

CLAIMS

1. A method for determining a susceptibility to cardiovascular disease in a human individual, comprising determining the presence or absence of at least one allele of at least one polymorphic marker in a nucleic acid sample obtained from the individual or in a genotype dataset derived from the individual, wherein the at least one polymorphic marker is selected from the polymorphic markers set forth in Table 10, and markers in linkage disequilibrium therewith, and wherein the presence of the at least one allele is indicative of a susceptibility to cardiovascular disease.
2. The method according to Claim 1, wherein the at least one polymorphic marker is located within the genomic segment with the sequence as set forth in SEQ ID NO:94.
3. The method according to Claim 1 or Claim 2, wherein the at least one polymorphic marker is in linkage disequilibrium with the CDKN2A and/or CDKN2B genes.
4. The method according to any of the preceding Claims, wherein the at least one polymorphic marker is selected from the markers set forth in Table 3 and Table 21.
5. The method according to any of the preceding Claims, wherein the at least one polymorphic marker is selected from rs10811650, rs10116277, rs1333040, rs10738607, rs4977574, rs6475608, D9S1870, rs2383207, rs1333045, rs1333046, rs10757278 and rs1333048.
6. The method according to any of the preceding Claims, wherein the at least one polymorphic marker is selected from rs1333040, rs10116277, rs2383207 and rs10757278.
7. The method according to any of the preceding Claims, wherein the at least one polymorphic marker is rs10757278.
8. The method according to any of the preceding Claims, further comprising assessing the frequency of at least one haplotype in the individual.
9. The method of any of the preceding claims, wherein the susceptibility conferred by the presence of the at least one allele or haplotype is increased susceptibility.
10. The method according to Claim 9, wherein the presence of allele T in rs1333040, allele T in rs10116277, allele G in rs2383207, allele G in rs10757278, allele X in DG9S1870 or allele D in D9S1814 is indicative of increased susceptibility to cardiovascular disease.

11. The method according to Claim 9 or 10, wherein the presence of the at least one allele or haplotype is indicative of increased susceptibility with a relative risk (RR) or odds ratio (OR) of at least 1.2.

12. The method according to Claim 9 or 10, wherein the presence of the at least one allele or haplotype is indicative of increased susceptibility with a relative risk (RR) or odds ratio (OR) of at least 1.3.

13. The method according to any of the claims 1-8, wherein the susceptibility conferred by the presence of the at least one allele or haplotype is decreased susceptibility.

14. The method according to any of the preceding Claims wherein the presence of the marker or haplotype is indicative of a different response rate of the subject to a particular treatment modality for a Cardiovascular disease.

15. The method according to Claim 14, wherein the treatment modality is a coronary stenosis method selected from balloon angioplasty, stenting, cutting balloon angioplasty, percutaneous transluminal coronary angioplasty (PTCA), directional coronary atherectomy, rotational coronary atherectomy, brachytherapy, drug-eluting stent (DES) insertion, metal stent insertion, and coronary artery surgery.

16. The method of claim 14, wherein the treatment modality is administration of a therapeutic agent for preventing and/or ameliorating symptoms associated with the Cardiovascular disease..

17. A method of identification of a marker for use in assessing susceptibility to cardiovascular disease, the method comprising

- a. identifying at least one polymorphic marker in linkage disequilibrium with at least one of the markers within LD Block C09 (SEQ ID NO:94);
- b. determining the genotype status of a sample of individuals diagnosed with, or having a susceptibility to, cardiovascular disease; and
- c. determining the genotype status of a sample of control individuals;

wherein a significant difference in frequency of at least one allele in at least one polymorphism in individuals diagnosed with, or having a susceptibility to, cardiovascular disease, as compared with the frequency of the at least one allele in the control sample is indicative of the at least one polymorphism being useful for assessing susceptibility to cardiovascular disease.

