

WHAT IS CLAIMED IS:

1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.
- 5 2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.
- 10 3. The isolated DNA of claim 1, wherein said DNA is an allelic variant of the nucleotide sequence set forth in SEQ ID NO:1.
34. The isolated DNA of claim 1 which contains BRCA1 regulatory sequences.
45. The isolated DNA of claim 2 which contains BRCA1 regulatory sequences.
- 15 6. The isolated DNA of claim 3 which contains BRCA1 regulatory sequences.
57. An isolated DNA having at least 15 nucleotides of the DNA of claim 1.
- 20 68. An isolated DNA having at least 15 nucleotides of the DNA of claim 2.
9. An isolated DNA having at least 15 nucleotides of the DNA of claim 3.
10. An isolated DNA coding for a mutated form of the BRCA1 polypeptide set forth in SEQ ID NO:2.
- 25 11. The isolated DNA of claim 10, wherein the DNA comprises a mutated form of the nucleotide sequence set forth in SEQ ID NO:1.
- 30 12. The isolated DNA of claim 11, wherein the mutation is a deletion mutation.

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13. The isolated DNA of claim 11, wherein the mutation is a nonsense mutation.

14. The isolated DNA of claim 11, wherein the mutation is an insertion mutation.

5 15. The isolated DNA of claim 11, wherein the mutation is missense mutation.

16. An isolated DNA having at least 15 nucleotides of the DNA of claim 10.

17. An isolated DNA having at least 15 nucleotides of the DNA of claim 11.

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18. The isolated DNA of claim 16, wherein the isolated DNA overlaps the mutation.

19. The isolated DNA of claim 17, wherein the isolated DNA overlaps the mutation.

15 20. The isolated DNA of claim 11 selected from the group consisting of:

(a) SEQ ID NO:1 having T at nucleotide position 4056;

(b) SEQ ID NO:1 having extra C at nucleotide position 5385;

(c) SEQ ID NO:1 having G at nucleotide position 5443; and,

(d) SEQ ID NO:1 having 11 base pairs at nucleotide positions 189-199 deleted.

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A replicative cloning vector which comprises the isolated DNA of claim 1 or parts thereof and a replicon operative in a host cell.

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A replicative cloning vector which comprises the isolated DNA of claim 2 or parts thereof and a replicon operative in a host cell.

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23. A replicative cloning vector which comprises the isolated DNA of claim 3 or parts thereof and a replicon operative in a host cell.

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24. A replicative cloning vector which comprises the isolated DNA of claim 10 or parts thereof and a replicon operative in a host cell.

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25. A replicative cloning vector which comprises the isolated DNA of claim 11 or parts thereof and a replicon operative in a host cell.

5 ~~10~~ 26. An expression system which comprises the isolated DNA of claim 1 or parts thereof operably linked to suitable control sequences.

~~11~~ 27. An expression system which comprises the isolated DNA of claim 2 or parts thereof operably linked to suitable control sequences.

10 28. An expression system which comprises the isolated DNA of claim 3 or parts thereof operably linked to suitable control sequences.

15 29. An expression system which comprises the isolated DNA of claim 10 or parts thereof operably linked to suitable control sequences.

30. An expression system which comprises the isolated DNA of claim 11 or parts thereof operably linked to suitable control sequences.

20 ~~12~~ ^{Host} 31. ~~Recombinant host cells transformed with the expression system of claim~~ ~~26~~ ¹⁰.

C ~~13~~ ^{Host} 32. ~~Recombinant host cells transformed with the expression system of claim~~ ~~27~~ ¹¹.

33. Recombinant host cells transformed with the expression system of claim 28.

25 34. Recombinant host cells transformed with the expression system of claim 29.

35. Recombinant host cells transformed with the expression system of claim 30.

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A method of producing ~~recombinant~~ BRCA1 polypeptide which comprises culturing the cells of claim ~~31~~¹³ under conditions effective for the production of said BRCA1 polypeptide and harvesting the ~~recombinant~~ BRCA1 polypeptide.

