Claims

1. A method for diagnosing a predisposition for breast and ovarian cancer in a human subject which comprises determining whether there is a germline alteration in the sequence of the BRCA1 gene or a BRCA1 gene regulatory sequence in a tissue sample of said subject, said alteration being indicative of a predisposition to said cancer.

2. A method for diagnosing a lesion of a human subject for neoplasia associated with the BRCA1 gene locus which comprises determining whether there is an alteration in the sequence of the BRCA1 gene or a BRCA1 gene regulatory sequence in a sample from said lesion, said alteration being indicative of neoplasia.

3. A method as claimed in claim 2 wherein said lesion is a breast or ovarian lesion.

4. A method as claimed in any one of claims 1 to 3 wherein the sequence of the BRCA1 gene in said sample is compared with the sequence of one or more wild-type BRCA1 gene sequences selected from the sequence set forth in SEQ.ID. No. 1 and wild-type allelic variants thereof.

5. A method as claimed in any one of claims 1 to 3 wherein the level and/or sequence of an expression product of the BRCA1 gene in said sample is investigated.

6. A method as claimed in claim 5 wherein said expression product is mRNA.

7. A method as claimed in claim 6 wherein mRNA of said sample is contacted with a BRCA1 gene probe under conditions suitable for hybridization of said probe to an RNA corresponding to said BRCA1 gene and hybridization of said probe is determined.

8. A method as claimed in any one of claims 1 to 4 wherein a BRCA1 gene probe is contacted with genomic DNA isolated from said sample under conditions suitable for hybridization of said probe to said gene and hybridization of said probe is determined.

9. A method as claimed in claim 7 or claim 8 wherein said probe is a mutant, allele specific probe.

10. A method as claimed in claim 5 wherein said expression product is the polypeptide encoded by the BRCA1 gene in said sample.

11. A method as claimed in claim 10 wherein said polypeptide is detected by immunoblotting or immunocytochemistry.

12. A method as claimed in claim 10 wherein binding interaction is assayed between the BRCA1 gene protein isolated from said sample and a binding partner capable of specifically binding the polypeptide expression product of a mutant BRCA1 allele and/or a binding partner for the BRCA1 polypeptide having the amino acid sequence set forth in SEQ.ID No:2.

13. A method as claimed in claim 12 wherein inhibition of biochemical activity of said binding partner is determined.

14. A method as claimed in any one of claims 1 to 3 and 5 which comprises determining whether there is an alteration in the regulatory regions of the BRCA1 gene present in said sample.

15. A method as claimed in any one of claims 1 to 4 which comprises determining whether there is an alteration in the germline sequence of the BRCA1 gene in said sample by observing shifts in electrophoretic mobility of single-stranded DNA from said sample on non-denaturing polyacrylamide gels.

16. A method as claimed in any one of claims 1 to 4 wherein all or part of the BRCA1 gene from said sample is amplified and the sequence of said amplified sequence is determined.

17. A method as claimed in any one of claims 1 to 4 wherein oligonucleotide primers are employed to determine whether a specific BRCA1 mutant allele can be identified in said sample by nucleic acid amplification.

18. A method as claimed in any one of claims 1 to 4 wherein all or part of the BRCA1 gene from said sample is cloned to produce a cloned sequence and the sequence of said cloned sequence is determined.

19. A method as claimed in any one of claims 1 to 6 which comprises determining whether there is a mismatch between molecules (1) BRCA1 gene genomic DNA or BRCA1 mRNA isolated from said sample, and (2) a nucleic acid probe complementary to human wild-type BRCA1 gene DNA, when molecules (1) and (2) are hybridized to each other to form a duplex.

20. A method as claimed in any one of claims 1 to 6 wherein amplification of BRCA1 gene sequences in said sample is carried out and hybridization of the amplified sequences to one or more nucleic acid probes which comprise a wild-type BRCA1 gene sequence or a mutant BRCA1 gene sequence including a mutation is determined.

21. A method as claimed in any one of claims 1 to 4 which comprises determining *in situ* hybridization of the BRCA1 gene in said sample with one or more nucleic acid probes which comprise a wild-type BRCA1 gene sequence or a mutant BRCA1 gene sequence including a mutation.

22. A method as claimed in any one of the preceding claims wherein the alteration screened for is a deletion mutation.

23. A method as claimed in any one of claims 1 to 21 wherein the alteration screened for is a point mutation.

24. A method as claimed in any one of claims 1 to 21 wherein the alteration screened for is an insertion mutation.

25. A method as claimed in any one of claims 1 to 21 wherein the alteration screened for is a mutation selected from the mutations set forth in Table 11.