-715],[797-858]
270	12-825-173	A	C	[1-34],[522-1001]
273	12-833-264	T	A	[1-86],[216-446],[558-1001]
274	12-833-279	G	A	[1-101],[231-461],[573-1001]
275	12-833-280	T	C	[1-102],[232-462],[574-1001]
276	12-833-373	G	A	[1-195],[325-555],[667-1001]
277	12-834-183	A	G	[295-990]
278	12-835-54	A	G	[1-1001]
279	12-836-134	C	T	[84-249],[354-587],[633-1001]
280	12-836-237	A	G	[1-147],[252-945]
281	12-836-238	A	T	[1-123],[228-919]
282	12-836-257	A	G	[1-123],[228-919]
283	12-836-275	A	C	[1-108],[213-904]
284	12-838-179	A	G	[1-519],[718-1001]
285	12-839-397	G	A	[1-43],[110-1001]
286	12-840-47	C	G	[1-553],[659-1001]
287	12-840-77	T	C	[1-583],[689-1001]
288	12-841-445	G	C	[1-502]
291	12-844-167	T	C	[186-1001]
292	12-845-364	G	A	[1-849]
293	12-846-209	A	T	[1-817]
294	12-847-123	A	G	[1-1001]
295	12-849-242	C	A	[1-27],[490-658]
298	10-336-232	A	G	[507-1001]
299	12-102-104	A	G	[1-630],[712-790]
300	12-102-111	A	G	[1-630],[712-790]
301	12-102-275	A	G	[1-581],[663-741],[834-851],[891-1001]
302	12-103-202	C	T	[188-767]
303	12-103-214	A	G	[176-755]
304	12-104-351	T	G	[1-20],[336-402],[438-511],[911-935]
305	12-105-435	A	G	[1-147],[492-924]
306	12-109-149	A	G	[1-59],[289-607]
307	12-109-197	A	G	[1-59],[289-607]
308	12-109-209	A	G	[1-59],[289-607]
309	12-109-284	A	G	[1-59],[289-607]
310	12-113-276	T	C	[1-1001]
311	12-115-57	A	G	[507-1001]
312	12-119-26	T	C	[1-569]
314	12-354-334	G	A	[1-750]

FIG.3E

315	12-357-140	C	T	[1-1001]
316	12-361-320	G	T	[1-201],[268-1001]
317	12-361-388	A	G	[1-133],[200-1001]
318	12-365-251	G	C	[1-41],[132-151],[232-622],[688-933]
319	12-374-261	G	A	[249-1001]
321	10-311-274	C	T	[125-305],[472-878]
322	10-314-76	C	T	[1-224],[290-535],[803-1001]
335	10-30-349	A	G	
340	12-884-203	C	T	[1-349],[464-1001]
342	10-479-350	C	T	[1-280],[446-1001]
343	10-479-394	A	G	[1-236],[402-1001]
345	12-854-64	A	G	[1-1001]
346	12-854-472	G	T	[1-1001]
347	12-855-194	T	G	[1-1001]
348	12-855-288	T	C	[1-1001]
349	12-855-423	T	G	[1-1001]
350	12-857-25	C	T	[221-985]
351	12-858-346	T	C	[1-1001]
352	12-858-443	G	A	[1-1001]
353	12-860-388	G	A	[1-30],[157-628],[831-1001]
354	12-861-270	C	T	[1-780]
355	12-862-349	A	G	[78-1001]
356	12-862-365	C	T	[62-1001]
357	12-862-452	G	T	[1-1000]
358	12-866-423	C	T	[1-434],[521-1001]
359	12-867-47	C	T	[81-769]
360	12-868-181	A	G	[306-1001]
361	12-868-198	A	G	[289-1001]
362	12-868-282	C	T	[205-1001]
363	12-869-128	A	C	[1-128],[908-1001]
365	12-872-52	A	G	[436-1001]
366	12-872-293	A	G	[185-1001]
367	12-873-185	T	C	[114-257],[288-377],[572-1001]
368	12-873-319	T	A	[1-139],[248-391],[422-511],[706-1001]
369	12-875-248	T	C	[1-408],[525-1001]
370	12-876-265	T	A	[1-1001]
371	12-876-280	C	G	[1-1001]
372	12-876-454	G	A	[1-1001]
373	12-877-59	C	T	[329-1001]
374	12-877-69	G	T	[319-1001]
375	12-877-79	C	T	[309-1001]
376	12-878-153	C	T	[207-937]
377	12-878-419	G	T	[1-629],[734-929]
378	12-879-67	G	C	[1-200],[261-460],[527-1001]
379	12-879-439	A	G	[1-89],[156-796]
380	12-881-210	A	G	[1-1001]
381	12-881-389	G	T	[1-841]
382	12-883-273	G	C	[1-56],[96-1001]
383	12-885-196	T	C	[1-1001]
384	12-885-333	C	G	[1-1001]
385	12-885-407	T	C	[1-1001]
386	12-885-410	C	G	[1-1001]
387	12-886-195	T	C	[1-815],[867-1001]
388	12-886-348	T	C	[1-968]
389	12-887-201	G	A	[1-59],[181-1001]
390	12-887-467	T	C	[295-325],[447-1001]
391	12-888-98	G	A	[1-717],[916-1001]

FIG.3F

392	12-888-203	C	A	[1-822]
393	12-888-315	T	G	[1-1001]
394	12-889-518	G	A	[1-89],[280-320],[441-1001]
395	12-894-266	T	C	[1-1001]
396	12-895-391	G	A	[148-1001]
397	12-896-140	T	A	[60-76],[126-1001]
398	12-897-115	T	C	[259-557]
399	12-897-225	G	A	[369-667]
400	12-898-49	G	A	[1-283],[372-781]
401	12-164-119	T	G	[1-646],[979-1001]
403	12-168-365	C	G	[1-600]
407	12-175-214	A	G	[1-154],[227-317],[391-660],[747-1001]
408	12-177-183	C	G	[1-837],[975-1001]
409	12-177-366	C	A	[1-1001]
427	10-47-103	A	C	
428	10-47-125	A	T	
433	10-40-222	A	G	
434	10-40-252	C	T	
442	10-388-379	C	T	[1-202],[383-1001]
443	10-389-116	A	G	[1-538],[693-1001]
444	10-389-349	C	T	[1-305],[460-1001]
445	10-391-94	A	G	[1-259],[301-575],[691-928]
446	12-277-147	A	T	[1-693]
447	12-278-413	A	G	[1-151],[365-733],[775-1001]
448	12-288-190	G	A	[1-701]
449	12-289-35	A	G	[1-791],[946-1001]
450	12-296-119	A	G	[451-550]
451	12-297-291	C	T	[1-1001]
452	12-298-105	G	A	[1-162],[348-1001]
453	12-300-126	A	G	[1-782]
454	12-300-410	A	C	[1-415],[447-498]
455	12-301-379	A	T	[1-627],[932-1001]
456	12-302-264	G	A	[1-1001]
458	12-310-105	G	C	[293-1001]
459	12-314-453	A	T	[1-392],[439-558],[643-799]
460	12-316-292	C	T	[1-460]
461	10-281-314	G	T	[1-282],[453-832],[921-1001]
462	10-268-381	C	T	[1-197],[383-895]
463	12-54-297	C	T	[97-326],[404-518],[658-1001]
464	10-276-407	C	T	[1-97],[510-615],[954-1001]
465	12-44-50	T	C	[220-534],[918-1001]
466	12-44-67	T	C	[237-551],[935-1001]
469	12-45-305	C	T	[1-63],[488-816]
470	12-46-92	A	G	[83-1001]
471	12-47-132	C	T	[1-184],[457-685],[799-871],[987-1001]
472	12-47-61	C	T	[72-255],[528-756],[870-942]
473	12-48-100	A	G	[1-1001]
474	12-48-323	A	G	[1-747]
475	12-48-369	C	T	[1-682]
476	12-48-37	C	T	[1-1001]
477	12-49-131	T	C	[1-609],[677-749],[920-1001]
478	12-49-53	G	A	[1-531],[599-671],[842-1001]
479	12-49-64	G	A	[1-542],[610-682],[853-1001]
480	12-51-234	T	C	[1-47],[182-541],[919-1001]
481	12-51-253	C	A	[1-66],[201-560],[938-1001]
482	12-51-370	G	A	[1-182],[317-676]
483	12-52-400	G	A	[1-100],[404-1001]

FIG.3G

484	12-57-192	G	A	[1-168],[286-752]
485	12-57-221	G	A	[1-197],[315-781]
486	12-57-510	C	A	[1-163],[251-486],[604-1010]
494	10-13-152	C	T	
510	12-561-270	C	T	[188-203],[496-642],[697-738]
511	12-563-87	C	T	[1-929]
512	12-564-64	G	T	[1-213],[381-1001]
513	12-564-214	C	T	[1-64],[232-1001]
514	12-568-207	G	T	[424-513],[613-1001]
515	12-568-365	G	T	[266-355],[455-1001]
516	12-568-367	G	T	[264-353],[453-1001]
517	12-571-337	G	C	[1-53],[327-897]
518	12-573-378	A	G	[1-335],[437-910]
519	10-294-256	G	C	[1-53],[327-897]
520	10-294-304	G	C	[279-849],[942-1001]
522	10-296-80	A	G	[359-397],[531-906]
523	10-296-373	A	G	[60-105],[239-623],[924-1001]
524	10-298-122	C	T	[1-565],[737-873]
525	10-298-158	A	G	[1-529],[701-837]
526	10-300-49	A	G	[285-643],[808-854]
527	10-300-185	C	T	[92-507],[672-718],[976-1001]
549	12-63-402	A	G	[1-472]
550	12-63-74	A	G	[1-472]
551	12-64-271	C	T	[1-787]
552	12-65-98	C	T	[112-272],[334-864]
553	12-70-147	A	C	[1-211],[491-1001]
554	12-70-397	C	T	[241-1001]
555	12-71-320	A	G	[1-1001]
556	12-73-150	C	T	[1-140],[275-607],[646-821]
557	12-73-49	A	G	[1-240],[375-707],[746-921]
558	12-73-56	A	T	[1-233],[368-700],[739-914]
559	12-74-38	G	A	[1-1001]
561	12-77-217	C	T	[1-822]
562	12-77-478	A	G	[1-562]
563	12-80-114	T	C	[1-1001]
564	12-80-233	G	A	[1-1001]
565	12-82-250	A	T	[404-454]
571	12-214-85	CCTAT	-	[1-101],[259-305]
572	12-215-272	T	-	[1-161],[254-499]
573	12-221-163	GTCCTCA	T	[1-64],[265-286]
574	12-225-82	T	-	[1-60],[368-598]
577	10-251-342	GG	C	[1-56],[156-301],[364-560]
578	10-395-367	A	-	[1-263],[367-717],[764-783]
579	12-730-58	ACAA	-	[162-251],[287-321],[517-767]
580	12-735-208	-	Deletion	[1-689],[779-805],[854-1002]
581	12-739-22	G	-	[1-39],[386-640],[791-1002]
582	12-540-363	T	-	[1-1002]
583	12-550-206	T	-	[380-1002]
587	12-834-290	G	-	[196-1002]
589	12-857-122	CTCT	-	[145-1002]
590	12-872-175	T	-	[1-41],[310-1102]
592	12-888-234	C	-	[1-850],[950-1002]
593	12-278-353	A	-	[1-208],[422-790],[832-1001]
595	12-44-181	C	-	[308-622],[983-1002]
602	12-570-239	T	C	[386,671],[724,727],[947,1001]
603	12-570-344	T	C	[1,51],[491,601],[727,776],[829,832]

FIG.3H

619	10-340-238	A	G	[231,310],[487,601]
620	10-342-301	Insertion	-	[432,576],[605,609],[676,722]
621	10-342-373	C	T	[360,504],[533,537],[604,650],[930,1001]
625	10-346-23	A	G	[1,144],[233,274],[305,347],[478,592],[696,945]
626	10-346-263	G	C	[1,37],[68,110],[241,355],[459,708]
627	10-346-305	C	T	[1,68],[199,313],[417,666],[961,1001]
629	10-350-332	C	T	[1,913]
630	10-350-72	C	T	[1,1001]
632	10-507-321	A	C	[1,308],[440,462],[552,652],[711,1000]
633	10-507-353	C	T	[1,276],[408,430],[520,620],[679,1000]
634	10-507-364	C	T	[1,265],[397,609],[668,1000]
635	10-507-405	C	T	[1,224],[356,378],[468,568],[627,1000]
636	10-508-191	C	T	[1,403],[442,444],[491,640],[942,1000]
637	10-508-245	C	T	[1,349],[388,390],[463,586],[888,1000]
638	10-510-173	ATTTA	TTTTTT	[243,380],[411,546]
647	10-517-100	G	C	[1,1000]
648	10-518-125	G	T	[1,1000]
649	10-518-194	A	G	[1,1000]
650	10-522-71	A	G	[1,806],[844,863],[911,920],[950,1000]

FIG.4A

SEQ ID NO.	BIALLELIC MARKER ID	ORIGINAL ALLELE	ALTERNATIVE ALLELE
11	10-204-326	G	A
12	10-32-357	C	A
13	10-33-175	C	T
14	10-33-211	C	T
15	10-33-234	A	C
16	10-33-270	G	A
17	10-33-327	T	C
18	10-34-290	G	T
20	10-35-390	C	T
21	10-36-164	G	A
26	12-206-366	T	C
29	10-347-111	G	C
30	10-347-165	C	T
33	10-347-271	A	T
34	10-347-348	G	A
36	10-349-47	T	C
38	10-349-142	C	G
41	10-339-32	C	T
43	10-341-319	C	T
46	12-198-128	G	A
47	12-206-81	G	A
49	12-214-129	C	T
50	12-214-151	G	C
51	12-214-360	G	C
69	10-231-23	G	A
70	10-233-386	A	G
79	10-227-282	A	G
80	10-240-241	A	G
83	10-252-209	G	A
95	12-384-336	C	T
96	12-384-451	G	C
97	12-385-123	C	T
106	12-400-217	A	G
107	12-400-280	A	G
162	12-749-240	G	A
163	12-749-255	G	T
175	12-757-384	T	C
185	10-372-279	T	C
186	10-375-136	T	C
187	10-376-281	A	T
188	10-369-392	C	T
222	10-87-73	C	T
223	10-87-74	A	T
224	10-87-80	A	G
225	10-87-140	C	T
226	10-88-81	T	C
227	10-89-41	G	A
228	10-90-35	G	A
229	10-91-274	T	G
231	10-94-197	G	A
232	10-94-198	T	G
234	10-207-386	C	G
235	10-207-409	G	C
236	10-118-307	G	A
237	10-173-247	G	A

FIG.4B

238	10-173-294	A	G
239	10-173-347	C	T
240	10-103-104	C	T
241	10-103-323	T	C
242	10-103-402	C	T
243	10-106-98	C	A
246	10-168-160	T	C
247	10-168-206	C	A
248	10-168-284	T	A
249	10-169-318	C	A
251	12-88-393	A	C
265	12-817-214	G	A
266	12-817-355	T	C
267	12-819-437	A	G
271	12-826-312	G	A
272	12-831-59	G	C
289	12-842-215	T	C
290	12-842-447	A	G
297	10-336-137	T	A
313	12-347-308	G	A
320	10-308-116	C	T
326	10-65-276	G	A
327	10-67-42	A	T
328	10-67-340	T	C
331	10-59-176	C	T
332	10-60-114	A	G
334	10-28-242	G	A
336	10-181-42	C	T
337	10-181-372	C	T
338	10-183-260	C	G
341	10-479-266	G	A
364	12-870-491	A	G
402	12-168-84	A	C
404	12-170-299	G	A
405	12-171-360	C	T
406	12-173-59	A	G
410	10-128-45	T	C
411	10-128-63	A	G
412	10-123-177	G	A
414	10-120-137	G	A
415	10-120-141	C	A
425	10-46-372	C	T
429	10-48-184	C	T
430	10-48-381	C	T
431	10-49-33	C	T
432	10-39-148	A	G
435	10-42-354	T	C
436	10-154-42	C	T
437	10-154-156	C	T
438	10-154-226	G	A
439	12-776-259	A	G
440	10-384-109	C	T
441	12-296-388	A	G
457	12-309-405	A	G
467	12-45-145	A	G
468	12-45-166	G	A
487	10-1-139	G	T