C 5 15
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A method of producing ~~recombinant~~ BRCA1 polypeptide which comprises culturing the cells of claim ~~32~~¹³ under conditions effective for the production of said BRCA1 polypeptide and harvesting the ~~recombinant~~ BRCA1 polypeptide.

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38. A method of producing recombinant BRCA1 polypeptide which comprises culturing the cells of claim 33 under conditions effective for the production of said BRCA1 polypeptide and harvesting the recombinant BRCA1 polypeptide.

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39. A preparation of human BRCA1 polypeptide substantially free of other human proteins, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.

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40. A preparation of human polypeptide substantially free of other human proteins, the amino acid sequence of said polypeptide having substantial sequence homology with the wild-type BRCA1 polypeptide having the amino acid sequence set forth in SEQ ID NO:2, and said human polypeptide having substantially similar function as the wild-type BRCA1 polypeptide.

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41. An antibody immunoreactive with a human BRCA1 polypeptide or portion thereof.

42. The antibody of claim 41 which is a polyclonal antibody.

43. The antibody of claim 41 which is a monoclonal antibody.

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A pair of single-stranded DNA primers for determination of a nucleotide sequence of a BRCA1 gene by a polymerase chain reaction, the sequence of said primers being derived from human chromosome 17q, wherein the use of said primers in a polymerase chain reaction results in the synthesis of DNA having all or part of the sequence of the BRCA1 gene.

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45. The pair of primers of claim 44 wherein said BRCA1 gene has the nucleotide sequence set forth in SEQ ID NO:1.

5 46. A method for identifying a mutant BRCA1 nucleotide sequence in a suspected mutant BRCA1 allele which comprises comparing the nucleotide sequence of the suspected mutant BRCA1 allele with the wild-type BRCA1 nucleotide sequence, wherein a difference between the suspected mutant and the wild-type sequences identifies a mutant BRCA1 nucleotide sequence.

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10 47. A kit for detecting mutations in the BRCA1 gene resulting in a susceptibility to breast and ovarian cancers comprising at least one oligonucleotide primer specific for a BRCA1 gene mutation and instructions relating to detecting mutations in the BRCA1 gene.

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15 48. A kit for detecting mutations in the BRCA1 gene resulting in a susceptibility to breast and ovarian cancers comprising at least one allele-specific oligonucleotide probe for a BRCA1 gene mutation and instructions relating to detecting mutations in the BRCA1 gene.

20 49. A method for supplying a wild-type BRCA1 gene function or a BRCA1 function substantially similar to the wild-type to a cell which has lost said gene function or has altered gene function by virtue of a mutation in the BRCA1 gene, comprising: introducing into the cell a nucleic acid which suppresses a transformed state of said cell, said nucleic acid selected from the group consisting of a wild-type BRCA1 gene nucleic acid, a portion of the wild-type BRCA1 gene nucleic acid, a nucleic acid substantially homologous and has substantially similar function to said wild-type BRCA1 gene nucleic acid and a portion of the nucleic acid substantially homologous to said wild-type BRCA1 gene nucleic acid.

25 50. The method of claim 49 wherein said nucleic acid is said wild-type BRCA1 gene nucleic acid.

51. The method of claim 49 wherein said nucleic acid is said portion of the wild-type BRCA1 gene nucleic acid.

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52. The method of claim 49 wherein said nucleic acid is said nucleic acid substantially homologous to the wild-type BRCA1 gene.
- 5 53. The method of claim 49 wherein said nucleic acid is said portion of the nucleic acid substantially homologous to the wild-type BRCA1 gene.
54. The method of claim 49 wherein said nucleic acid contains the BRCA1 gene regulatory sequences.
- 10 55. The method of claim 50 wherein said nucleic acid contains the BRCA1 gene regulatory sequences.
56. The method of claim 51 wherein said nucleic acid contains the BRCA1 gene regulatory sequences.
- 15 57. The method of claim 52 wherein said nucleic acid contains the BRCA1 gene regulatory sequences.
58. The method of claim 53 wherein said nucleic acid contains the BRCA1 gene regulatory sequences.
- 20 59. The method of claim 49 wherein said nucleic acid is incorporated into the genome of said cell.
60. The method of claim 50 wherein said nucleic acid is incorporated into the genome of said cell.
- 25 61. The method of claim 51 wherein said nucleic acid is incorporated into the genome of said cell.
62. The method of claim 52 wherein said nucleic acid is incorporated into the genome of said cell.
- 30 63. The method of claim 53 wherein said nucleic acid is incorporated into the genome of said cell.