18. The method according to Claim 17, wherein an increase in frequency of the at least one allele in the at least one polymorphism in individuals diagnosed with, or

having a susceptibility to, cardiovascular disease, as compared with the frequency of the at least one allele in the control sample is indicative of the at least one polymorphism being useful for assessing increased susceptibility to cardiovascular disease.

- 5 19. The method according to Claim 17 or Claim 18, wherein a decrease in frequency of the at least one allele in the at least one polymorphism in individuals diagnosed with, or having a susceptibility to, cardiovascular disease, as compared with the frequency of the at least one allele in the control sample is indicative of the at least one polymorphism being useful for assessing decreased susceptibility to, or protection against, cardiovascular disease.
- 10 20. The method according to any of the Claims 17-19, wherein the at least one marker within LD Block C09 is selected from the markers set forth in Table 10.
21. The method according to any of the Claims 17-20, wherein the at least one marker within LD Block C09 is selected from the markers set forth in Table 3 and
- 15 Table 21.
22. The method according to any of the Claims 17-21, wherein the at least one marker within LD Block C09 is selected from rs1333040, rs10116277, rs2383207 and rs10757278.
- 20 23. A method of genotyping a nucleic acid sample obtained from a human individual at risk for, or diagnosed with, cardiovascular disease, comprising determining the presence or absence of at least one allele of at least one polymorphic marker in the sample, wherein the at least one marker is selected from the group consisting of the markers set forth in Table 3 and Table 21, and markers in linkage disequilibrium therewith, and wherein the presence or absence of the at least one
- 25 allele of the at least one polymorphic marker is indicative of a susceptibility of cardiovascular disease.
24. The method of Claim 23, wherein the at least one marker is selected from rs10811650, rs10116277, rs1333040, rs10738607, rs4977574, rs6475608, D9S1870, rs2383207, rs1333045, rs1333046, rs10757278 and rs1333048.
- 30 25. The method according to Claim 23 or 24, wherein genotyping comprises amplifying a segment of a nucleic acid that comprises the at least one polymorphic marker by Polymerase Chain Reaction (PCR), using a nucleotide primer pair flanking the at least one polymorphic marker.
- 35 26. The method according to any of the Claims 23 - 25, wherein genotyping is performed using a process selected from allele-specific probe hybridization, allele-specific primer extension, allele-specific amplification, nucleic acid sequencing, 5'-

exonuclease digestion, molecular beacon assay, oligonucleotide ligation assay, size analysis, and single-stranded conformation analysis.

27. The method according to Claim 25, wherein the process comprises allele-specific probe hybridization.

5 28. The method according to Claim 27, wherein the process comprises DNA sequencing.

29. The method according to any of the Claims 23 ~ 27, comprising:

10 4) contacting copies of the nucleic acid with a detection oligonucleotide probe and an enhancer oligonucleotide probe under conditions for specific hybridization of the oligonucleotide probe with the nucleic acid;

wherein

a) the detection oligonucleotide probe is from 5-100 nucleotides in length and specifically hybridizes to a first segment of the nucleic acid whose nucleotide sequence is given by SEQ ID NO:94;

15 b) the detection oligonucleotide probe comprises a detectable label at its 3' terminus and a quenching moiety at its 5' terminus;

20 c) the enhancer oligonucleotide is from 5-100 nucleotides in length and is complementary to a second segment of the nucleotide sequence that is 5' relative to the oligonucleotide probe, such that the enhancer oligonucleotide is located 3' relative to the detection oligonucleotide probe when both oligonucleotides are hybridized to the nucleic acid; and

25 d) a single base gap exists between the first segment and the second segment, such that when the oligonucleotide probe and the enhancer oligonucleotide probe are both hybridized to the nucleic acid, a single base gap exists between the oligonucleotides;

5) treating the nucleic acid with an endonuclease that will cleave the detectable label from the 3' terminus of the detection probe to release free detectable label when the detection probe is hybridized to the nucleic acid; and

30 6) measuring free detectable label, wherein the presence of the free detectable label indicates that the detection probe specifically hybridizes to the first segment of the nucleic acid, and indicates the sequence of the polymorphic site as the complement of the detection probe.