FIG.4C

488	10-1-212	G	T
489	10-1-241	C	A
491	10-9-185	T	C
492	10-9-264	C	G
493	10-11-22	T	C
495	10-13-256	C	T
496	10-13-282	T	C
497	10-15-281	T	G
498	10-17-142	C	T
499	10-18-302	C	T
500	10-23-331	G	A
501	10-25-152	T	C
502	10-25-258	C	T
503	10-3-103	C	T
504	10-3-144	T	C
505	10-3-275	G	T
506	10-5-227	A	C
507	10-7-155	T	C
508	10-7-383	C	T
509	10-7-98	G	C
533	10-20-274	A	G
534	10-24-90	A	C
536	10-24-221	G	T
546	10-8-92	T	C
547	10-8-94	C	T
548	12-61-472	C	T
560	12-76-238	G	T
566	10-176-85	C	T
567	10-176-51	C	T
568	10-176-207	G	T
569	10-176-397	C	A
570	10-177-219	A	C
575	10-234-179	AA	-
576	10-235-272	T	-
584	10-207-410	-	C
585	10-171-254	GG	-
586	12-94-110	-	AATT
588	10-55-115	TTATA	-
591	12-882-40	A	-
594	12-283-386	T	-
598	10-485-256	A	G
599	10-485-257	T	C
600	10-474-320	Insertion A	-
601	10-387-371	T	C
604	12-570-393	C	T
605	12-570-421	T	G
606	12-570-62	Insertion TG	-
607	10-4-144	C	A
608	10-4-161	A	C
609	10-4-270	G	C
610	10-4-340	A	G
611	10-4-369	C	T
612	10-4-420	G	T
613	10-13-396	Insertion AAT	-

FIG.4D

614	10-509-284	C	T
616	10-339-124	C	T
617	10-340-112	C	A
618	10-340-130	T	A
622	10-343-231	Insertion C	-
623	10-343-278	C	T
624	10-346-141	G	A
628	10-349-216	Insertion CTG	-
631	10-507-170	A	G
639	10-511-337	Deletion	-
640	10-512-36	G	C
641	10-511-62	C	T
642	10-512-318	G	A
643	10-513-250	G	A
644	10-513-262	T	C
645	10-513-352	G	A
646	10-513-365	G	A

FIG.5

SEQ ID NO.	BIALLELIC MARKER ID	1 ST ALLELE	2 ND ALLELE
22	10-498-192	A	G
31	10-347-203	A	G
32	10-347-220	A	G
37	10-349-97	A	G
39	10-349-224	G	T
42	10-341-116	A	G
81	10-249-185	A	G
123	10-397-201	G	T
189	10-371-257	A	C
230	10-93-133	C	T
244	10-106-288	C	T
245	10-106-378	C	T
296	10-336-58	C	T
323	10-306-265	A	G
324	10-52-386	C	T
325	10-62-240	G	C
329	10-55-265	C	T
330	10-57-278	C	T
333	10-27-176	A	G
339	10-475-163	A	G
344	10-482-145	A	G
413	10-123-402	A	G
416	10-179-39	C	T
417	10-180-65	G	C
418	10-179-257	G	T
426	10-46-36	T	A
521	10-295-201	G	T
528	10-10-328	G	A
529	10-12-52	C	T
530	10-14-46	C	T
532	10-20-111	A	C
535	10-24-204	A	G
537	10-24-234	A	G
538	10-24-288	A	G
539	10-24-311	G	C
541	10-8-39	A	C
542	10-8-120	A	G
543	10-8-154	G	C
544	10-8-101	A	T
545	10-8-86	C	T
596	10-370-132	C	T
597	10-370-254	C	T
615	10-509-295	Insertion and Deletion	

FIG.6A

SEQ ID NO.	POSITION RANGE OF NOVEL SEQUENCE
26	[569-588],[815-956]
29	[1-97],[203-450],[747-956]
30	[1-43],[149-396],[693-956]
31	[111-358],[655-956]
32	[94-341],[638-956]
33	[44-291],[588-956]
34	[1-214],[511-844]
36	[734-843]
37	[684-793]
38	[639-748]
39	[557-666]
41	[217-319],[721-781]
42	[1-96],[276-387],[881-956]
43	[72-184],[678-820]
46	[1-56],[193-400]
47	[855-874]
49	[1-101],[259-305]
50	[1-101],[259-305]
51	[1-101],[259-305]
79	[1-311],[512-1001]
80	[709-1001]
81	[1-231],[723-741]
83	[291-476]
95	[1-138],[532-662],[970-1001]
96	[59-254],[648-778],[918-1001]
97	[318-757]
106	[88-182],[309-461],[798-843]
107	[1-119],[246-398],[735-780]
123	[1-449],[568-1001]
162	[264-407],[801-833]
163	[249-392],[786-818]
175	[1-419]
185	[267-360],[549-599],[651-807],[851-1001]
186	[1-459],[691-1001]
187	[1-311],[557-1001]
188	[1-155],[662-1001]
189	[1-39],[554-1001]
251	[746-1001]
265	[315-445],[873-1001]
266	[174-304],[732-1001]
271	[1-173],[572-844],[884-917]
272	[1-75],[556-576]
289	[1-191]
290	[160-421]
296	[1-151],[681-1001]
297	[1-72],[602-1001]
313	[1-319]
320	[592-1001]
339	[1-24],[804-1001]
341	[1-364],[530-1001]
364	[1-270],[554-1001]
402	[1-319]
404	[1-319],[767-830]
405	[1-222],[639-1001]
439	[1-73],[608-900]

FIG.6B

440	[1-40],[732-1001]
441	[182-281]
457	[1-315],[838-1001]
467	[1-222],[647-1001]
468	[1-201],[626-954]
521	[1-138],[281-412],[529-880]
548	[60-80]
560	[539-810]
588	[406-418]
591	[150-320],[777-824],[864-1002]
594	[300-450]
596	[196-237],[920-1001]
597	[74-115],[798-1001]
598	[557-1001]
599	[556-1001]
600	[256-267],[669-670],[833-835]
604	[1-100],[540-650],[776-825],[878-881],[969-985]
605	[1-128],[568-678],[804-853],[906-909],[997-1001]
606	[210-320],[446-495],[548-551],[771-1001]
607	[1-54]
608	[1-54]
609	[1-54]
610	[1-54]
611	[1-54]
612	[1-54]
613	[1-30],[138-179]
614	[725-814]
615	[714-803]
616	[1-252],[634-713],[890-1001]
617	[106-155],[357-436],[613-727]
618	[88-137],[339-418],[595-709]
622	[138-178],[592-638],[863-1001]
623	[91-131],[545-591],[816-1001]
624	[1-29],[118-159],[190-232],[363-477],[581-830]
628	[587-698]
631	[199-459],[591-613],[703-803],[862-1000]
641	[1-159],[190-325]
646	[1-20]

FIG.7A

SEQ ID NO.	POSITION RANGE OF MICROSEQUENCING PRIMERS	COMPLEMENTARY POSITION RANGE OF MICROSEQUENCING PRIMERS
1	458-477	479-498
2	459-477*	479-498
3	458-477	479-498
4	458-477	479-498
5	458-477	479-498
6	458-477	479-498
7	458-477	479-498
8	458-477	479-498
9	458-477	479-498
10	458-477	479-498
11	458-477	479-497*
12	459-477*	479-498
13	459-477*	479-498
14	458-477	479-498
15	459-477*	479-498
16	459-477*	479-498
17	459-477*	479-498
18	458-477	479-498
19	459-477*	479-498
20	459-477*	479-498
21	458-477	479-497*
22	458-477	479-498
23	458-477	479-497*
24	458-477	479-498
25	459-477*	479-498
26	459-477*	479-498
27	458-477	479-498
28	458-477	479-498
29	458-477	479-498
30	458-477	479-498
31	459-477*	479-498
32	458-477	479-497*
33	458-477	479-498
34	458-477	479-498
35	458-477	479-498
36	458-477	479-498
37	458-477	479-497*
38	458-477	479-498
39	458-477	479-497*
40	458-477	479-498
41	458-477	479-498
42	458-477	479-497*
43	458-477	479-498
44	100-118*	120-139
45	224-242*	244-263
46	108-127	129-148
47	458-477	479-498
48	16-34*	36-55
49	110-128*	130-149
50	131-150	152-171
51	338-357	359-378
52	446-465	467-486
53	398-417	419-437*
54	209-228	230-248*
55	235-254	256-275

FIG.7B

56	458-477	479-498
57	282-301	303-322
58	159-178	180-199
59	188-206*	208-227
60	521-539*	541-560
61	147-165*	167-185*
62	435-454	456-475
63	312-331	333-352
64	331-350	352-371
65	344-363	365-384
66	79-98	100-119
67	127-146	148-167
68	245-264	266-285
69	480-499	501-519*
70	481-500	502-520*
71	482-500*	502-521
72	481-500	502-521
73	482-500*	502-521
74	481-500	502-521
75	481-500	502-521
76	481-500	502-521
77	481-500	502-521
78	481-500	502-521
79	481-500	502-520*
80	481-500	502-521
81	481-500	502-521
82	481-500	502-521
83	481-500	502-521
84	482-500*	502-521
85	480-499	501-520
86	481-500	502-521
87	481-500	502-521
88	481-500	502-521
89	481-500	502-521
90	481-500	502-521
91	482-500*	502-521
92	481-500	502-521
93	481-500	502-521
94	481-500	502-521
95	481-500	502-521
96	481-500	502-521
97	238-257	259-278
98	481-500	502-521
99	423-442	444-462*
100	293-312	314-333
101	481-500	502-520*
102	481-500	502-521
103	481-500	502-521
104	481-500	502-521
105	365-384	386-405
106	482-500*	502-521
107	481-500	502-521
108	360-379	381-400
109	303-322	324-343
110	297-316	318-337
111	481-500	502-521
112	481-500	502-521

FIG.7C

113	481-500	502-521
114	481-500	502-521
115	482-500*	502-521
116	209-228	230-249
117	466-485	487-506
118	481-500	502-521
119	481-500	502-521
120	481-500	502-521
121	481-500	502-521
122	481-500	502-521
123	481-500	502-521
124	481-500	502-521
125	481-500	502-521
126	477-496	498-517
127	481-500	502-521
128	481-500	502-521
129	481-500	502-521
130	481-500	502-521
131	481-500	502-521
132	481-500	502-521
133	481-500	502-521
134	481-500	502-521
135	481-500	502-521
136	481-500	502-521
137	481-500	502-521
138	481-500	502-521
139	481-500	502-521
140	481-500	502-521
141	481-500	502-521
142	481-500	502-520*
143	481-500	502-521
144	481-500	502-521
145	481-500	502-521
146	481-500	502-521
147	482-500*	502-521
148	481-500	502-521
149	481-500	502-520*
150	482-500*	502-521
151	481-500	502-521
152	481-500	502-521
153	481-500	502-521
154	481-500	502-521
155	481-500	502-521
156	481-500	502-521
157	481-500	502-521
158	481-500	502-521
159	481-500	502-521
160	481-500	502-521
161	481-500	502-521
162	481-500	502-521
163	481-500	502-521
164	488-507	509-528
165	481-500	502-521
166	481-500	502-521
167	481-500	502-521
168	481-500	502-521
169	481-500	502-521

FIG.7D

170	481-500	502-521
171	481-500	502-521
172	481-500	502-521
173	481-500	502-521
174	481-500	502-521
175	481-500	502-521
176	481-500	502-521
177	481-500	502-521
178	481-500	502-521
179	521-540	542-561
180	481-500	502-521
181	481-500	502-521
182	481-500	502-521
183	481-500	502-521
184	481-500	502-521
185	481-500	502-521
186	481-500	502-521
187	481-500	502-521
188	481-500	502-521
189	481-500	502-521
190	481-500	502-521
191	481-500	502-521
192	481-500	502-521
193	481-500	502-520*
194	481-500	502-521
195	481-500	502-520*
196	482-500*	502-521
197	481-500	502-521
198	481-500	502-520*
199	481-500	502-521
200	481-500	502-521
201	482-500*	502-521
202	481-500	502-521
203	481-500	502-520*
204	481-500	502-521
205	481-500	502-521
206	481-500	502-521
207	481-500	502-521
208	481-500	502-521
209	481-500	502-521
210	481-500	502-521
211	481-500	502-521
212	481-500	502-521
213	481-500	502-521
214	481-500	502-521
215	481-500	502-521
216	481-500	502-521
217	481-500	502-521
218	481-500	502-521
219	481-500	502-521
220	481-500	502-521
221	481-500	502-521
222	52-71	73-92
223	53-72	74-93
224	59-78	80-99
225	118-137	139-158
226	62-80*	82-101

FIG.7E

227	21-40	42-61
228	15-34	36-54*
229	254-273	275-294
230	113-132	134-153
231	178-196*	198-217
232	178-197	199-218
233	342-361	363-382
234	368-386*	388-407
235	390-408*	410-429
236	287-306	308-326*
237	227-246	248-267
238	274-293	295-313*
239	328-346*	348-367
240	84-103	105-124
241	304-322*	324-343
242	383-402	404-423
243	78-97	99-118
244	269-287*	289-308
245	361-379*	381-400
246	141-159*	161-180
247	187-205*	207-226
248	263-282	284-303
249	297-316	318-337
250	481-500	502-520*
251	481-500	502-521
252	482-500*	502-521
253	481-500	502-521
254	481-500	502-521
255	501-520	522-541
256	482-500*	502-521
257	481-500	502-521
258	482-500*	502-521
259	482-500*	502-521
260	481-500	502-521
261	481-500	502-521
262	481-500	502-521
263	480-499	501-520
264	481-500	502-521
265	481-500	502-521
266	481-500	502-521
267	481-500	502-521
268	481-500	502-521
269	481-500	502-521
270	481-500	502-521
271	481-500	502-521
272	481-500	502-521
273	481-500	502-521
274	481-500	502-521
275	482-501	503-522
276	481-500	502-521
277	463-482	484-503
278	481-500	502-521
279	481-500	502-521
280	480-499	501-520
281	456-475	477-496
282	478-497	499-518
283	481-500	502-521

FIG.7F

284	481-500	502-521
285	481-500	502-521
286	481-500	502-521
287	481-500	502-521
288	425-444	446-465
289	481-500	502-521
290	479-498	500-519
291	481-500	502-521
292	481-500	502-521
293	481-500	502-521
294	481-500	502-521
295	481-500	502-521
296	481-500	502-521
297	481-500	502-521
298	481-500	502-521
299	359-378	380-399
300	366-385	387-406
301	481-500	502-521
302	482-500*	502-521
303	481-500	502-521
304	481-500	502-520*
305	419-438	440-459
306	258-277	279-297*
307	306-325	327-346
308	318-337	339-358
309	393-412	414-433
310	482-500*	502-521
311	481-500	502-520*
312	482-500*	502-521
313	481-500	502-521
314	482-500*	502-521
315	481-500	502-520*
316	481-500	502-520*
317	482-500*	502-521
318	482-500*	502-521
319	482-500*	502-521
320	481-500	502-521
321	481-500	502-521
322	481-500	502-521
323	481-500	502-521
324	366-385	387-406
325	221-239*	241-260
326	256-275	277-295*
327	22-41	43-62
328	322-340*	342-361
329	245-263*	265-284
330	259-277*	279-298
331	157-175*	177-196
332	94-113	115-134
333	156-175	177-195*
334	222-241	243-261*
335	330-349	351-369*
336	23-41*	43-62
337	355-373*	375-394
338	239-258	260-279
339	481-500	502-521
340	482-500*	502-521

