Title: METHOD AND APPARATUS FOR CORRELATING LEVELS OF BIOMARKER PRODUCTS WITH DISEASE
as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(Ui))

Published:
— with international search report
— with amended claims

Date of publication of the amended claims: 28 June 2007

Published:
For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.
1. A method of testing for one or more colorectal pathologies in a test subject, the method comprising:

(a) providing data representing a level of one or more products of each of at least two biomarkers in a sample isolated and/or derived from said test subject, wherein said biomarkers are genes selected from the group consisting of BCNPl, CD163, CDA, MS4A1, BANK1, and MGC20553; and

(b) applying to said data a formula based on (i) a dataset representing levels of one or more products of each of said biomarkers in each subject of a reference population having said one or more pathologies, and (ii) a dataset representing levels of one or more products of each of said biomarkers in each subject of a reference population not having said one or more pathologies, thus providing an indication of a probability that said test subject has said one or more colorectal pathologies.

2. A computer-based method for testing for one or more colorectal pathologies in a test subject, the method comprising:

inputting, to a computer, data representing a level of products of each of at least two biomarkers in a sample isolated and/or derived from a test subject, wherein said biomarkers are genes selected from the group consisting of BCNPl, CD163, CDA, MS4A1, BANK1 and MGC20553; and

causing said computer to apply to said data, a formula based on (i) a dataset representing levels of one or more products of each of said biomarkers in each subject of a reference population having said one or more pathologies, and (ii) a dataset representing levels of one or more products of each of said biomarkers in each subject of a reference population not having said one or more pathologies, thus providing an indication of a probability that said test subject has said one or more colorectal pathologies.

3. The method of claims 1 or 2, wherein said formula has a form:

\[ V = C + \sum \beta_i X_i \]

wherein \( V \) is a value indicating a probability that said test subject has said one or more colorectal pathologies, \( X_i \) is a level of products of an \( i \)th biomarker of said biomarkers, \( \beta_i \) is a coefficient, and \( C \) is a constant.
4. The method of claims 1 or 2, wherein said formula has a form:
\[ V = C + \sum \beta_i \frac{X_i}{X_j}, \]

wherein \( V \) is a value indicating a probability that said test subject has said one or more colorectal pathologies, \( X_i \) is a level of products of an \( i \)-th biomarker of said biomarkers, \( X_j \) is a level of products of an \( j \)-th biomarker of said biomarkers where the \( z \)-th biomarker is not the \( y \)-th biomarker, \( \beta_i \) is a coefficient and \( C \) is a constant.

5. The method of claims 1 or 2, wherein said formula is derived by logistic regression.

6. The method of claims 1 or 2, wherein said sample is selected from the group consisting of blood, lymph and lymphoid tissue.

7. The method of claims 1 or 2 wherein said products in said sample are RNA.

8. The method of claims 1 or 2, wherein said sample is selected from the group consisting of a sample of serum-reduced blood, a sample of erythrocyte-reduced blood, a sample of serum-reduced and erythrocyte-reduced blood, a sample of unfractionated cells of lysed blood, and a sample of fractionated blood.

9. The method of claims 1 or 2, wherein said products in said sample are RNA, and whereas said data represents a level of cDNA, EST and/or PCR product derived from said RNA.

10. A kit comprising packaging and containing at least two primer sets, wherein each set of which is able to generate an amplification product by selective amplification of at least a portion of a polynucleotide complementary to one or more RNA products of a biomarker, wherein said biomarker is a gene selected from the group consisting of: BCNPI, CD163, CDA, MS4A1, BANK1, and MGC20553; and wherein each set of said primer sets is selective for a different biomarker of said group.

11. The kit of claim 10, wherein said polynucleotide is selected from the group consisting of total RNA, mRNA, DNA, cDNA and EST.
12. The kit of claim 10, further comprising two or more oligonucleotide probes, wherein each of said probes is capable of selectively hybridizing to either a sense or an antisense strand of said amplification product.

13. The kit of claims 10, 11 or 12, further comprising two or more components selected from the group consisting of: a thermostable polymerase, a reverse transcriptase, deoxynucleotide triphosphates, nucleotide triphosphates and enzyme buffer.

14. The kit of claims 10, 11, 12 or 13, further comprising a computer-readable medium encoded with instructions for applying a formula to data representing levels of said amplification product in a sample isolated and/or derived from a test subject, wherein said formula is said based on (i) a dataset representing levels of one or more products of each of said biomarkers in each subject of a reference population having one or more colorectal pathologies, and (ii) a dataset representing levels of one or more products of each of said biomarkers in each subject of a reference population not having said one or more pathologies, thus providing an indication of a probability that said test subject has said one or more colorectal pathologies.

15. The kit of claim 14, wherein said formula has a form:

\[ V = C + \sum \beta_i X_i, \]

wherein \( V \) is a value indicating a probability that said test subject has said one or more colorectal pathologies, \( X_i \) is a level of products of an \( i \)th biomarker of said biomarkers, \( \beta_i \) is a coefficient, and \( C \) is a constant.