30. A method of assessing an individual for probability of response to a therapeutic agent for preventing and/or ameliorating symptoms associated with cardiovascular disease, comprising: determining the presence or absence of at least one allele of at least one polymorphic marker in a nucleic acid sample obtained from the individual, wherein the at least one polymorphic marker is selected from the group consisting of the polymorphic markers set forth in Table 3 and Table 21, and markers in linkage disequilibrium therewith, wherein the presence of the at least one allele of the at least one marker is indicative of a probability of a positive response to the therapeutic agent.
31. A method of predicting prognosis of an individual diagnosed with cardiovascular disease, the method comprising determining the presence or absence of at least one allele of at least one polymorphic marker in a nucleic acid sample obtained from the individual, wherein the at least one polymorphic marker is selected from the group consisting of the polymorphic markers set forth in Tables 3 and 21, and markers in linkage disequilibrium therewith, wherein the presence of the at least one allele is indicative of a worse prognosis of the cardiovascular disease in the individual.
32. A method of monitoring progress of treatment of an individual undergoing treatment for cardiovascular disease, the method comprising determining the presence or absence of at least one allele of at least one polymorphic marker in a nucleic acid sample obtained from the individual, wherein the at least one polymorphic marker is selected from the markers set forth in Tables 3 and 21, and markers in linkage disequilibrium therewith, wherein the presence of the at least one allele is indicative of the treatment outcome of the individual.
33. The method according to any of the Claims 30-32, wherein the at least one polymorphic marker is selected from rs10811650, rs10116277, rs1333040, rs10738607, rs4977574, rs6475608, D9S1870, rs2383207, rs1333045, rs1333046, rs10757278 and rs1333048, and markers in linkage disequilibrium therewith.
34. The method of any of the preceding Claims, further comprising assessing at least one biomarker in a sample from the individual.
35. The method of Claim 34, wherein the biomarker is a cardiac marker or an inflammatory marker.
36. The method of Claim 34 or Claim 35, wherein the at least one biomarker is selected from creatin kinase, troponin, glycogen phosphorylase, C-reactive protein (CRP), serum amyloid A, fibrinogen, interleukin-6, tissue necrosis factor-alpha, soluble vascular cell adhesion molecules (sVCAM), soluble intervascular adhesion

molecules (sICAM), E-selectin, matrix metalloprotease type-1, matrix metalloprotease type-2, matrix metalloprotease type-3, matrix metalloprotease type-9, serum sCD40L, leukotrienes, leukotriene metabolites, Interleukin-6, tissue necrosis factor-alpha, myeloperoxidase (MPO), and N-tyrosine.

- 5 37. The method of Claim 36, wherein the leukotriene is selected from LTB₄, LTC₄, LTD₄ and LTE₄.
38. The method of any of the preceding claims, further comprising analyzing a sample comprising genomic DNA from a human individual or a genotype dataset derived from a human individual for the presence or absence of at least one at-risk allele of at least one at-risk variant for cardiovascular disease not in linkage disequilibrium with any one of the markers set forth in Table 10.
- 10 39. The method of any of the claims 1-6, comprising determining the presence or absence of at least one allele in at least two polymorphic markers, wherein the presence of the at least one allele in the at least two polymorphic markers is indicative of an increased susceptibility to cardiovascular disease.
- 15 40. The method of any of the preceding Claims, further comprising analyzing non-genetic information to make risk assessment, diagnosis, or prognosis of the individual.
41. The method of Claim 40, wherein the non-genetic information is selected from age, gender, ethnicity, socioeconomic status, previous disease diagnosis, medical history of subject, family history of cardiovascular disease, biochemical measurements, and clinical measurements.
- 20 42. The method of any of the Claims 34 - 41, further comprising calculating combined risk.
- 25 43. The method according to any of the preceding Claims, wherein linkage disequilibrium is characterized by a particular numeric cutoff value for the linkage disequilibrium measures r^2 and/or $|D'|$.
44. The method according to Claim 43, wherein wherein linkage disequilibrium is characterized by a cutoff value for r^2 of greater than 0.2.
- 30 45. The method according to Claim 43 or Claim 44, wherein linkage disequilibrium is characterized by a cutoff value for r^2 of greater than 0.5.
46. The method according to Claim 42, wherein linkage disequilibrium is characterized by a cutoff value for r^2 of greater than 0.2 and/or $|D'|$ of greater than 0.8.