FIG.7G

341	481-500	502-521
342	481-500	502-521
343	481-500	502-521
344	481-500	502-521
345	481-500	502-521
346	481-500	502-521
347	481-500	502-521
348	481-500	502-521
349	481-500	502-521
350	456-475	477-496
351	482-500*	502-521
352	481-500	502-521
353	481-500	502-521
354	481-500	502-521
355	481-500	502-521
356	481-500	502-521
357	481-500	502-521
358	482-500*	502-521
359	481-500	502-521
360	481-500	502-521
361	481-500	502-521
362	481-500	502-521
363	481-500	502-521
364	481-500	502-521
365	481-500	502-521
366	481-500	502-521
367	481-500	502-521
368	481-500	502-521
369	482-500*	502-521
370	481-500	502-521
371	481-500	502-521
372	481-500	502-521
373	481-500	502-521
374	481-500	502-521
375	481-500	502-521
376	481-500	502-521
377	481-500	502-521
378	481-500	502-521
379	481-500	502-521
380	481-500	502-521
381	481-500	502-521
382	481-500	502-521
383	481-500	502-521
384	481-500	502-521
385	481-500	502-521
386	481-500	502-521
387	482-500*	502-521
388	481-500	502-521
389	481-500	502-521
390	481-500	502-521
391	481-500	502-521
392	482-500*	502-521
393	481-500	502-521
394	459-478	480-499
395	481-500	502-521
396	481-500	502-520*
397	481-500	502-521

FIG.7H

398	481-500	502-521
399	481-500	502-521
400	508-527	529-548
401	481-500	502-520*
402	482-500*	502-521
403	481-500	502-521
404	481-500	502-520*
405	482-500*	502-521
406	481-500	502-520*
407	481-500	502-520*
408	481-500	502-520*
409	481-500	502-521
410	26-44*	46-65
411	43-62	64-83
412	157-176	178-197
413	382-401	403-422
414	117-135*	137-156
415	121-139*	141-160
416	19-38	40-59
417	46-64*	66-85
418	237-256	258-276*
425	350-368*	370-389
426	15-34	36-55
427	82-101	103-122
428	105-123*	125-144
429	164-182*	184-203
430	362-381	383-402
431	14-32*	34-53
432	130-149	151-169*
433	202-221	223-241*
434	230-249	251-270
435	334-353	355-373*
436	22-41	43-62
437	137-155*	157-176
438	206-225	227-246
439	481-500	502-521
440	481-500	502-521
441	482-500*	502-521
442	481-500	502-521
443	481-500	502-521
444	481-500	502-521
445	481-500	502-521
446	482-500*	502-521
447	482-500*	502-521
448	481-500	502-521
449	481-500	502-521
450	481-500	502-521
451	481-500	502-521
452	481-500	502-521
453	481-500	502-521
454	481-500	502-521
455	481-500	502-521
456	481-500	502-521
457	481-500	502-521
458	481-500	502-521
459	482-500*	502-521
460	481-500	502-520*

FIG.7I

461	481-500	502-521
462	481-500	502-521
463	482-500*	502-521
464	481-500	502-521
465	482-500*	502-521
466	481-500	502-521
467	481-500	502-521
468	481-500	502-521
469	481-500	502-521
470	481-500	502-520*
471	482-500*	502-521
472	481-500	502-521
473	481-500	502-521
474	481-500	502-521
475	481-500	502-521
476	481-500	502-521
477	482-500*	502-521
478	481-500	502-521
479	481-500	502-521
480	483-500*	502-521
481	481-500	502-521
482	481-500	502-521
483	481-500	502-521
484	481-500	502-520*
485	482-500*	502-520*
486	481-500	502-521
487	119-138	140-158*
488	192-211	213-231*
489	222-240*	242-261
491	166-184*	186-205
492	245-263*	265-284
493	2-21	23-42
494	133-151*	153-172
495	237-255*	257-276
496	263-281*	283-302
497	261-280	282-301
498	123-141*	143-162
499	282-301	303-322
500	311-330	332-351
501	133-151*	153-172
502	238-257	259-278
503	84-102*	104-123
504	125-143*	145-164
505	255-274	276-294*
506	208-226*	228-247
507	136-154*	156-175
508	361-380	382-401
509	78-97	99-118
510	481-500	502-520*
511	482-500*	502-521
512	481-500	502-520*
513	481-500	502-521
514	481-500	502-521
515	481-500	502-521
516	481-500	502-521
517	482-500*	502-521
518	482-500*	502-521

FIG.7J

519	481-500	502-521
520	481-500	502-521
521	481-500	502-521
522	481-500	502-521
523	481-500	502-521
524	481-500	502-521
525	481-500	502-521
526	481-500	502-521
527	481-500	502-521
528	307-326	328-346*
529	32-51	53-72
530	27-45*	47-66
532	91-109*	111-130
533	253-272	274-292*
534	71-89*	91-110
535	184-203	205-223*
536	201-220	222-241
537	214-233	235-253*
538	268-287	289-308
539	291-310	312-331
541	20-38*	40-59
542	100-119	121-140
543	134-153	155-174
544	81-100	102-119*
545	67-85*	87-106
546	72-91	93-112
547	74-93	95-114
548	481-500	502-521
549	396-415	417-436
550	68-87	89-108
551	268-286*	288-307
552	419-438	440-459
553	482-500*	502-521
554	482-500*	502-521
555	481-500	502-520*
556	481-500	502-521
557	482-500*	502-521
558	481-500	502-521
559	481-500	502-520*
560	481-500	502-520*
561	481-500	502-521
562	481-500	502-520*
563	481-500	502-521
564	481-500	502-520*
565	230-249	251-270
566	66-84*	86-105
567	31-50	52-71
568	187-206	208-227
569	378-396*	398-416*
570	200-218*	220-239
571	65-84	-
572	251-270	-
573	143-162	-
574	62-81	-
575	195-213*	-
576	471-490	-
577	478-497	-

FIG.7K

578	477-496	-
579	478-497	-
580	-	459-477*
581	-	498-516*
582	478-497	-
583	477-496	-
584	389-408	-
585	235-254	-
586	479-497 *	-
587	478-497	-
588	95-113 *	-
589	478-497	-
590	478-497	-
591	478-497	-
592	478-497	-
593	479-498	-
594	478-497	-
595	438-457	-
596	481-500	502-521
597	481-500	502-521
598	481-500	502-521
599	481-500	502-521
600	481-500	-
601	481-500	502-521
602	481-500	502-521
603	481-500	502-521
604	481-500	502-521
605	481-500	502-521
606	-	502-521
607	121-140	142-161
608	138-157	159-178
609	247-266	268-287
610	317-336	338-357
611	346-365	367-386
612	397-416	418-437
613	374-395	-
614	481-500	502-521
615	481-500	-
616	481-500	502-521
617	481-500	502-521
618	481-500	502-521
619	481-500	502-521
620	481-500	-
621	481-500	502-521
622	481-500	-
623	481-500	502-521
624	481-500	502-520*
625	480-499	501-520
626	481-500	502-521
627	481-500	502-521
628	481-500	-

FIG.7L

629	481-500	502-521
630	481-500	502-521
631	481-500	502-521
632	481-500	502-521
633	481-500	502-521
634	481-500	502-521
635	481-500	502-521
636	481-500	502-521
637	481-500	502-521
638	481-500	-
639	481-500	-
640	481-500	502-521
641	481-500	502-521
642	481-500	502-521
643	481-500	502-521
644	481-500	502-521
645	481-500	502-521
646	481-500	502-521
647	481-500	502-521
648	481-500	502-521
649	481-500	502-521
650	481-500	502-521

FIG.8A

SEQ ID NO.	POSITION RANGE OF AMPLIFICATION PRIMERS	COMPLEMENTARY POSITION RANGE OF AMPLIFICATION PRIMERS
1	361-379	761-780
2	181-199	581-600
3	164-182	564-583
4	324-343	536-553
5	294-310	743-760
6	221-237	670-687
7	70-86	519-536
8	326-343	760-780
9	307-324	557-575
10	237-254	487-505
11	153-170	590-607
12	121-139	522-541
13	304-322	705-723
14	268-286	669-687
15	245-263	646-664
16	209-227	610-628
17	152-170	553-571
18	189-206	525-542
19	120-137	526-543
20	88-105	494-511
21	315-334	741-760
22	287-306	621-638
23	266-286	764-782
24	271-291	769-787
25	238-257	617-637
26	222-239	635-654
27	140-157	553-572
28	405-422	826-845
29	368-385	789-808
30	314-331	735-754
31	276-293	697-716
32	259-276	680-699
33	209-226	630-649
34	132-149	553-572
35	90-109	488-507
36	432-451	829-848
37	382-401	779-798
38	337-356	734-753
39	255-274	652-671
40	114-133	511-530
41	447-464	845-864
42	363-380	771-789
43	160-177	568-586
44	1-20	450-469
45	1-19	380-399
46	1-20	380-400
47	398-415	835-854
48	1-21	487-507
49	1-20	429-448
50	1-20	429-448
51	1-20	429-448
52	1-20	479-499
53	1-20	467-486

FIG.8B

54	1-20	465-485
55	1-20	465-485
56	76-96	505-525
57	1-21	387-407
58	1-20	449-468
59	1-20	449-468
60	1-19	581-598
61	1-19	490-508
62	1-19	490-508
63	1-21	437-456
64	1-21	437-456
65	1-20	401-420
66	1-19	470-490
67	1-19	470-490
68	1-19	470-490
69	478-495	879-898
70	119-137	540-557
71	183-200	603-620
72	138-157	538-556
73	472-490	900-917
74	431-449	859-876
75	374-392	802-819
76	243-261	671-688
77	113-131	541-558
78	161-179	561-580
79	220-238	620-638
80	261-279	595-614
81	317-335	720-738
82	374-393	732-751
83	293-312	701-720
84	470-488	901-921
85	185-203	590-609
86	90-107	509-528
87	83-103	652-671
88	140-160	709-728
89	361-381	930-949
90	437-456	885-905
91	298-318	727-747
92	385-404	832-852
93	332-351	779-799
94	234-253	681-701
95	347-367	816-836
96	463-483	932-952
97	136-155	591-611
98	75-94	530-550
99	290-310	669-688
100	290-310	669-688
101	325-343	756-776
102	71-90	503-519
103	136-154	571-590
104	417-435	930-949
105	5-23	530-549
106	285-304	749-769
107	222-241	686-706

FIG.8C

108	4-22	446-466
109	198-218	634-654
110	53-70	504-523
111	450-468	881-899
112	93-111	524-542
113	285-303	746-766
114	103-121	564-584
115	147-165	587-607
116	9-29	435-455
117	187-206	636-656
118	406-425	797-816
119	384-403	775-794
120	354-373	745-764
121	216-235	607-626
122	402-420	735-752
123	301-319	707-724
124	324-341	618-635
125	134-153	533-552
126	478-495	906-924
127	399-416	827-845
128	178-195	606-624
129	475-493	879-896
130	179-197	583-600
131	265-284	694-714
132	277-295	720-740
133	360-378	867-887
134	309-327	816-836
135	442-462	898-918
136	383-403	839-859
137	365-385	821-841
138	356-376	812-832
139	104-124	560-580
140	389-408	879-898
141	338-357	828-847
142	337-356	827-846
143	57-76	547-566
144	301-320	682-701
145	10-30	524-542
146	386-406	844-862
147	47-67	547-566
148	268-288	768-787
149	478-498	903-922
150	391-410	828-846
151	385-404	822-840
152	316-336	745-765
153	378-398	807-827
154	427-447	856-876
155	67-86	512-530
156	112-131	557-575
157	380-399	825-843
158	387-406	832-850
159	183-201	672-692
160	321-340	767-787
161	200-219	646-666

FIG.8D

162	262-281	761-780
163	247-266	746-765
164	1-21	527-544
165	42-62	568-585
166	153-173	679-696
167	441-461	967-984
168	364-382	900-920
169	127-145	663-683
170	330-349	769-788
171	284-303	723-742
172	176-195	615-634
173	110-129	549-568
174	222-242	688-708
175	118-135	628-647
176	245-264	749-768
177	128-147	632-651
178	79-98	583-602
179	1-21	545-563
180	116-136	660-678
181	355-373	811-828
182	403-421	859-876
183	74-94	649-668
184	408-428	983-1002
185	224-242	627-646
186	366-385	765-784
187	221-239	646-665
188	111-129	512-531
189	246-263	661-679
190	114-133	610-627
191	9-28	505-522
192	107-126	537-557
193	405-424	891-911
194	216-234	653-673
195	180-198	617-637
196	129-149	661-678
197	220-240	752-769
198	352-372	849-867
199	349-369	856-875
200	461-481	968-987
201	369-389	798-817
202	110-130	539-558
203	329-346	723-741
204	62-79	567-587
205	130-150	558-578
206	131-151	559-579
207	267-284	795-815
208	304-324	770-787
209	216-234	712-731
210	188-207	659-674
211	172-192	645-663
212	194-214	674-693
213	63-83	543-562
214	236-256	687-705
215	268-288	719-737

FIG.8E

216	335-355	786-804
217	463-482	899-918
218	72-91	508-527
219	115-135	555-573
220	236-256	681-700
221	290-310	735-754
222	1-18	345-362
223	1-18	345-362
224	1-18	345-362
225	1-18	345-362
226	1-18	349-368
227	1-19	401-420
228	1-18	409-427
229	1-18	402-420
230	1-19	407-426
231	1-19	403-420
232	1-19	403-420
233	1-18	363-380
234	1-12	444-464
235	1-12	444-464
236	1-18	343-361
237	1-19	418-435
238	1-19	418-435
239	1-19	418-435
240	1-19	420-439
241	1-19	420-439
242	1-19	420-439
243	1-19	406-424
244	1-19	406-424
245	1-19	406-424
246	1-18	354-371
247	1-18	354-371
248	1-18	354-371
249	1-20	408-425
250	130-149	562-579
251	444-464	875-894
252	133-151	564-584
253	411-429	842-862
254	292-312	819-839
255	6-26	533-553
256	101-121	547-564
257	419-437	866-886
258	347-366	776-796
259	253-273	749-768
260	127-146	656-675
261	408-428	849-859
262	119-139	560-570
263	118-138	559-569
264	111-131	552-562
265	288-307	791-810
266	147-166	650-669
267	65-84	527-546
268	17-37	542-562
269	438-458	963-983

FIG.8F

270	329-347	774-794
271	337-357	792-811
272	92-112	540-559
273	315-335	746-764
274	330-350	761-779
275	331-351	762-780
276	424-444	855-873
277	306-326	737-757
278	449-468	879-898
279	368-386	909-929
280	266-284	807-827
281	242-260	783-803
282	242-260	783-803
283	227-245	768-788
284	323-342	895-915
285	448-468	877-897
286	98-118	527-547
287	128-148	557-577
288	1-21	483-502
289	248-268	697-715
290	478-498	927-945
291	245-265	649-667
292	415-435	843-863
293	294-312	786-796
294	379-397	835-855
295	293-312	723-742
296	444-462	845-863
297	365-383	766-784
298	270-288	671-689
299	276-296	733-753
300	276-296	733-753
301	227-247	684-704
302	301-318	733-751
303	289-306	721-739
304	373-393	831-851
305	5-23	442-462
306	130-148	577-597
307	130-148	577-597
308	130-148	577-597
309	130-148	577-597
310	288-307	756-775
311	445-463	901-921
312	41-61	509-526
313	195-213	636-656
314	307-327	816-834
315	362-381	794-814
316	182-200	677-696
317	114-132	609-628
318	252-270	697-717
319	262-280	741-761
320	386-403	754-771
321	228-245	632-651
322	426-443	827-846
323	238-255	660-678