64. The method of claim 54 wherein said nucleic acid is incorporated into the genome of said cell.

65. The method of claim 55 wherein said nucleic acid is incorporated into the genome of said cell.

5 66. The method of claim 56 wherein said nucleic acid is incorporated into the genome of said cell.

67. The method of claim 57 wherein said nucleic acid is incorporated into the genome of said cell.

68. The method of claim 58 wherein said nucleic acid is incorporated into the genome of said cell.

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69. A method for supplying a wild-type BRCA1 gene function or a BRCA1 function substantially similar to the wild-type to a cell which has lost said gene function or has altered gene function by virtue of a mutation in the BRCA1 gene, comprising: introducing into the cell a molecule which suppresses a transformed state of said cell, said molecule selected from the group consisting of a wild-type BRCA1 polypeptide, a portion of said wild-type BRCA1 polypeptide, a polypeptide substantially homologous to said wild-type BRCA1 polypeptide, a portion of said polypeptide substantially homologous to said wild-type BRCA1 polypeptide and a molecule which mimics the function of said wild-type BRCA1 polypeptide.

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20 70. The method of claim 69 wherein said molecule is said wild-type BRCA1 polypeptide.

71. The method of claim 69 wherein said molecule is said portion of the wild-type BRCA1 polypeptide.

25 72. The method of claim 69 wherein said molecule is said polypeptide substantially homologous to the wild-type BRCA1 polypeptide.

73. The method of claim 69 wherein said molecule is said portion of said polypeptide substantially homologous to the wild-type BRCA1 polypeptide.

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74. The method of claim 69 wherein said molecule is said molecule which mimics the function of said wild-type BRCA1 polypeptide.

5 75. A method for screening potential cancer therapeutics which comprises: combining (i) a BRCA1 binding partner, (ii) a BRCA1 polypeptide selected from the group consisting of a polypeptide having the amino acid sequence set forth in SEQ ID NO:2 and a polypeptide having a portion of said amino acid sequence which binds to said binding partner and (iii) a compound suspected of being a cancer therapeutic and determining the amount of binding of the BRCA1 polypeptide to its binding partner.

10 76. A method for screening potential cancer therapeutics which comprises: combining a BRCA1 binding partner and a compound suspected of being a cancer therapeutic and measuring the biological activity of the binding partner.

15 *had Cz* 77. A method for screening potential cancer therapeutics which comprises: growing a transformed eukaryotic host cell containing an altered BRCA1 gene in the presence of a compound suspected of being a cancer therapeutic and determining the rate of growth of said host cell.

20 78. A method for screening potential cancer therapeutics which comprises: administering a compound suspected of being a cancer therapeutic to a transgenic animal which carries an altered BRCA1 allele from a second animal in its genome and determining the development or growth of a cancer lesion.

25 79. A transgenic animal which carries an altered BRCA1 allele.

80. The transgenic animal of claim 79 wherein the altered BRCA1 allele contains a deletion.

81. The transgenic animal of claim 79 wherein the altered BRCA1 allele contains a nonsense mutation.

82. The transgenic animal of claim 79 wherein the altered BRCA1 allele contains a frameshift mutation.

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83. The transgenic animal of claim 79 wherein the altered BRCA1 allele contains a missense mutation.

84. The transgenic animal of claim 79 wherein the altered BRCA1 allele is a disrupted allele.

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