47. The method according to any of the preceding Claims, wherein the Cardiovascular disease is at least one of Myocardial Infarction, Coronary Artery Disease, Percutaneous Transluminal Coronary Angioplasty (PTCA), Coronary Artery Bypass Surgery (CABG), Restenosis, Peripheral Arterial Disease, Stroke, Abdominal Aorta Aneurysm and Intracranial Aneurysm.
48. The method according to Claim 47, wherein the Cardiovascular disease is at least one of Myocardial Infarction, Coronary Artery Disease, Restenosis, Intracranial Aneurysm and Abdominal Aorta Aneurysm.
49. The method according to Claim 47, wherein the Stroke is Large Artery Atherosclerotic Stroke or Cardiolgenic Stroke.
50. The method according to Claim 47 or 48, wherein Myocardial Infarction is an early onset Myocardial Infarction.
51. The method according to Claim 50, wherein the Cardiovascular Disease is Myocardial Infarction and/or Coronary Artery Disease with an early onset before age 50 for males and 60 for females.
52. A kit for assessing susceptibility to cardiovascular disease in a human individual, the kit comprising reagents for selectively detecting at least one allele of at least one polymorphic marker in the genome of the individual, wherein the polymorphic marker is selected from the markers set forth in Tables 10, and markers in linkage disequilibrium therewith, and wherein the presence of the at least one allele is indicative of a susceptibility to cardiovascular disease.
53. The kit of Claim 52, wherein the at least one polymorphic marker is selected from rs10811650, rs10116277, rs1333040, rs10738607, rs4977574, rs6475608, D9S1870, rs2383207, rs1333045, rs1333046, rs10757278 and rs1333048.
54. The method kit according to Claim 52 or Claim 53, wherein the at least one polymorphic marker is selected from rs1333040, rs10116277, rs2383207 and rs10757278.
55. The kit according to Claim 55, wherein the at least one polymorphic marker is selected from rs10757278 and markers in linkage disequilibrium therewith.
56. The kit according to any of the Claims 52-55, wherein linkage disequilibrium is characterized by a particular numeric cutoff value for the linkage disequilibrium measures r^2 and/or $|D'|$.
57. The kit according to Claim 56, wherein wherein linkage disequilibrium is characterized by a cutoff value for r^2 of greater than 0.2.

58. The kit according to Claim 56 or Claim 57, wherein linkage disequilibrium is characterized by a cutoff value for r^2 of greater than 0.5.

59. The method according to Claim 56, wherein linkage disequilibrium is characterized by a cutoff value for r^2 of greater than 0.2 and/or $|D'|$ of greater than 0.8.

5 60. The kit according to any of the Claims 52 - 59, wherein the reagents comprise at least one contiguous oligonucleotide that hybridizes to a fragment of the genome of the individual comprising the at least one polymorphic marker, a buffer and a detectable label.

10 61. The kit according to any of the Claims 52 - 60, wherein the reagents comprise at least one pair of oligonucleotides that hybridize to opposite strands of a genomic nucleic acid segment obtained from the subject, wherein each oligonucleotide primer pair is designed to selectively amplify a fragment of the genome of the individual that includes one polymorphic marker, and wherein the fragment is at least 30 base pairs in size.

15 62. The kit according to Claim 60 or 61, wherein the at least one oligonucleotide is completely complementary to the genome of the individual.