16. The kit of claim 14, wherein said formula has a form:

\[ V = C + \sum \beta_j(X_j/X_i) , \]

wherein \( V \) is a value indicating a probability that said test subject has said one or more colorectal pathologies, \( X_i \) is a level of products of an \( i \)th biomarker of said biomarkers, \( X_j \) is a level of products of a \( j \)th biomarker of said biomarkers where the \( i \)th biomarker is not the \( j \)th biomarker, \( \beta_j \) is a coefficient, and \( C \) is a constant.

17. The kit of claims 14, 15 or 16, wherein said sample is selected from the group consisting of blood, lymph and lymphoid tissue.
18. The kit of claims 14, 15 or 16, wherein said sample is selected from the group consisting of a sample of serum-reduced blood, a sample of erythrocyte-reduced blood, a sample of serum-reduced and erythrocyte-reduced blood, a sample of unfractionated cells of lysed blood and a sample of fractionated blood.

19. A computer-readable medium having instructions stored thereon that are operable when executed by a computer to apply a formula to data representing a level of one or more products of each of at least two biomarkers in a sample isolated and/or derived from a test subject, wherein said biomarkers are genes selected from the group consisting of BCNPl, CDI 63, CDA, MS4A1, BANK1, and MGC20553, wherein said formula is based on (i) a dataset representing levels of one or more products of each of said biomarkers in each subject of a reference population having one or more colorectal pathologies, and (ii) a dataset representing levels of one or more products of each of said biomarkers in each subject of a reference population not having said one or more pathologies, thus providing an indication of a probability that said test subject has said one or more colorectal pathologies.

20. The computer-readable medium of claim 19, wherein said formula has a form:

\[ V = c + \sum \beta_i x_i \]

wherein \( V \) is a value indicating a probability that said test subject has said one or more colorectal pathologies, \( x_i \) is a level of products of an \( i \)th biomarker of said biomarkers, \( \beta_i \) is a coefficient, and \( c \) is a constant.

21. The computer-readable medium of claim 19, wherein said formula has a form:

\[ V = C + \sum \beta_j (X_j / X_{ij}) \]

wherein \( V \) is a value indicating a probability that said test subject has said one or more colorectal pathologies, \( X_j \) is a level of products of an \( i \)th biomarker of said biomarkers, and \( X_{ij} \) is a level of products of a \( j \)th biomarker of said biomarkers, where the \( z \)th biomarker is not the \( z \)th biomarker, \( \beta_j \) is a coefficient and \( C \) is a constant.

22. The computer-readable medium of claim 19 wherein said formula is derived by logistic regression.
23. The computer-readable medium of claim 19 wherein said sample is selected from the group consisting of blood, lymph and lymphoid tissue.

24. The computer-readable medium of claims 19 wherein said products in said sample are RNA.

25. The computer-readable medium of claim 19, wherein said sample is selected from the group consisting of a sample of serum-reduced blood, a sample of erythrocyte-reduced blood, a sample of serum-reduced and erythrocyte-reduced blood, a sample of unfractionated cells of lysed blood, and a sample of fractionated blood.

26. The computer-readable medium of claim 19 wherein said products in said sample are RNA, and whereas said data represents a level of cDNA, EST and/or PCR product derived from said RNA.

27. A computer system for providing an indication of a probability that a test subject has one or more colorectal pathologies, the computer system comprising a processor; and

a memory configured with instructions that, when executed, cause said processor to provide a user with said indication, wherein said instructions comprise applying a formula to data representing a level of one or more products of each of at least two biomarkers in a sample isolated and/or derived from said test subject, wherein said biomarkers are genes selected from the group consisting of BCNPI, CD163, CDA, MS4A1, BANK1, and MGC20553; and wherein said formula is based on (i) a dataset representing levels of one or more products of each of said biomarkers in each subject of a reference population having said one or more pathologies, and (ii) a dataset representing levels of one or more products of each of said biomarkers in each subject of a reference population not having said one or more pathologies, thus providing said indication of said probability that said test subject has said one or more colorectal pathologies.

28. The system of claim 27, wherein said formula has a form:

\[ V = C + \Sigma \beta_i x_i \]
wherein $V_i$ is a value indicating a probability that said test subject has said one or more colorectal pathologies, $X_i$ is a level of products of an $i$th biomarker of said biomarkers, $\beta_i$ is a coefficient, and $C$ is a constant.

29. The system of claim 27, wherein said formula has a form:

$$V = C + \sum \beta_j (X_i / X_j)$$

wherein $V$ is a value indicating a probability that said test subject has said one or more colorectal pathologies, $X_i$ is a level of products of an $i$th biomarker of said biomarkers, and $X_j$ is a level of products of a $j$th biomarker of said biomarkers, where the $j$th biomarker is not the $i$th biomarker, $\beta_j$ is a coefficient, and $C$ is a constant.

30. The system of claim 27, wherein said formula is derived by logistic regression.

31. The system of claim 27, wherein said sample is selected from the group consisting of blood, lymph and lymphoid tissue.

32. The system of claim 27, wherein said products in said sample are RNA.

33. The system of claim 27 wherein said sample is selected from the group consisting of a sample of serum-reduced blood, a sample of erythrocyte-reduced blood, a sample of serum-reduced and erythrocyte-reduced blood, a sample of unfractionated cells of lysed blood, and a sample of fractionated blood.

34. The system of claim 27 wherein said products in said sample are RNA, and whereas said data represents a level of cDNA, EST and/or PCR product derived from said RNA.