FIG.8G

324	1-18	412-429
325	1-20	419-438
326	1-19	408-425
327	2-20	403-422
328	2-20	403-422
329	1-17	405-418
330	1-19	410-429
331	1-19	401-420
332	1-20	409-428
333	1-18	290-307
334	3-20	410-429
335	1-18	368-385
336	1-18	424-443
337	1-18	424-443
338	1-18	430-447
339	340-358	739-758
340	299-317	817-837
341	236-253	638-657
342	152-169	554-573
343	108-125	510-529
344	357-374	779-798
345	438-457	942-962
346	30-49	534-554
347	234-254	674-694
348	328-348	768-788
349	463-483	903-923
350	452-471	965-985
351	371-391	827-846
352	468-488	924-943
353	367-387	866-885
354	232-251	668-688
355	153-171	607-626
356	137-155	591-610
357	50-68	504-523
358	79-98	589-609
359	455-474	898-918
360	322-340	789-809
361	305-323	772-792
362	221-239	688-708
363	374-394	813-833
364	11-31	528-548
365	450-470	893-911
366	209-229	652-670
367	151-169	667-685
368	285-303	801-819
369	251-271	727-747
370	242-261	745-765
371	257-276	760-780
372	431-450	934-954
373	443-462	875-895
374	433-452	865-885
375	423-442	855-875
376	349-369	839-859
377	83-103	573-593

FIG.8H

378	435-453	951-971
379	64-82	580-600
380	292-311	723-743
381	113-132	544-564
382	229-248	674-694
383	235-255	677-696
384	372-392	814-833
385	446-466	888-907
386	449-469	891-910
387	246-266	674-694
388	399-419	827-847
389	184-204	683-701
390	450-470	949-967
391	148-168	578-598
392	253-273	683-703
393	365-385	795-815
394	426-445	976-995
395	309-329	745-765
396	348-368	870-889
397	138-158	622-640
398	106-126	595-615
399	216-236	705-725
400	6-26	558-576
401	116-134	600-619
402	105-125	566-584
403	386-406	847-865
404	296-315	781-799
405	142-160	521-541
406	443-460	901-921
407	287-306	765-785
408	217-236	664-683
409	399-418	846-865
410	1-20	349-366
411	1-20	349-366
412	1-18	412-429
413	1-18	412-429
414	1-16	333-349
415	1-16	333-349
416	1-18	400-420
417	1-18	407-424
418	1-18	400-420
425	1-18	398-417
426	1-18	398-417
427	1-20	404-423
428	1-20	404-423
429	1-18	403-421
430	1-18	403-421
431	1-19	402-419
432	1-20	405-422
433	1-18	335-352
434	1-18	335-352
435	1-18	413-432
436	1-19	283-300
437	1-19	283-300

FIG.8I

438	1-19	283-300
439	243-263	674-692
440	393-412	802-819
441	114-134	543-563
442	123-141	542-561
443	386-403	792-809
444	153-170	559-576
445	409-426	821-838
446	355-374	783-803
447	90-109	600-620
448	199-219	670-690
449	467-486	915-935
450	383-403	812-832
451	211-229	688-707
452	33-53	586-605
453	376-395	840-860
454	92-111	556-576
455	124-142	553-573
456	286-306	745-764
457	456-475	884-904
458	397-415	826-845
459	49-67	536-556
460	210-229	679-698
461	188-207	600-617
462	121-138	521-540
463	210-228	647-667
464	95-113	511-530
465	147-166	530-550
466	164-183	547-567
467	357-375	804-824
468	336-354	783-803
469	198-216	645-665
470	410-429	792-811
471	370-388	756-776
472	441-459	827-847
473	403-421	904-921
474	180-198	681-698
475	134-152	635-652
476	466-484	967-984
477	180-200	613-630
478	102-122	535-552
479	113-133	546-563
480	329-347	717-734
481	348-366	736-753
482	464-482	852-869
483	451-471	881-900
484	151-168	672-692
485	180-197	701-721
486	469-486	990-1010
487	1-20	429-448
488	1-20	429-448
489	1-20	429-448
491	1-18	332-351
492	1-18	332-351

FIG.8J

493	1-18	402-421
494	1-19	402-420
495	1-19	402-420
496	1-19	402-420
497	1-20	409-428
498	1-20	413-431
499	1-19	403-422
500	1-19	427-446
501	1-18	408-427
502	1-18	408-427
503	1-19	411-430
504	1-19	411-430
505	1-19	411-430
506	1-20	404-421
507	1-20	399-418
508	1-20	399-418
509	1-20	399-418
510	232-252	703-723
511	415-433	862-882
512	438-456	920-940
513	289-307	771-791
514	295-313	812-829
515	137-155	654-671
516	135-153	652-669
517	165-183	647-667
518	124-144	590-610
519	246-264	650-669
520	198-216	602-621
521	301-320	701-720
522	423-440	833-850
523	131-148	541-558
524	384-401	806-825
525	348-365	770-789
526	453-470	802-820
527	317-334	666-684
528	1-20	414-433
529	1-18	330-349
530	1-18	414-431
532	1-19	400-419
533	1-19	400-419
534	1-20	416-435
535	1-20	416-435
536	1-20	416-435
537	1-20	416-435
538	1-20	416-435
539	1-20	416-435
541	1-20	427-446
542	1-20	427-446
543	1-20	427-446
544	1-20	427-446
545	1-20	427-446
546	1-20	427-446
547	1-20	427-446
548	39-57	548-568

FIG.8K

549	15-35	445-464
550	15-35	445-464
551	19-38	407-425
552	342-360	777-797
553	355-374	784-804
554	105-124	534-554
555	187-206	703-721
556	353-370	799-818
557	453-470	899-918
558	446-463	892-911
559	88-106	519-538
560	264-283	671-689
561	288-306	772-792
562	28-46	512-532
563	101-121	595-614
564	220-240	714-733
565	1-21	436-454
566	1-18	404-423
567	1-18	404-423
568	1-18	404-423
569	1-18	404-423
570	1-18	400-419
571	1-20	429-448
572	1-20	479-499
573	1-21	387-407
574	1-19	581-598
575	36-56	346-366
576	220-237	553-571
577	157-176	515-534
578	140-159	531-550
579	441-459	948-968
580	133-153	647-665
581	476-494	907-927
582	425-445	939-957
583	292-310	788-807
584	1-18	443-463
585	1-19	333-351
586	389-409	916-936
587	207-227	638-658
588	1-19	401-418
589	376-395	889-909
590	324-344	767-785
591	459-478	904-924
592	281-301	711-731
593	147-166	657-677
594	114-132	547-567
595	235-254	618-638
596	371-389	772-791
597	249-267	650-669
598	246-264	652-669
599	245-263	651-668
600	182-199	590-609
601	131-149	535-552

FIG.8L

602	255-274	719-738
603	360-379	824-843
604	409-428	873-892
605	437-456	901-920
606	79-98	543-562
607	1-18	427-444
608	1-18	427-444
609	1-18	427-444
610	1-18	427-444
611	1-18	427-444
613	1-19	402-420
614	218-235	618-637
615	207-224	607-626
616	379-396	776-795
617	390-408	791-809
618	372-390	773-791
619	264-282	665-683
620	201-220	606-623
621	129-148	534-551
622	271-288	684-703
623	224-241	637-656
624	363-381	763-780
625	478-496	878-895
626	241-259	641-658
627	199-217	599-616
628	286-305	683-702
629	172-189	513-532
630	430-447	771-790
631	332-350	739-758
632	181-199	588-607
633	149-167	556-575
634	138-156	545-564
635	97-115	504-523
636	311-328	727-746
637	257-274	673-692
638	329-347	729-748
639	165-182	569-587
640	147-164	551-569
641	440-457	844-862
642	184-203	607-626
643	252-269	660-677
644	240-257	648-665
645	150-167	558-575
646	137-154	545-562
647	402-420	722-740
648	378-396	630-648
649	309-327	561-579
650	431-449	885-903

FIG.9A

SEQ ID NO.	POSITION RANGE OF PROBES
1	466-490
2	466-490
3	466-490
4	466-490
5	466-490
6	466-490
7	466-490
8	466-490
9	466-490
10	466-490
11	466-490
12	466-490
13	466-490
14	466-490
15	466-490
16	466-490
17	466-490
18	466-490
19	466-490
20	466-490
21	466-490
22	466-490
23	466-490
24	466-490
25	466-490
26	466-490
27	466-490
28	466-490
29	466-490
30	466-490
31	466-490
32	466-490
33	466-490
34	466-490
35	466-490
36	466-490
37	466-490
38	466-490
39	466-490
40	466-490
41	466-490
42	466-490
43	466-490
44	107-131
45	231-255
46	116-140
47	466-490
48	23-47
49	117-141
50	139-163
51	346-370
52	454-478
53	406-430
54	217-241
55	243-267

56	466-490
57	290-314
58	167-191
59	195-219
60	528-552
61	154-178
62	443-467
63	320-344
64	339-363
65	352-376
66	87-111
67	135-159
68	253-277
69	488-512
70	489-513
71	489-513
72	489-513
73	489-513
74	489-513
75	489-513
76	489-513
77	489-513
78	489-513
79	489-513
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81	489-513
82	489-513
83	489-513
84	489-513
85	488-512
86	489-513
87	489-513
88	489-513
89	489-513
90	489-513
91	489-513
92	489-513
93	489-513
94	489-513
95	489-513
96	489-513
97	246-270
98	489-513
99	431-455
100	301-325
101	489-513
102	489-513
103	489-513
104	489-513
105	373-397
106	489-513
107	489-513
108	368-392
109	311-335
110	305-329
111	489-513
112	489-513

FIG.9B

113	489-513
114	489-513
115	489-513
116	217-241
117	474-498
118	489-513
119	489-513
120	489-513
121	489-513
122	489-513
123	489-513
124	489-513
125	489-513
126	485-509
127	489-513
128	489-513
129	489-513
130	489-513
131	489-513
132	489-513
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156	489-513
157	489-513
158	489-513
159	489-513
160	489-513
161	489-513
162	489-513
163	489-513
164	496-520
165	489-513
166	489-513
167	489-513
168	489-513
169	489-513

170	489-513
171	489-513
172	489-513
173	489-513
174	489-513
175	489-513
176	489-513
177	489-513
178	489-513
179	529-553
180	489-513
181	489-513
182	489-513
183	489-513
184	489-513
185	489-513
186	489-513
187	489-513
188	489-513
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194	489-513
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210	489-513
211	489-513
212	489-513
213	489-513
214	489-513
215	489-513
216	489-513
217	489-513
218	489-513
219	489-513
220	489-513
221	489-513
222	60-84
223	61-85
224	67-91
225	126-150
226	69-93

FIG.9C

227	29-53
228	23-47
229	262-286
230	121-145
231	185-209
232	186-210
233	350-374
234	375-399
235	397-421
236	295-319
237	235-259
238	282-306
239	335-359
240	92-116
241	311-335
242	391-415
243	86-110
244	276-300
245	368-392
246	148-172
247	194-218
248	271-295
249	305-329
250	489-513
251	489-513
252	489-513
253	489-513
254	489-513
255	509-533
256	489-513
257	489-513
258	489-513
259	489-513
260	489-513
261	489-513
262	489-513
263	488-512
264	489-513
265	489-513
266	489-513
267	489-513
268	489-513
269	489-513
270	489-513
271	489-513
272	489-513
273	489-513
274	489-513
275	490-514
276	489-513
277	471-495
278	489-513
279	489-513
280	488-512
281	464-488
282	486-510
283	489-513

284	489-513
285	489-513
286	489-513
287	489-513
288	433-457
289	489-513
290	487-511
291	489-513
292	489-513
293	489-513
294	489-513
295	489-513
296	489-513
297	489-513
298	489-513
299	367-391
300	374-398
301	489-513
302	489-513
303	489-513
304	489-513
305	427-451
306	266-290
307	314-338
308	326-350
309	401-425
310	489-513
311	489-513
312	489-513
313	489-513
314	489-513
315	489-513
316	489-513
317	489-513
318	489-513
319	489-513
320	489-513
321	489-513
322	489-513
323	489-513
324	374-398
325	228-252
326	264-288
327	30-54
328	329-353
329	252-276
330	266-290
331	164-188
332	102-126
333	164-188
334	230-254
335	338-362
336	30-54
337	362-386
338	247-271
339	489-513
340	489-513

FIG.9D

341	489-513
342	489-513
343	489-513
344	489-513
345	489-513
346	489-513
347	489-513
348	489-513
349	489-513
350	464-488
351	489-513
352	489-513
353	489-513
354	489-513
355	489-513
356	489-513
357	489-513
358	489-513
359	489-513
360	489-513
361	489-513
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381	489-513
382	489-513
383	489-513
384	489-513
385	489-513
386	489-513
387	489-513
388	489-513
389	489-513
390	489-513
391	489-513
392	489-513
393	489-513
394	467-491
395	489-513
396	489-513
397	489-513

398	489-513
399	489-513
400	516-540
401	489-513
402	489-513
403	489-513
404	489-513
405	489-513
406	489-513
407	489-513
408	489-513
409	489-513
410	33-57
411	51-75
412	165-189
413	390-414
414	124-148
415	128-152
416	27-51
417	53-77
418	245-269
425	357-381
426	23-47
427	90-114
428	112-136
429	171-195
430	370-394
431	21-45
432	138-162
433	210-234
434	238-262
435	342-366
436	30-54
437	144-168
438	214-238
439	489-513
440	489-513
441	489-513
442	489-513
443	489-513
444	489-513
445	489-513
446	489-513
447	489-513
448	489-513
449	489-513
450	489-513
451	489-513
452	489-513
453	489-513
454	489-513
455	489-513
456	489-513
457	489-513
458	489-513
459	489-513
460	489-513

FIG.9E

461	489-513
462	489-513
463	489-513
464	489-513
465	489-513
466	489-513
467	489-513
468	489-513
469	489-513
470	489-513
471	489-513
472	489-513
473	489-513
474	489-513
475	489-513
476	489-513
477	489-513
478	489-513
479	489-513
480	489-513
481	489-513
482	489-513
483	489-513
484	489-513
485	489-513
486	489-513
487	127-151
488	200-224
489	229-253
491	173-197
492	252-276
493	10-34
494	140-164
495	244-268
496	270-294
497	269-293
498	130-154
499	290-314
500	319-343
501	140-164
502	246-270
503	91-115
504	132-156
505	263-287
506	215-239
507	143-167
508	369-393
509	86-110
510	489-513
511	489-513
512	489-513
513	489-513
514	489-513
515	489-513
516	489-513
517	489-513
518	489-513

519	489-513
520	489-513
521	489-513
522	489-513
523	489-513
524	489-513
525	489-513
526	489-513
527	489-513
528	315-339
529	40-64
530	34-58
532	98-122
533	261-285
534	78-102
535	192-216
536	209-233
537	222-246
538	276-300
539	299-323
541	27-51
542	108-132
543	142-166
544	89-113
545	74-98
546	80-104
547	82-106
548	489-513
549	404-428
550	76-100
551	275-299
552	427-451
553	489-513
554	489-513
555	489-513
556	489-513
557	489-513
558	489-513
559	489-513
560	489-513
561	489-513
562	489-513
563	489-513
564	489-513
565	238-262
566	73-97
567	39-63
568	195-219
569	385-409
570	207-231
596	489-513
597	489-513
598	489-513
599	489-513
601	489-513
602	489-513

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FIG.9F**58/76**

603	489-513
604	489-513
605	489-513
607	129-153
608	146-170
609	255-279
610	325-349
611	354-378
612	405-429
614	489-513
616	489-513
617	489-513
618	489-513
619	489-513
621	489-513
623	489-513
624	489-513
625	488-512
626	489-513
627	489-513
629	489-513
630	489-513
631	489-513
632	489-513
633	489-513
634	489-513
635	489-513
636	489-513
637	489-513
640	489-513
641	489-513
642	489-513
643	489-513
644	489-513
645	489-513
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647	489-513
648	489-513
649	489-513
650	489-513