63. The kit according to any of the Claims 60 - 62, wherein the oligonucleotide is about 18 to about 50 nucleotides in length.

20 64. The kit according any of the Claims 60 - 63, wherein the oligonucleotide is 20-30 nucleotides in length.

65. The kit according to any of the Claims 52 - 64, wherein the kit comprises:

a. a detection oligonucleotide probe that is from 5-100 nucleotides in length;

b. an enhancer oligonucleotide probe that is from 5-100 nucleotides in length; and

25 c. an endonuclease enzyme;

wherein the detection oligonucleotide probe specifically hybridizes to a first segment of the nucleic acid whose nucleotide sequence is set forth in SEQ ID NO:94; and

30 wherein the detection oligonucleotide probe comprises a detectable label at its 3' terminus and a quenching moiety at its 5' terminus;

wherein the enhancer oligonucleotide is from 5-100 nucleotides in length and is complementary to a second segment of the nucleotide sequence that is 5' relative

to the oligonucleotide probe, such that the enhancer oligonucleotide is located 3' relative to the detection oligonucleotide probe when both oligonucleotides are hybridized to the nucleic acid;

wherein a single base gap exists between the first segment and the second segment, such that when the oligonucleotide probe and the enhancer oligonucleotide probe are both hybridized to the nucleic acid, a single base gap exists between the oligonucleotides; and

wherein treating the nucleic acid with the endonuclease will cleave the detectable label from the 3' terminus of the detection probe to release free detectable label when the detection probe is hybridized to the nucleic acid.

66. Use of an oligonucleotide probe in the manufacture of a reagent for diagnosing and/or assessing susceptibility to cardiovascular disease in a human individual, wherein the probe hybridizes to a segment of a nucleic acid whose nucleotide sequence is set forth in SEQ ID NO:94, wherein the probe is 15-500 nucleotides in length.

67. A computer-readable medium on which is stored:

- a. an identifier for at least one polymorphic marker;
- b. an indicator of the frequency of at least one allele of said at least one polymorphic marker in a plurality of individuals diagnosed with cardiovascular disease; and
- c. an indicator of the frequency of the least one allele of said at least one polymorphic markers in a plurality of reference individuals;

wherein the at least one polymorphic marker is selected from the polymorphic markers set forth in Table 10, and polymorphic markers in linkage disequilibrium therewith.

68. The medium according to Claim 67, wherein the polymorphic marker is selected from rs10811650, rs10116277, rs1333040, rs10738607, rs4977574, rs6475608, D9S1870, rs2383207, rs1333045, rs1333046, rs10757278 and rs1333048, and markers in linkage disequilibrium therewith.

69. The medium according to claim 67 or 68, further comprising information about the ancestry of the plurality of individuals.

70. An apparatus for determining a genetic indicator for cardiovascular disease in a human individual, comprising:

a computer readable memory; and

a routine stored on the computer readable memory;

wherein the routine is adapted to be executed on a processor to analyze marker and/or haplotype information for at least one human individual with respect to at least one polymorphic marker selected from the markers set forth in Table 10, and markers in linkage disequilibrium therewith, and generate an output based on the marker or haplotype information, wherein the output comprises a risk measure of the at least one marker or haplotype as a genetic indicator of cardiovascular disease for the human individual.

71. The apparatus of Claim 70, wherein the routine further comprises an indicator of the frequency of at least one allele of at least one polymorphic marker or at least one haplotype in a plurality of individuals diagnosed with cardiovascular disease, and an indicator of the frequency of at the least one allele of at least one polymorphic marker or at least one haplotype in a plurality of reference individuals, and wherein a risk measure is based on a comparison of the at least one marker and/or haplotype status for the human individual to the indicator of the frequency of the at least one marker and/or haplotype information for the plurality of individuals diagnosed with cardiovascular disease.

72. The apparatus according to Claim 70 or 71, wherein the at least one polymorphic marker is selected from rs10811650, rs10116277, rs1333040, rs10738607, rs4977574, rs6475608, D9S1870, rs2383207, rs1333045, rs1333046, rs10757278 and rs1333048, and markers in linkage disequilibrium therewith.

73. The apparatus or medium according to any of the claims 67 - 72, wherein linkage disequilibrium is characterized by numerical values of r^2 of at least 0.2 and/or values of $|D'|$ of at least 0.8.

74. The apparatus of any of the Claims 70 - 73, wherein the risk measure is characterized by an Odds Ratio (OR) or a Relative Risk (RR).

CLAIMS

1. A method for determining a susceptibility to arterial disease in a human individual, comprising determining the presence or absence of at least one allele of at least one polymorphic marker in a nucleic acid sample obtained from the individual or in a genotype dataset derived from the individual, wherein the at least one polymorphic marker is selected from the polymorphic markers rs10116277, rs1333040, and rs2383207, DG9S1870 and D9S1814, and markers in linkage disequilibrium therewith, and wherein the presence of the at least one allele is indicative of a susceptibility to the arterial disease, wherein linkage disequilibrium is characterized by a numeric cutoff value for $r^2 > 0.2$.
2. The method according to Claim 1, wherein the at least one polymorphic marker is selected from the markers set forth in Table 3 and Table 21.
3. The method according to any of the preceding Claims, wherein the at least one polymorphic marker is rs10757278.
4. The method according to Claim 1, further comprising assessing the frequency of at least one haplotype in the individual.
5. The method of any of the preceding claims, wherein the susceptibility conferred by the presence of the at least one allele or haplotype is increased susceptibility.
6. The method according to Claim 5, wherein the presence of allele T in rs1333040, allele T in rs10116277, allele G in rs2383207, allele G in rs10757278, allele X in DG9S1870 or allele 0 in D9S1814 is indicative of increased susceptibility to cardiovascular disease.
7. The method according to Claim 5 or 6, wherein the presence of the at least one allele or haplotype is indicative of increased susceptibility with a relative risk (RR) or odds ratio (OR) of at least 1.2.
8. The method according to Claim 5 or 6, wherein the presence of the at least one allele or haplotype is indicative of increased susceptibility with a relative risk (RR) or odds ratio (OR) of at least 1.3.
9. The method according to any of the claims 1-4, wherein the susceptibility conferred by the presence of the at least one allele or haplotype is decreased susceptibility.
10. The method of any of the preceding Claims, further comprising assessing at least one biomarker in a sample from the individual.

11. The method of Claim 10, wherein the biomarker is a cardiac marker or an inflammatory marker.
12. The method of Claim 10 or Claim 11, wherein the at least one biomarker is selected from creatin kinase, troponin, glycogen phosphorylase, C-reactive protein (CRP), serum amyloid A, fibrinogen, interleukin-6, tissue necrosis factor-alpha, soluble vascular cell adhesion molecules (sVCAM), soluble intervascular adhesion molecules (sICAM), E-selectin, matrix metalloprotease type-1, matrix metalloprotease type-2, matrix metalloprotease type-3, matrix metalloprotease type-9, serum sCD40L, leukotrienes, leukotriene metabolites, interleukin-6, tissue necrosis factor-alpha, myeloperoxidase (MPO), and N-tyrosine.
13. The method of Claim 12, wherein the leukotriene is selected from LTB₄, LTC₄, LTD₄ and LTE₄.
14. The method of any of the preceding claims, further comprising analyzing a sample comprising genomic DNA from a human individual or a genotype dataset derived from a human individual for the presence or absence of at least one at-risk allele of at least one at-risk variant for cardiovascular disease not in linkage disequilibrium with any one of the markers set forth in Table 10.
15. The method of claim 1, comprising determining the presence or absence of at least one allele in at least two polymorphic markers, wherein the presence of the at least one allele in the at least two polymorphic markers is indicative of an increased susceptibility to cardiovascular disease.
16. The method of any of the preceding Claims, further comprising analyzing non-genetic information to make risk assessment, diagnosis, or prognosis of the individual.
17. The method of Claim 16, wherein the non-genetic information is selected from age, gender, ethnicity, socioeconomic status, previous disease diagnosis, medical history of subject, family history of cardiovascular disease, biochemical measurements, and clinical measurements.
18. The method of any of the Claims 10-17, further comprising calculating combined risk.
19. The method according to Claim 1 wherein linkage disequilibrium is characterized by a cutoff value for r^2 of greater than 0.5.
20. The method according to Claim 18, wherein linkage disequilibrium is characterized by a cutoff value for r^2 of greater than 0.2 and/or $|D'|$ of greater than 0.8.