FIG.10

FLAP gene

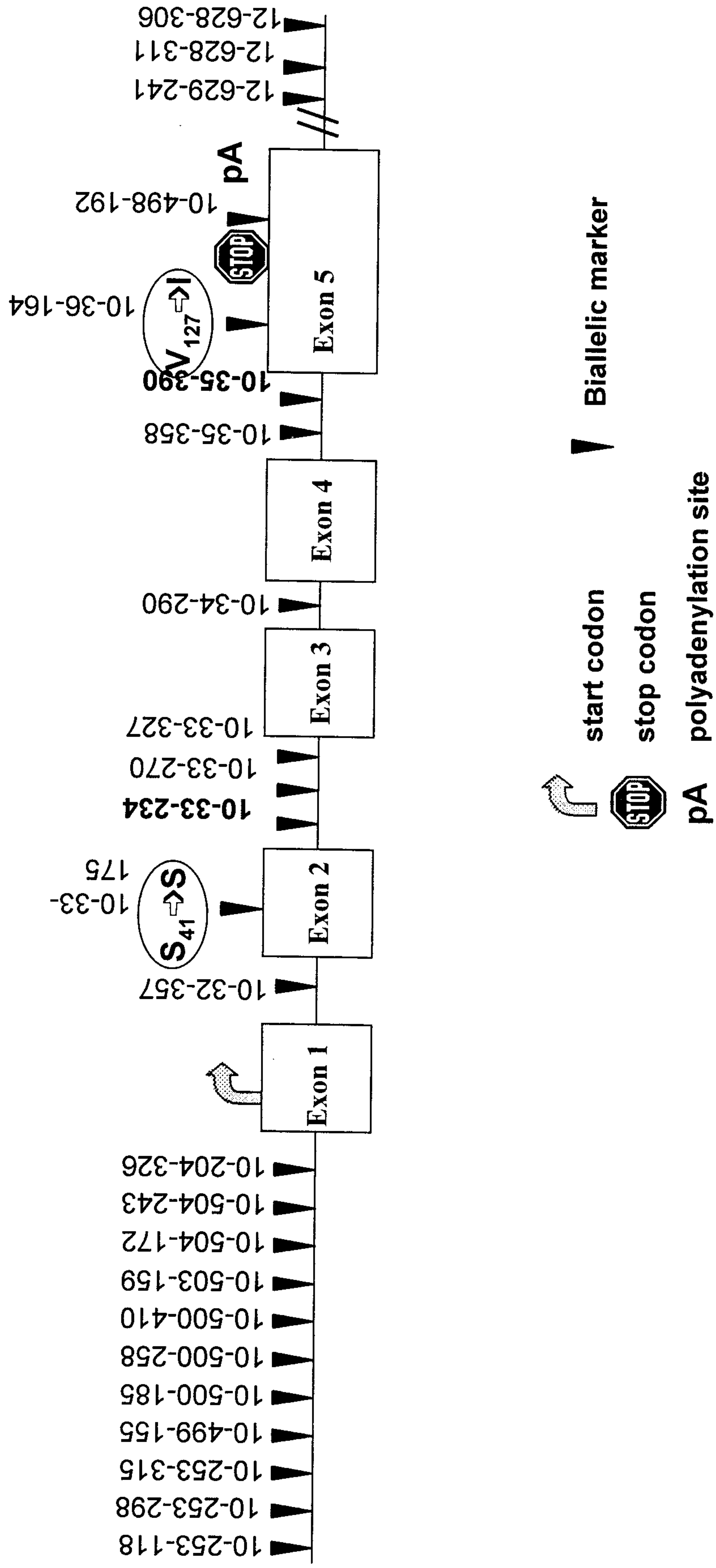


FIG.11

ASSOCIATION STUDIES BETWEEN THE FLAP BIALLELIC MARKERS AND ASTHMA
290 asthmatic individuals vs 280 caucasian US controls

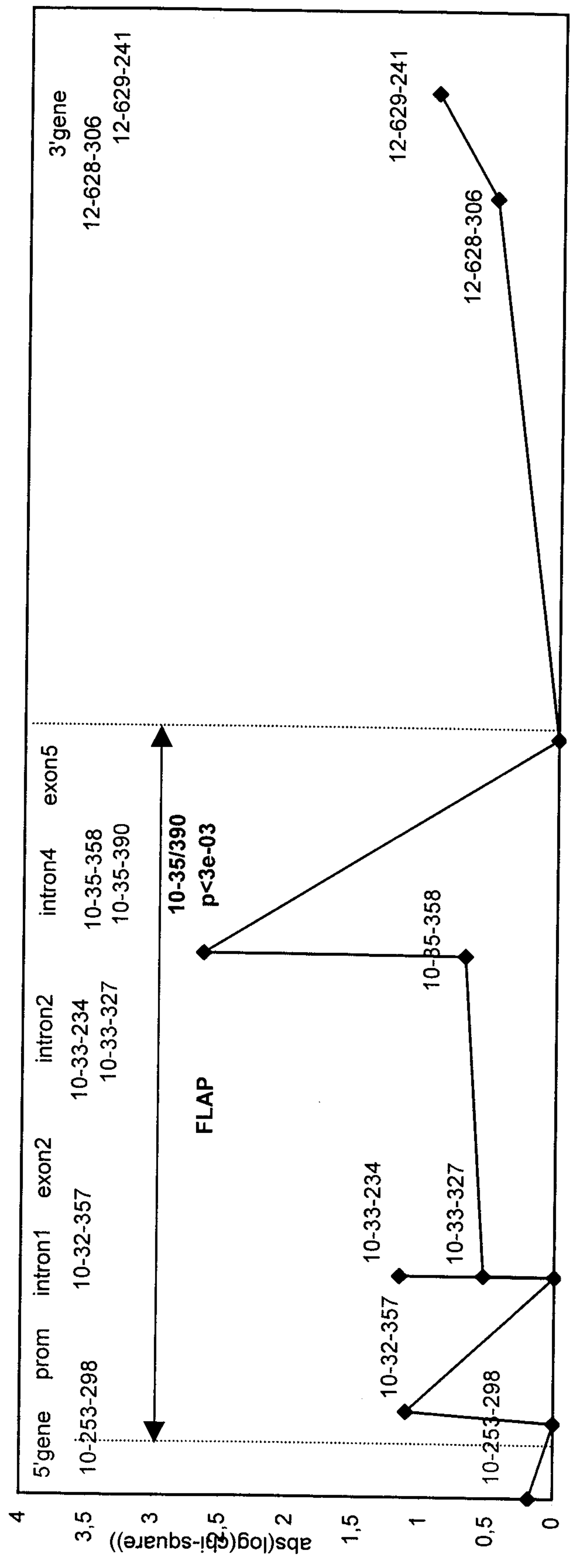


FIG.12 HAPLOTYPE FREQUENCY ANALYSIS

MARKERS		10-253-298	10-33-175	10-33-234	10-33-327	10-35-358	10-35-390	12-628-306	12-629-241	ESTIMATED FREQUENCIES				
FLAP		5' gene	exon 2	intron 2		intron 4		3' gene		Frequencies haplotype		Odds ratio	Chi-S	Pvalue (1df)
cases/controls		287/186	295/174	295/274	295/270	291/280	295/272	284/185	283/182	cases	controls			
case/controls freq %		95/95 (C)	99/98 (C)	49/44 (A)	78/76 (T)	72/69 (G)	31/23 (C)	88/90 (C)	76/72 (G)					
diff.freq.all. (cases - controls)		0,5	1,8	5,3	2,6	3,4	9	2,1	4,6					
pvalue		6,55E-01	1,35E-02	6,93E-02	2,94E-01	2,06E-01	2,29E-03	3,17E-01	1,14E-01					
1	293 vs 265			A		T				0.283	0.197	1.61	11.18	(8.2e-04)
2	281 vs 177			A				G		0.305	0.210	1.65	9.97	(1.6e-03)
3	293 vs 261				T		T			0.307	0.224	1.53	9.62	(1.8e-03)
4	289 vs 271					G	T			0.304	0.231	1.46	7.77	(5.2e-03)
5	293 vs 168		C				T			0.309	0.226	1.53	7.26	(6.9e-03)
6	293 vs 265			A	T					0.276	0.208	1.46	7.17	(7.3e-03)
7	282 vs 178						T	G		0.314	0.233	1.50	7.01	(7.7e-03)
37	281 vs 176			A			T	C		0.265	0.171	1.76	11.04	(8.6e-04)
38	280 vs 173			A			T		G	0.292	0.194	1.71	10.71	(1.0e-03)
39	289 vs 264			A		G	T			0.283	0.199	1.59	10.56	(1.1e-03)
40	278 vs 175			A				C	G	0.271	0.180	1.70	9.94	(1.6e-03)
41	284 vs 176	C		A			T			0.287	0.195	1.66	9.77	(1.7e-03)
121	277 vs 171			A			T	C	G	0.265	0.169	1.77	11.07	(8.6e-04)
122	278 vs 173			A		G	T		G	0.290	0.195	1.69	10.29	(1.3e-03)
123	279 vs 176			A		G	T	C		0.264	0.175	1.70	9.80	(1.7e-03)
124	276 vs 175			A		G		C	G	0.271	0.181	1.69	9.72	(1.7e-03)
125	280 vs 174	C		A			T	C		0.265	0.176	1.69	9.68	(1.8e-03)
247	275 vs 171			A		G	T	C	G	0.265	0.170	1.77	10.91	(9.1e-04)
248	276 vs 169	C		A			T	C	G	0.265	0.172	1.74	10.30	(1.3e-03)
373	274 vs 169	C		A		G	T	C	G	0.265	0.172	1.73	10.13	(1.4e-03)
457	273 vs 163	C		A	T	G	T	C	G	0.247	0.167	1.64	7.74	(5.2e-03)

FIG.13

HAPLOTYPE FREQUENCY ANALYSIS
PERMUTATIONS TEST RESULTS (>1000 Iterations)

Markers	10-33-234		10-35-390	
	intron 2		intron 4	
ALT vs US	A		T	
cases vs US controls	5.3 (51 vs 56)	6.93E-02	9 (31 vs 23)	2.29E-03
ASSOCIATION	diff all.	Freq	pvalue	Freq

HAPLOTYPE (AT)	sample sizes cases vs controls	haplotype		p-excess	odds-ratio	chi-S	P value		PERMUTATIONS TEST RESULTS		
		frequencies	controls						Av. Chi-S	Max Chi-S	> lter / nb of lter.
Asthmatics vs US controls	293 vs 265	0,283	0,197	10,7	1,61	11,18	8,20E-04		1,2	7,4	0/1000
									1,2	12,9	1/10 000

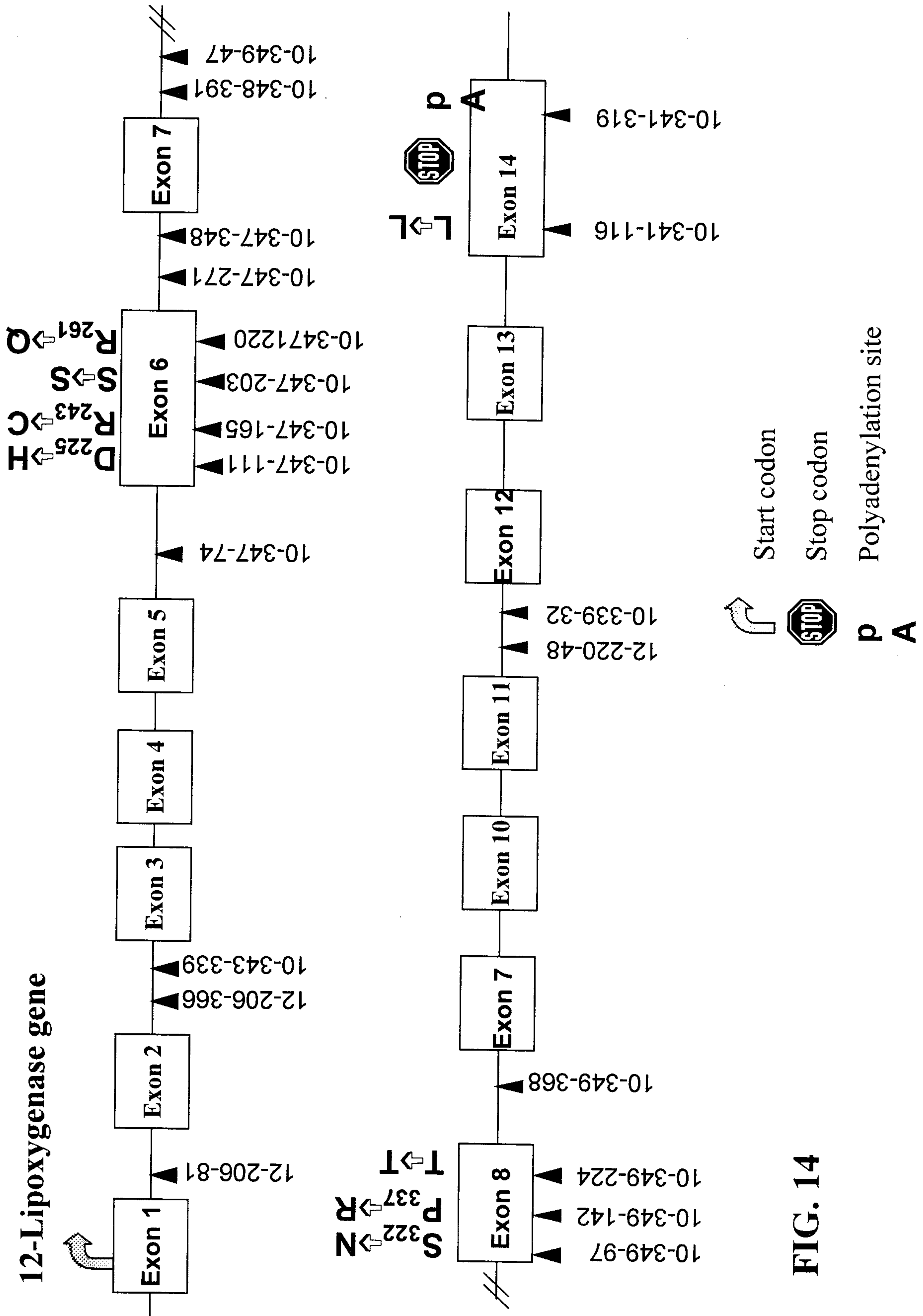


FIG. 14

FIG.15

HAPLOTYPE FREQUENCY ANALYSIS
(Asthma)

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297 Asthmatics vs 186 US controls randoms

MARKERS		ESTIMATED FREQUENCIES											
12-lipoxygenase		12-208-35	12-226-167	12-206-366	10-347-203	10-347-220	10-349-97	10-349-224	12-196-119	12-214-129	12-216-421	12-219-230	12-223-207
		5' gene		intron 2	exon 6		exon 8						
cases / controls frequency % (case/controls) diff freq. all. (cases controls) pvalue	284/182	288/188	272/89	285/184	274/184	282/182	271/177	281/184	282/181	288/182	288/187	287/186	
	59/58 (T)	62/59 (C)	57/62 (T)	57/58 (A)	58/60 (G)	59/60 (A)	57/60 (G)	70/71 (T)	61/61 (T)	61/64 (G)	64/68 (A)	62/62 (T)	
	0.9	3.4	-4.6	-1.2	-1.7	-1.9	-3.1	-1.2	-0.7	-2.9	-4.2	0.8	
	7.52e-01	2.94e-01	2.73e-01	6.55e-01	5.84e-01	5.27e-01	3.43e-01	6.55e-01	7.52e-01	3.71e-01	1.80e-01	7.52e-01	*
	*	*	*	*	*	*	*	*	*	*	*	*	
		haplotype frequencies											

FIG.16A

ALLELE FREQUENCY ANALYSIS
(Asthma)

CASES (297 ALT) vs CONTROLS (186 US CAUCASIAN)

MARKERS		12-197/244	12-208/35	12-226/167	12-206/366	10-346/141	10-347/111	10-347/165	10-347/203	10-347/220
PROTEIN 12-LO		5'gene		in2		ex5		ex6		
cases / controls		277/180	284/182	288/188	272/189	285/185	284/180	268/185	280/184	283/184
frequency % (case/controls)		66/67 (T)	58/57 (T)	62/58 (C)	57/61 (T)	99/100 (G)	99/100 (G)	99/100 (C)	57/58 (A)	57/59 (G)
diff freq. all. (cases - controls)		-1.0	0.9	3.4	-4.6	-0.4	-0.2	-0.2	-1.1	-2.1
pvalue		7.52e-01	7.52e-01	2.94e-01	2.73e-01	HOM	HOM	5.92e-01#	6.55e-01	4.80e-01
Test	cases vs	*	*	*	*			*	*	*
	controls									
Hardy Weinberg		0.034 (HWD)	-0.002 (HWE)	-0.001 (HWE)	-0.014 (HWE)	0.000 (HWD)	0.000 (HWD)	0.000 (HWD)	-0.011 (HWE)	-0.005 (HWE)
		0.054 (HWD)	-0.020 (HWE)	0.022 (HWE)	0.000 (HWE)	0.000 (HWD)	0.000 (HWD)	0.000 (HWD)	0.012 (HWE)	0.021 (HWE)

MARKERS		10-349/97	10-349/224	10-341/116	12-196/119	12-214/129	12-216/421	12-219/230	12-223/207
PROTEIN 12-LO		ex8		ex14	markers in bac				

cases / controls		287/182	277/177	286/176	281/184	282/181	288/182	288/187	287/186
frequency % (case/controls)		59/60 (A)	56/60 (G)	89/89 (G)	69/70 (T)	60/61 (T)	61/64 (G)	63/67 (A)	62/61 (T)
diff freq. all. (cases - controls)		-1.4	-4.1	0.1	-1.2	-0.7	-2.9	-4.2	0.8
pvalue		6.55e-01	2.06e-01	7.52e-01	6.55e-01	7.52e-01	3.71e-01	1.80e-01	7.52e-01
Test	cases vs	*	*	*	*	*	*	*	*
	controls								
Hardy Weinberg		0.003 (HWE)	-0.010 (HWE)	-0.008 (HWE)	0.012 (HWE)	-0.013 (HWE)	-0.012 (HWE)	-0.010 (HWE)	0.012 (HWD)
		0.008 (HWE)	-0.004 (HWE)	-0.000 (HWE)	0.030 (HWE)	0.016 (HWE)	0.024 (HWE)	-0.001 (HWE)	-0.019 (HWD)

FIG.16B

HAPLOTYPE FREQUENCY ANALYSIS (Asthma)

CASES (297 ALT) vs CONTROLS (186 US CAUCASIAN)

haplotype 1	PT2	265 vs 86
haplotype 2	PT2	267 vs 89
haplotype 3	PT2	266 vs 88
haplotype 4	PT2	271 vs 87
haplotype 5	PT2	271 vs 174
haplotype 6	PT2	285 vs 175
haplotype 7	PT3	282 vs 174
haplotype 8	PT3	287 vs 176
haplotype 9	PT3	277 vs 176
haplotype 10	PT3	275 vs 176
haplotype 11	PT3	283 vs 179
haplotype 12	PT3	266 vs 171
haplotype 13	PT3	248 vs 85
haplotype 14	PT3	271 vs 168
haplotype 15	PT3	261 vs 86
haplotype 16	PT3	276 vs 176
haplotype 17	PT3	280 vs 178
haplotype 18	PT3	268 vs 170
haplotype 19	PT3	249 vs 88
haplotype 20	PT3	264 vs 86
haplotype 21	PT3	261 vs 85
haplotype 22	PT3	264 vs 84
haplotype 23	PT3	248 vs 87
haplotype 24	PT3	261 vs 86
haplotype 25	PT3	268 vs 164
haplotype 26	PT3	265 vs 89
haplotype 27	PT4	280 vs 173
haplotype 28	PT4	274 vs 174
haplotype 29	PT4	275 vs 171
haplotype 30	PT4	276 vs 175
haplotype 31	PT4	269 vs 172
haplotype 32	PT4	280 vs 165
haplotype 33	PT4	270 vs 172
haplotype 34	PT4	282 vs 169
haplotype 35	PT4	267 vs 167
haplotype 36	PT4	285 vs 167
haplotype 37	PT4	277 vs 172
haplotype 38	PT4	275 vs 171
haplotype 39	PT4	276 vs 162
haplotype 40	PT4	245 vs 85
haplotype 41	PT4	268 vs 81

Marker 1	Marker 2	Marker 3	Marker 4	Haplotype
12-206/366	10-349/224			CT
12-206/366	10-347/220			CA
12-206/366	10-347/203			CG
12-206/366	10-349/97			CG
12-197/244	12-214/129			CC
10-341/116	12-223/207			AT
10-349/97	12-214/129	12-219/230		ACG
10-349/97	12-216/421	12-219/230		AAG
10-347/220	12-214/129	12-219/230		GCG
10-347/203	12-214/129	12-219/230		ACG
10-347/220	12-216/421	12-219/230		GAG
12-197/244	10-347/203	12-214/129		CAC
12-206/366	10-347/165	10-349/224		CCT
12-197/244	10-349/97	12-214/129		CAC
12-206/366	10-347/220	10-349/224		CAT
12-226/167	10-349/224	12-223/207		CTT
10-347/203	12-216/421	12-219/230		AAG
12-197/244	10-347/220	12-214/129		CGC
12-206/366	10-347/165	10-347/220		CCA
12-206/366	10-346/141	10-349/224		CGT
12-206/366	10-347/203	10-349/224		CGT
12-206/366	10-349/97	10-349/224		CGT
12-206/366	10-347/165	10-347/203		CCG
12-206/366	10-347/111	10-349/224		CGT
12-197/244	10-347/111	12-214/129		CGC
12-206/366	10-346/141	10-347/220		CGA
10-349/97	12-196/119	12-216/421	12-219/230	ATAG
10-347/203	12-196/119	12-216/421	12-219/230	ATAG
10-349/97	12-196/119	12-214/129	12-219/230	ATCG
10-347/220	12-196/119	12-216/421	12-219/230	GTAG
10-347/203	12-196/119	12-214/129	12-219/230	ATCG
10-349/97	10-341/116	12-214/129	12-219/230	AGCG
10-347/220	12-196/119	12-214/129	12-219/230	GTCG
10-349/97	12-214/129	12-216/421	12-219/230	ACAG
10-347/220	12-208/35	12-214/129	12-223/207	CTCC
10-349/97	10-341/116	12-216/421	12-219/230	AGAG
10-347/220	12-214/129	12-216/421	12-219/230	GCAG
10-347/203	12-214/129	12-216/421	12-219/230	ACAG
12-208/35	10-341/116	12-214/129	12-219/230	AGCG
12-206/366	10-347/165	10-347/220	10-349/224	CCAT
12-208/35	12-206/366	10-349/97	12-216/421	TCCG

ESTIMATED FREQUENCIES						PERMUTATIONS TEST RESULTS		
Haplotype frequencies		p-excess	Odds ratio	Chi-S	Pvalue (1df)	Av. Chi-S	Max Chi-s	> lter / nb of lter
cases	controls							
0.424	0.265	21.72	2.05	13.97	(1.8e-04)	2.2	8.3	[0/100]
0.423	0.274	20.56	1.94	12.55	(3.9e-04)	2.3	9.3	[0/100]
0.421	0.277	19.96	1.90	11.64	(6.3e-04)	2.1	7.1	[0/100]
0.408	0.270	18.88	1.86	10.69	(1.1e-03)	1.7	5.9	[0/100]
0.148	0.077	7.66	2.08	10.03	(1.5e-03)	1.8	9.7	[0/100]
0.042	0.008	3.45	5.48	8.95	(2.7e-03)	1.4	9.9	[2/100]
0.125	0.041	8.73	3.32	17.87	(2.3e-05)	1.8	8.5	[0/100]
0.126	0.043	8.67	3.23	17.65	(2.6e-05)	1.5	13.6	[0/100]
0.119	0.040	8.28	3.27	16.90	(3.7e-05)	3.0	15.4	[0/100]
0.115	0.037	8.05	3.35	16.64	(4.4e-05)	2.4	19.2	[1/100]
0.119	0.041	8.11	3.15	16.40	(5.1e-05)	2.6	14.4	[0/100]
0.070	0.012	5.96	6.46	15.97	(6.3e-05)	1.9	11.3	[0/100]
0.427	0.255	23.11	2.18	15.86	(6.7e-05)	2.7	18.8	[1/100]
0.069	0.012	5.83	6.37	15.34	(8.7e-05)	1.8	10.4	[0/100]
0.423	0.256	22.45	2.13	15.27	(9.2e-05)	2.4	7.8	[0/100]
0.137	0.055	8.64	2.72	15.27	(9.2e-05)	1.4	7.1	[0/100]
0.112	0.039	7.59	3.12	15.15	(9.7e-05)	2.2	21.1	[2/100]
0.067	0.012	5.60	6.10	14.68	(1.3e-04)	2.0	12.7	[0/100]
0.428	0.265	22.14	2.07	14.54	(1.3e-04)	2.8	9.4	[0/100]
0.426	0.265	21.94	2.06	14.23	(1.6e-04)	2.6	11.2	[0/100]
0.418	0.259	21.40	2.05	13.71	(2.0e-04)	2.2	8.3	[0/100]
0.411	0.253	21.19	2.06	13.68	(2.1e-04)	2.4	7.2	[0/100]
0.425	0.268	21.54	2.03	13.55	(2.3e-04)	2.2	8.5	[0/100]
0.421	0.265	21.30	2.02	13.43	(2.4e-04)	2.1	6.1	[0/100]
0.151	0.068	8.89	2.44	13.33	(2.5e-04)	1.9	25.3	[1/100]
0.426	0.274	21.00	1.97	13.04	(3.0e-04)	2.3	7.0	[0/100]
0.124	0.035	9.20	3.90	20.63	(5.4e-06)	1.5	11.6	[0/100]
0.117	0.031	8.89	4.14	20.59	(5.7e-06)	2.7	19.0	[0/100]
0.126	0.037	9.21	3.72	19.86	(8.2e-06)	2.0	11.8	[0/100]
0.121	0.035	8.92	3.80	19.84	(8.2e-06)	2.4	14.7	[0/100]
0.120	0.034	8.90	3.86	19.61	(9.1e-06)	2.4	12.2	[0/100]
0.127	0.038	9.30	3.73	19.55	(9.5e-06)	1.9	16.0	[0/100]
0.124	0.037	9.00	3.68	19.31	(1.1e-05)	2.8	19.3	[0/100]
0.124	0.038	9.00	3.62	18.98	(1.3e-05)	1.8	10.5	[0/100]
0.055	0.000	5.49	100.00	18.96	(1.3e-05)	2.6	21.7	[2/100]
0.127	0.039	9.12	3.55	18.89	(1.4e-05)	2.0	12.3	[0/100]
0.120	0.036	8.71	3.62	18.59	(1.6e-05)	2.3	25.8	[1/100]
0.116	0.033	8.52	3.80	18.57	(1.6e-05)	2.7	21.6	[1/100]
0.054	0.000	5.40	0.00	18.10	(2.0e-05)	2.7	18.6	[1/100]
0.429	0.246	24.18	2.30	17.77	(2.5e-05)	3.0	7.5	[0/100]
0.196	0.056	14.80	4.09	17.76	(2.5e-05)	1.8	15.1	[0/100]

FIG.17

HAPLOTYPE FREQUENCY ANALYSIS

(Zyflo secondary effects)

WO 00/47771

89 ALT+ vs 208 ALT-

MARKERS	12-208-35	12-226-167	12-206-366	10-347-203	10-347-220	10-349-97	10-349-224	12-196-119	12-214-129	12-216-421	12-219230	12-223-207
12-lipoxygenase	5' gene		intron 2	exon 6		exon 8						

ESTIMATED FREQUENCIES

Size (cases / controls)	87/197	89/199	86/186	88/197	86/188	86/196	86/185	86/195	89/193	89/199	89/199	88/199	haplotype frequencies		Chi-S	Pvalue (1df)
frequency % (case/controls)	58/59 (T)	61/63 (C)	55/58 (T)	56/58 (A)	56/59 (G)	58/59 (A)	54/59 (G)	72/69 (T)	59/61 (T)	58/63 (G)	67/62 (A)	62/63 (T)	cases	controls	ratio	
diff freq. all. (cases - controls)	-0.8	-2.1	-3.7	-2.2	-3.0	-1.4	-4.8	3.4	-2.4	-4.7	4.5	-0.6	7.52e-01	7.52e-01	*	
p value	7.52e-01	5.84e-01	4.03e-01	5.84e-01	4.80e-01	7.52e-01	2.73e-01	4.03e-01	5.84e-01	2.73e-01	2.94e-01	7.52e-01				

1	87 vs 197	A	G					C					0.123	0.070	1.87	4.34	(3.6e-02)
2	83 vs 184				A								0.209	0.140	1.63	4.09	(4.3e-02)
3	85 vs 185						T			A		T	0.151	0.048	3.53	16.76	(4.2e-05)
4	85 vs 186			C						A		T	0.148	0.059	2.77	11.62	(6.3e-04)
5	85 vs 179						T		C			T	0.151	0.066	2.52	9.85	(1.7e-03)
6	85 vs 180			C					C			T	0.149	0.070	2.34	8.42	(3.6e-03)
7	86 vs 188				A					A		T	0.157	0.076	2.25	8.36	(3.8e-03)
8	82 vs 174			C			T			A		T	0.158	0.040	4.56	21.85	(2.9e-06)
9	85 vs 179						T		C	A		T	0.157	0.052	3.37	16.03	(6.0e-05)
10	83 vs 177				A					A		T	0.162	0.057	3.22	15.30	(9.2e-05)
11	82 vs 183					G	T			A		T	0.147	0.050	3.23	14.18	(1.6e-04)
12	85 vs 183						T			A		T	0.143	0.049	3.21	13.97	(1.8e-04)
13	82 vs 168			C			T		C			T	0.156	0.058	3.02	13.08	(3.0e-04)
14	84 vs 175			C	A					A		T	0.155	0.062	2.78	11.77	(5.9e-04)
15	84 vs 184			C		G				A		T	0.147	0.059	2.74	11.22	(7.8e-04)
16	85 vs 180			C					C	A		T	0.145	0.058	2.74	11.05	(8.6e-04)
17	82 vs 181						T	T		A		T	0.132	0.050	2.85	10.62	(1.1e-03)
18	83 vs 187	A						T		A		T	0.148	0.066	2.48	9.50	(2.1e-03)
19	83 vs 171				A		T		C			T	0.162	0.074	2.41	9.29	(2.3e-03)
20	83 vs 174			C			T			A	A	T	0.111	0.041	2.92	9.24	(2.3e-03)
21	82 vs 178					G	T		C			T	0.152	0.068	2.45	9.22	(2.3e-03)
22	82 vs 168			C			T		C	A		T	0.161	0.043	4.27	20.43	(6.0e-06)
23	82 vs 172			C		G	T			A		T	0.146	0.040	4.07	18.03	(2.1e-05)
24	81 vs 166			C	A		T			A		T	0.160	0.047	3.82	17.77	(2.5e-05)
25	80 vs 171			C			T	T		A		T	0.137	0.037	4.17	17.18	(3.4e-05)

FIG.18A

ALLELE FREQUENCY ANALYSIS (Zyflo secondary effects)

CASES (85 ALT+) vs CONTROLS (208 ALT-)

MARKERS		
PROTEIN 12-LO		
cases / controls		
frequency % (case/controls)		
diff freq. all. (cases - controls)		
pvalue		
Test	cases vs controls	
Hardy Weinberg		