21. The method according to any of the preceding Claims, wherein the Arterial disease is at least one of Myocardial Infarction, Coronary Artery Disease, Percutaneous Transluminal Coronary Angioplasty (PTCA), Coronary Artery Bypass Surgery (CABG), Restenosis, Peripheral Arterial Disease, Stroke, Abdominal Aorta Aneurysm and Intracranial Aneurysm.
22. The method according to Claim 21, wherein the Arterial disease is at least one of Myocardial Infarction, Coronary Artery Disease, Restenosis, Intracranial Aneurysm and Abdominal Aorta Aneurysm.
23. The method according to Claim 20, wherein the Stroke is Large Artery Atherosclerotic Stroke or Cardiogenic Stroke.
24. The method according to Claim 21 or 22, wherein Myocardial Infarction is an early onset Myocardial Infarction.
25. The method according to Claim 24, wherein the Cardiovascular Disease is Myocardial Infarction and/or Coronary Artery Disease with an early onset before age 50 for males and 60 for females.
26. Use of an oligonucleotide probe in the manufacture of a reagent for diagnosing and/or assessing susceptibility to arterial disease in a human individual, wherein the probe hybridizes to a segment of a nucleic acid whose nucleotide sequence is set forth in SEQ ID NO:94 that comprises at least one polymorphic site selected from the group consisting of rs10116277, rs1333040, D9S1870, rs2383207, and D9S1814, and markers in linkage disequilibrium therewith, wherein the probe is 15-500 nucleotides in length, wherein linkage disequilibrium is characterized by a numeric cutoff value for $r^2 > 0.2$.
27. An apparatus for determining a genetic indicator for arterial disease in a human individual, comprising:
 - a computer readable memory; and
 - a routine stored on the computer readable memory;
 wherein the routine is adapted to be executed on a processor to analyze marker and/or haplotype information for at least one human individual with respect to at least one polymorphic marker selected from the group consisting of rs10116277, rs1333040, D9S1870, rs2383207, and D9S1814, and markers in linkage disequilibrium therewith wherein linkage disequilibrium is characterized by a numeric cutoff value for $r^2 > 0.2$, and generate an output based on the marker or haplotype

information, wherein the output comprises a risk measure of the at least one marker or haplotype as a genetic indicator of arterial disease for the human individual.

28. The apparatus of Claim 27, wherein the routine further comprises an indicator of the frequency of at least one allele of at least one polymorphic marker or at least one haplotype in a plurality of individuals diagnosed with arterial disease, and an indicator of the frequency of the at least one allele of at least one polymorphic marker or at least one haplotype in a plurality of reference individuals, and wherein a risk measure is based on a comparison of the at least one marker and/or haplotype status for the human individual to the indicator of the frequency of the at least one marker and/or haplotype information for the plurality of individuals diagnosed with cardiovascular disease.
29. The apparatus according to claim 27 or 28, wherein linkage disequilibrium is characterized by numerical values of r^2 of at least 0.2 and/or values of $|D'|$ of at least 0.8.
30. The apparatus of any of the Claims 27 - 29, wherein the risk measure is characterized by an Odds Ratio (OR) or a Relative Risk (RR).