12-197/244	12-208/35	12-226/167	12-206/366	10-346/141	10-347/111	10-347/165	10-347/203	10-347/220
5'gene				ex5	ex6			
81/196	87/197	89/199	86/186	88/197	88/196	69/199	83/197	87/196
70/65(T)	58/59(T)	61/63(C)	55/58(T)	100/99(G)	99/100(G)	100/99(C)	56/58(A)	43/57(G)
5.8	-0.8	-2.1	-3.7	0.5	-0.6	0.3	-1.8	0.1
1.80e-01	7.52e-01	5.84e-01	4.03e-01	HOM	HOM	7.43e-01#	6.55e-01	7.52e-01
*	*	*	*			*	*	*
-0.001 (HWE)	0.008 (HWE)	-0.020 (HWE)	-0.031 (HWE)	0.000 (HWD)	0.000 (HWD)	0.000 (HWD)	-0.037 (HWE)	-0.020 (HWE)
0.048 (HWD)	-0.007 (HWE)	0.007 (HWE)	-0.007 (HWE)	0.000 (HWD)	0.000 (HWD)	0.000 (HWD)	0.000 (HWE)	0.002 (HWE)

MARKERS		
PROTEIN 12-LO		
cases / controls		
frequency % (case/controls)		
diff freq. all. (cases - controls)		
pvalue		
Test	cases vs controls	
Hardy Weinberg		

10-349/97	10-349/224	10-341/116	12-196/119	12-214/129	12-216/421	12-219/230	12-223/207
ex8		ex14	markers in bac				
89/198	83/194	89/197	86/195	89/193	89/199	89/199	88/199
59/59(A)	54/57(G)	90/89(G)	72/69(T)	59/61(T)	58/63(G)	67/62(G)	62/63(T)
-0.1	-3.0	1.6	3.4	-2.4	-4.7	4.5	-0.6
7.52e-01	4.80e-01	5.27e-01	4.03e-01	5.84e-01	2.73e-01	2.94e-01	7.52e-01
*	*	*	*	*	*	*	*
0.000 (HWE)	-0.029 (HWE)	0.002 (HWE)	0.015 (HWE)	-0.011 (HWE)	-0.031 (HWE)	0.002 (HWE)	0.037 (HWE)
0.004 (HWE)	-0.003 (HWE)	0.764 (HWD)	0.010 (HWE)	-0.014 (HWE)	-0.004 (HWE)	-0.016 (HWE)	0.001 (HWE)

FIG.18B

HAPLOTYPE FREQUENCY ANALYSIS
(Zyflo secondary effects)

CASES (85 ALT+) vs CONTROLS (208 ALT-)

	MARKER 1	MARKER 2	MARKER 3	MARKER 4	MARKER 5	HAPLOTYPE
haplotype 1	12-197/244	12-196/119				TT
haplotype 2	12-208/35	12-226/167				AG
haplotype 3	12-206/366	12-196/119				CC
haplotype 4	10-347/220	12-196/119				GT
haplotype 5	10-347/203	12-196/119				GC
haplotype 6	10-349/224	12-216/421	12-223/207			TAT
haplotype 7	12-206/366	12-216/421	12-223/207			CAT
haplotype 8	12-197/244	12-206/366	12-196/119			TTT
haplotype 9	12-197/244	10-347/220	12-196/119			TGT
haplotype 10	12-197/244	10-349/224	12-196/119			TGT
haplotype 11	12-197/244	10-349/224	12-216/421			CTA
haplotype 12	12-197/244	10-347/203	12-196/119			TAT
haplotype 13	12-206/366	10-349/224	12-216/421	12-223/207		CTAT
haplotype 14	12-206/366	10-346/141	12-216/421	12-223/207		CGAT
haplotype 15	10-349/224	12-214/129	12-216/421	12-223/207		TCAT
haplotype 16	12-206/366	10-347/203	12-216/421	12-223/207		CGAT
haplotype 17	10-347/111	10-349/224	12-216/421	12-223/207		GTAT
haplotype 18	10-346/141	10-349/224	12-216/421	12-223/207		GTAT
haplotype 19	10-347/220	10-349/224	12-216/421	12-223/207		ATAT
haplotype 20	12-206/366	10-347/220	12-216/421	12-223/207		CAAT
haplotype 21	12-206/366	10-347/111	12-216/421	12-223/207		CGAT
haplotype 22	12-197/244	10-346/141	10-349/224	12-196/119		TGGT
haplotype 23	12-206/366	12-214/129	12-216/421	12-223/207		CCAT
haplotype 24	10-347/203	10-349/224	12-216/421	12-223/207		GTAT
haplotype 25	10-347/203	10-341/116	12-214/129	12-223/207		GGCT
haplotype 26	12-197/244	12-208/35	12-196/119	12-216/421	12-219/230	TATGA
haplotype 27	12-197/244	12-208/35	10-349/97	12-196/119	12-223/207	TTATC
haplotype 28	12-197/244	12-208/35	12-196/119	12-214/129	12-219/230	TATTA
haplotype 29	12-197/244	12-208/35	10-347/220	12-196/119	12-223/207	TTGTC
haplotype 30	12-197/244	12-208/35	12-206/366	10-341/116	12-196/119	TTTGT

ESTIMATED FREQUENCIES						PERMUTATIONS TEST RESULTS		
Haplotype frequencies		p-excess	Odds ratio	Chi-S	Pvalue (1df)	Av. Chi-S	Max Chi-s	> lter / No. of lter
cases	controls							
0.542	0.436	18.89	1.53	5.11	(2.3e-02)	1.7	6.7	[3/100]
0.123	0.070	5.73	1.87	4.34	(3.6e-02)	1.1	7.3	[4/100]
0.205	0.139	7.68	1.60	3.75	(5.1e-02)	1.3	8.0	[11/100]
0.486	0.400	14.25	1.41	3.49	(6.1e-02)	1.0	5.3	[8/100]
0.207	0.144	7.46	1.56	3.43	(6.1e-02)	1.3	10.3	[9/100]
0.158	0.064	10.09	2.76	12.35	(4.3e-04)	2.1	11.0	[0/100]
0.148	0.059	9.44	2.77	11.62	(6.3e-04)	2.8	24.7	[3/100]
0.434	0.286	20.67	1.91	10.62	(1.1e-03)	1.8	10.9	[1/100]
0.433	0.291	19.96	1.86	9.98	(1.6e-03)	1.7	9.3	[0/100]
0.435	0.293	20.17	1.86	9.88	(1.7e-03)	1.8	6.9	[0/100]
0.137	0.056	8.56	2.66	9.76	(1.7e-03)	1.6	11.3	[1/100]
0.431	0.294	19.42	1.82	9.13	(2.4e-03)	1.3	6.1	[0/100]
0.160	0.058	10.82	3.10	14.38	(1.5e-04)	2.0	13.9	[0/100]
0.158	0.058	10.62	3.04	14.20	(1.6e-04)	3.3	23.7	[2/100]
0.161	0.063	10.50	2.86	13.12	(2.8e-04)	2.9	25.2	[3/100]
0.153	0.059	10.03	2.89	12.50	(3.9e-04)	2.7	13.0	[1/100]
0.159	0.064	10.14	2.77	12.33	(4.3e-04)	2.3	15.7	[2/100]
0.158	0.065	9.96	2.70	11.85	(5.6e-04)	2.6	18.1	[3/100]
0.159	0.066	10.02	2.69	11.78	(5.9e-04)	2.2	9.9	[0/100]
0.150	0.059	9.60	2.79	11.72	(5.9e-04)	2.3	17.1	[3/100]
0.148	0.059	9.42	2.76	11.45	(7.0e-04)	2.0	12.3	[1/100]
0.435	0.284	21.12	1.94	11.16	(8.2e-04)	2.0	8.7	[0/100]
0.145	0.058	9.20	2.74	11.03	(8.6e-04)	2.3	15.7	[3/100]
0.156	0.065	9.65	2.63	11.00	(8.6e-04)	1.7	14.4	[3/100]
0.125	0.046	8.22	2.94	10.86	(9.6e-04)	1.8	18.8	[2/100]
0.138	0.050	9.27	3.06	12.24	(4.5e-04)	2.6	13.2	[2/100]
0.127	0.045	8.56	3.08	11.42	(7.0e-04)	1.6	10.3	[0/100]
0.126	0.047	8.30	2.93	10.42	(1.2e-03)	2.4	14.6	[4/100]
0.121	0.048	7.63	2.71	8.84	(2.9e-03)	1.4	9.5	[1/100]
0.195	0.099	10.67	2.21	8.82	(2.9e-03)	1.3	7.3	[0/100]

FIG.19

Summary of
Association Study Results and Permutation Tests

12-Lipoxygenase	12-206-366	10-347-203	10-349-224	12-196-119	12-216-421	12-219-230	12-223-207	MARKERS	
	intron 2	exon 6	exon 8						
	C			T			T	HAPLOTYPE 8 Zylfo secondary effects (ALT+ vs ALT-)	
				A			A		
				T			T	HAPLOTYPE 14 Asthma (ALT vs US)	
	A			A			A		
	4,03E-01	5,84E-01	7,52E-01	4,03E-01	2,73E-01	2,94E-01	7,52E-01	pvalue	ALT+ vs ALT-
	-3,7	-2,2	-1,4	3,4	-4,7	4,5	-0,6	diff all. Freq	
	2,73E-01	6,55E-01	5,27E-01	6,55E-01	3,71E-01	1,80E-01	7,52E-01	pvalue	ALT vs caucasian US
	-4,6	-1,2	-1,9	-1,2	-2,9	-4,2	0,8	diff all. Freq	

70/76

HAPLOTYPE 8 (ALT+ vs ALT-) Zylfo secondary effects
ALT+ vs ALT-
ALT vs caucasian US

sample sizes cases vs controls	haplotype frequencies		odds-ratio	chi-S	P value	PERMUTATIONS TEST RESULTS		
	cases	controls				Av. Chi-S	Max Chi-S	> Iter / nb of Iter.
82 vs 174	0,158	0,04	4,56	21,85	2,90E-06	3,1	29,9	5/1 000
256 vs 83	0,059	0		10,12	1,40E-03	3,3	40,9	77/10 000
						3,5	37,6	82/1 000

HAPLOTYPE 14 (ALT vs US) Asthma
ALT+ vs ALT-
ALT vs caucasian US

sample sizes cases vs controls	haplotype frequencies		odds-ratio	chi-S	P value	PERMUTATIONS TEST RESULTS		
	cases	controls				Av. Chi-S	Max Chi-S	> Iter / nb of Iter.
85 vs 193	0,097	0,109	-1,34	0,18	6,50E-01	2,1	24,1	785/1 000
278 vs 174	0,118	0,031	4,18	21,01	4,40E-06	2,8	38,6	39/10 000
						2,8	29,9	7/1 000

FIG.20

PERMUTATIONS TEST RESULTS

PROTEIN PEC12L												
12-206/366	10-349/97	10-349/224	12-196/119	12-214/129	12-216/421	12-219/230	12-223/207	MARKERS				
in2	ex8	ex8	in bac (not localization in Bac: 3' or 5' gene)									
C			T		A			T				
			A		C			HAPLOTYPE 1 (ALT+ vs ALT-)				
			A		T			HAPLOTYPE 2 (ALT vs US)				
					A			HAPLOTYPE 3				
4.03e-01	7.52e-01	4.80e-01	4.03e-01	5.84e-01	2.73e-01	2.94e-01	7.52e-01	pvalue				
-3.7	-0.1	-3.0	3.4	-2.4	-4.7	4.5	-0.6	diff all. Freq				
(54 vs 58)	(58 vs 59)	(54 vs 57)	(72 vs 68)	(58 vs 61)	(57 vs 62)	(66 vs 62)	(61 vs 62)	(cases vs				
2.73e-01	6.55e-01	2.06e-01	6.55e-01	7.52e-01	3.71e-01	1.80e-01	7.52e-01	pvalue	ALT+ vs ALT-			
-4.6	-1.4	-4.1	-1.2	-0.7	-2.9	-4.2	0.8	diff all. Freq				
(57 vs 61)	(59 vs 60)	(56 vs 60)	(69 vs 70)	(60 vs 61)	(61 vs 64)	(63 vs 67)	(62 vs 61)	(cases vs	ALT vs caucasian US			

Zyflo secondary effects

HAPLOTYPE 1 (ALT+ vs ALT-) (Zyflo secondary effects)CTAT
ALT+ vs ALT-
ALT+ vs ALT- (1)
ALT+ vs ALT- (2)
ALT vs caucasian US

sample sizes cases vs controls	haplotype frequencies		p-excess	odds- ratio	chi-S	P value	PERMUTATIONS TEST RESULTS		
							Av. Chi-S	Max Chi-S	> iter / nb of iter.
81 vs 183	0,16	0,058	10,82	3,10	14,38	1,50E-04	2,7	13,9	0/100
81 vs 99	0,16	0,065	10,11	2,72	8,28	4,00E-03	3,3	33,6	18/1000
81 vs 84	0,16	0,044	12,12	4,15	12,23	4,50E-04	2,7	23,1	118/1000
264 vs 83	0,071	0	302,77#	7,08	12,37	4,30E-04	2,6	19,6	20/1000
						***TH	2,6	23	25/1000

Asthma gene

HAPLOTYPE 2 (ALT vs US) (Asthma gene)ACG
ALT+ vs ALT-
ALT+ vs ALT- (1)
ALT+ vs ALT- (2)
ALT vs caucasian US

sample sizes cases vs controls	haplotype frequencies		p-excess	odds- ratio	chi-S	P value	PERMUTATIONS TEST RESULTS		
							Av. Chi-S	Max Chi-S	> iter / nb of iter.
89 vs 193	0,131	0,121	1,14	1,10	0,11	6,50E-01	1,3	18,1	760/1000
89 vs 104	0,131	0,115	1,84	1,16	0,20	5,80E-01	1,5	14,6	683/1000
89 vs 89	0,131	0,134	-0,26	0,98	0,00	7,50E-01	1,4	16,2	946/1000
282 vs 174	0,125	0,041	8,73	3,32	17,87	2,30E-05	1,8	8,5	0/100
						*****	2	19,9	2/1000

HAPLOTYPE 3 (ALT vs US)
(Asthma gene) ATAG

ALT+ vs ALT-
ALT+ vs ALT- (1)
ALT+ vs ALT- (2)
ALT vs caucasian US

sample sizes cases vs controls	haplotype frequencies		p-excess	odds- ratio	chi-S	P value	PERMUTATIONS TEST RESULTS		
							Av. Chi-S	Max Chi-S	> iter / nb of iter.
86 vs 194	0,123	0,114	1,04	1,09	0,10	7,50E-01	1,5	15,5	816/1000
86 vs 100	0,123	0,108	1,69	1,16	0,21	5,80E-01	1,6	16,6	735/1000
86 vs 94	0,123	0,11	1,54	1,14	0,16	6,50E-01	1,5	19,3	750/1000
280 vs 173	0,124	0,035	9,2	3,9	20,63	5,40E-06	1,5	11,6	0/100
						*****	2	18,7	0/1000

FIG.21

Allele Frequency

PROTEINS	Marker	ALT+					ALT-					US caucasian				
		size	A	C	G	T	size	A	C	G	T	size	A	C	G	T
12-LO	12-197/244	81		29.63		70.37	196		35.46		64.54	180		32.78		67.22
2	12-208/35	87	41.95			58.05	197	41.12			58.88	182	42.31			57.69
3	12-226/167	89		60.67	39.33		199		62.81	37.19		188		58.78	41.22	
4	12-206/366	86		45.35		54.65	186		41.67		58.33	89		38.20		61.80
5	10-346/141	88			HOM		197	0.51		99.49		185			HOM	
6	10-347/111	88		0.57	99.43		196			HOM		180			HOM	
7	10-347/165	69		HOM			199		99.75		0.25	185		HOM		
8	10-347/203	83	56.02		43.98		197	57.87		42.13		184	58.42		41.58	
9	10-347/220	87	42.53		57.47		196	42.60		57.40		184	40.49		59.51	
10	10-349/97	89	58.99		41.01		198	59.09		40.91		182	60.44		39.56	
11	10-349/224	83			54.22	45.78	194			57.22	42.78	177			60.45	39.55
12	10-341/116	89	9.55		90.45		197	11.17		88.83		176	10.80		89.20	
13	12-196/119	86		27.91		72.09	195		31.28		68.72	184		29.08		70.92
14	12-214/129	89		41.01		58.99	193		38.60		61.40	181		38.67		61.33
15	12-216/421	89	42.13		57.87		199	37.44		62.56		182	35.99		64.01	
16	12-219/230	89	66.85		33.15		199	62.31		37.69		187	67.91		32.09	
17	12-223/207	88		38.07		61.93	199		37.44		62.56	186		38.44		61.56

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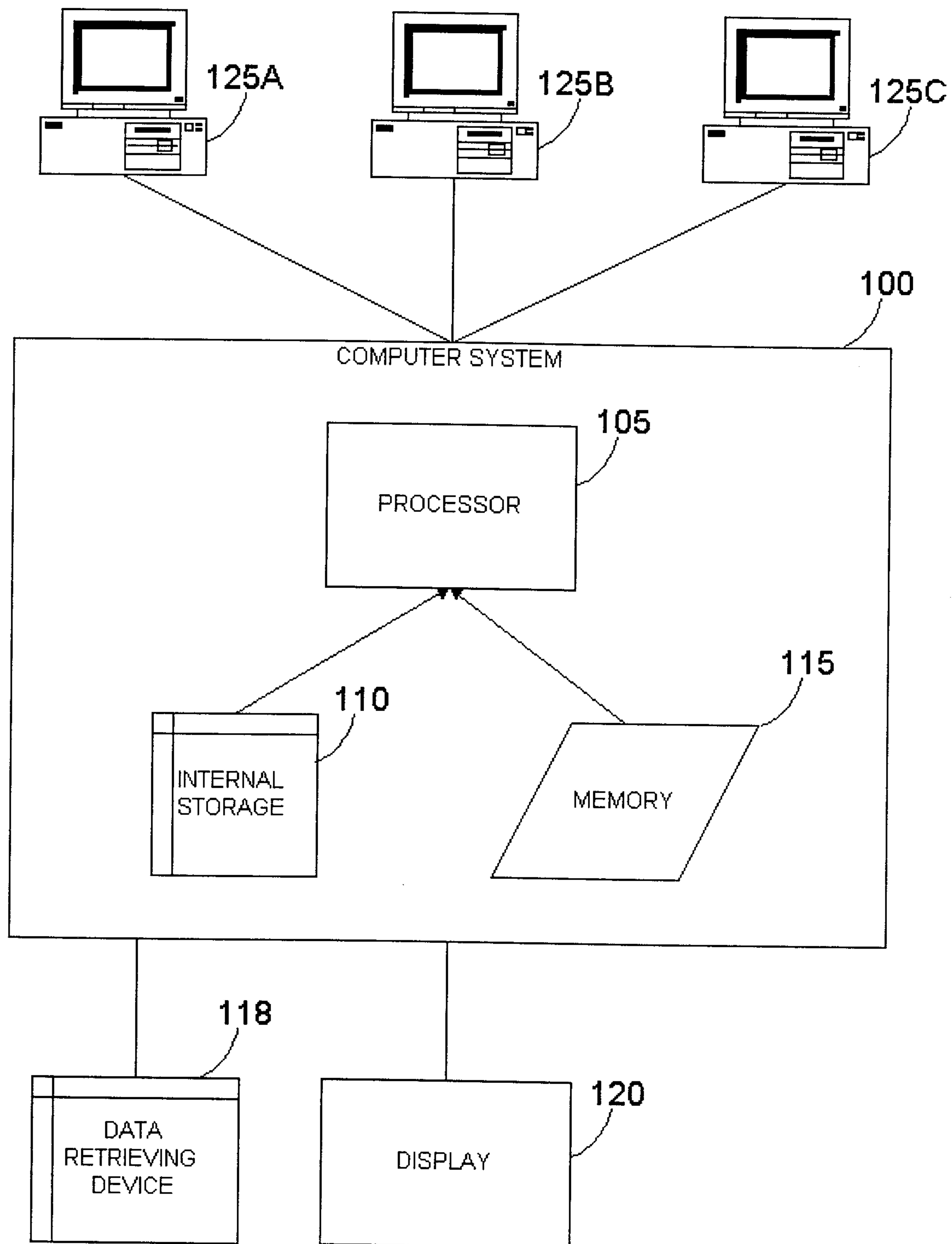


FIG.22

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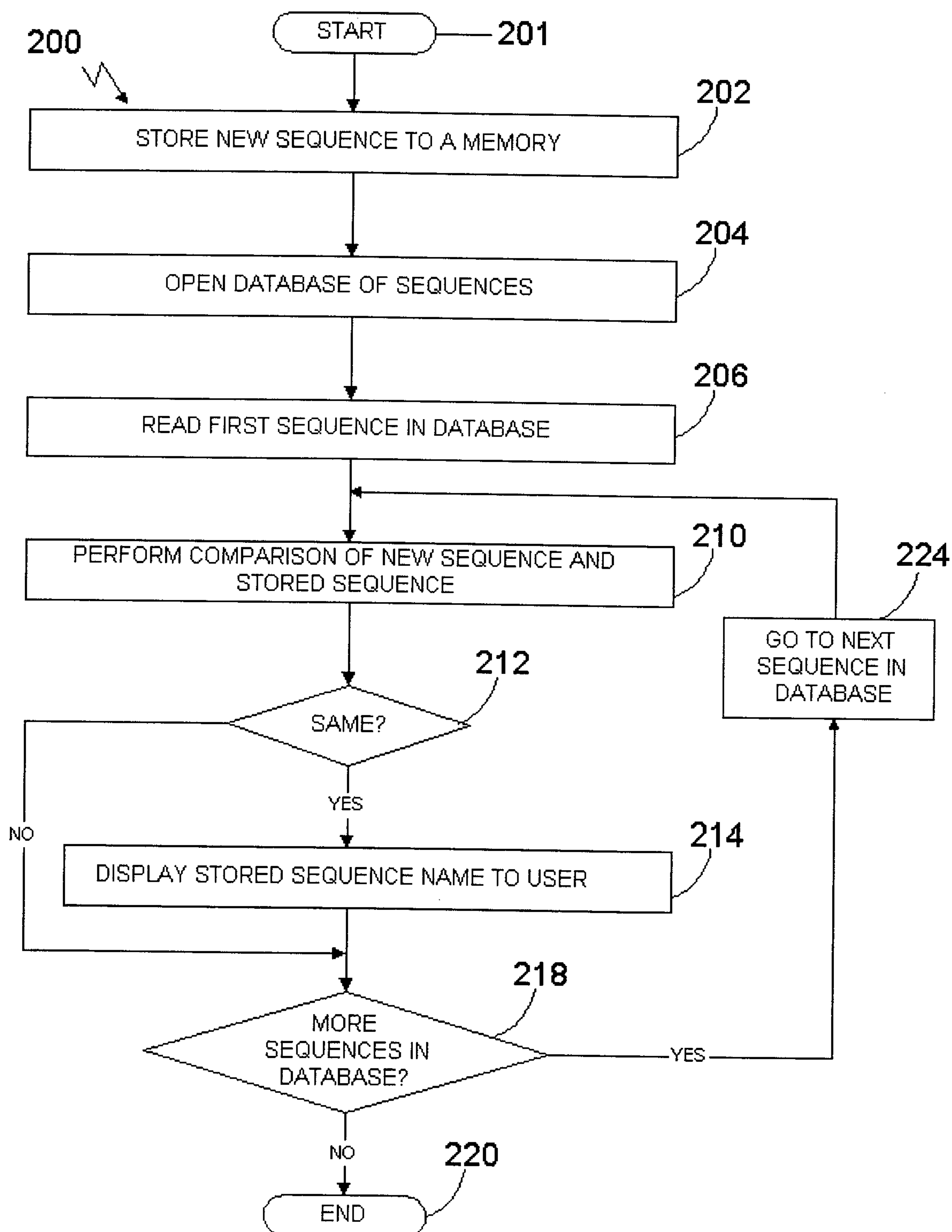


FIG.23

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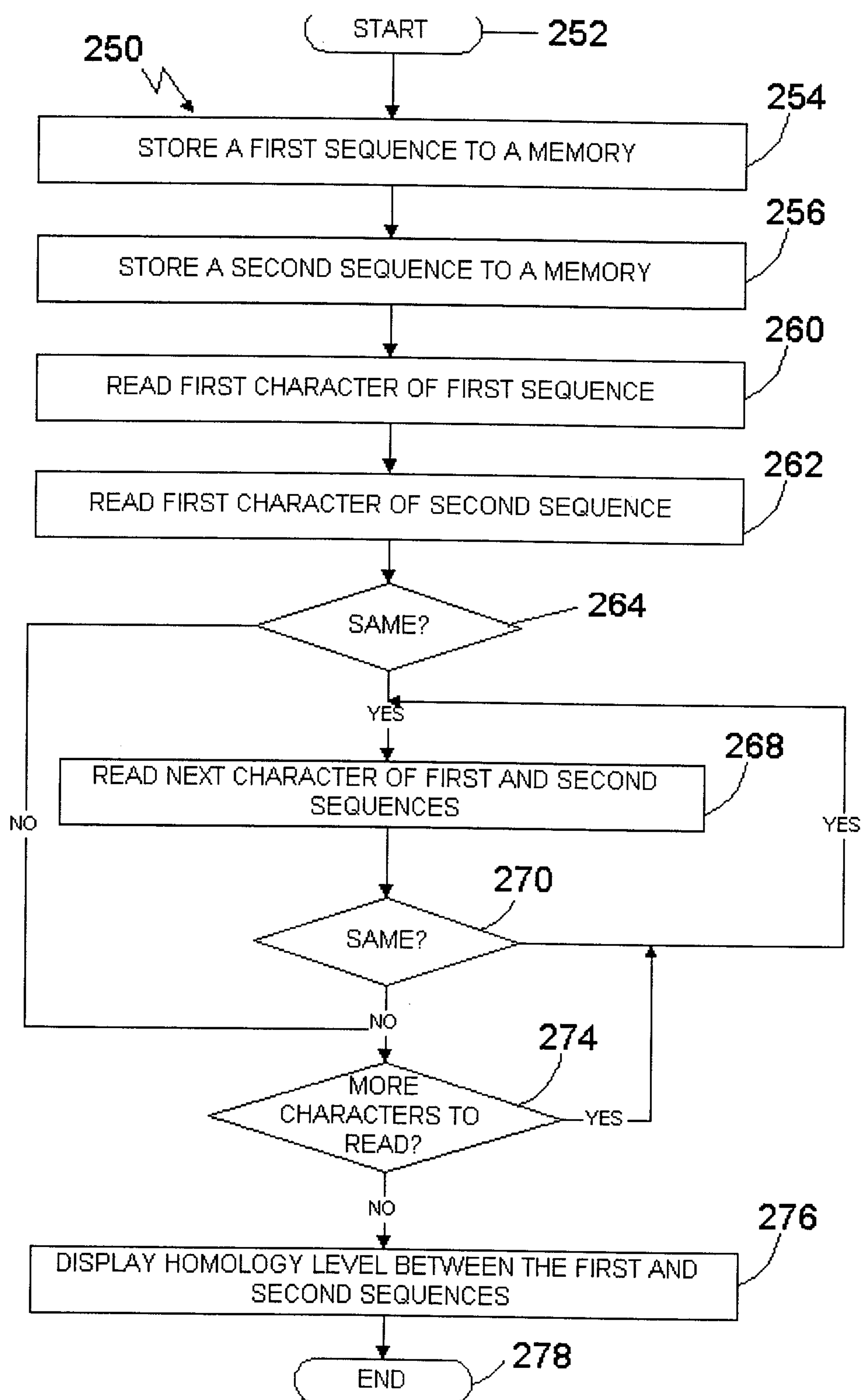


FIG.24

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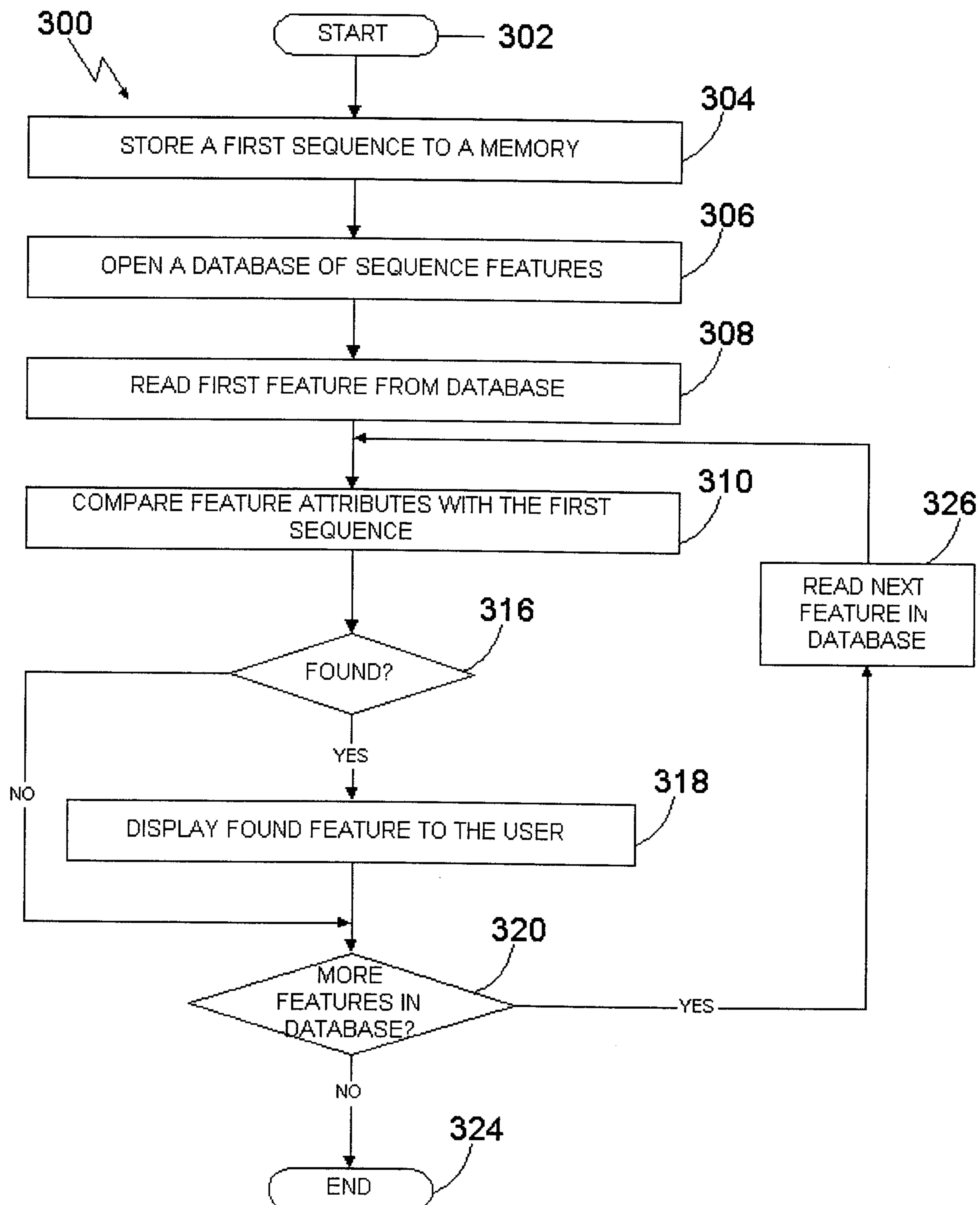


FIG.25