METHOD OF DETERMINING AND TREATING BREAST CANCER

FIELD OF THE INVENTION

[0001] The present invention relates generally to the field of molecular biology. In particular, the present invention relates to the use of biomarkers for the detection of cancer.

BACKGROUND

[0002] Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer mortality among women worldwide. The gold standard for breast cancer screening is mammography. However, this modality yields significant false-positive results that require additional diagnostic imaging procedures and tissue biopsies. In a large study of 702,154 cases in the United States, 171,829 had abnormal screening mammogram results with only <2% (2,599/171,829) found to be true positives. As a result, a large majority of these women with abnormal screening mammograms were subjected to invasive and expensive diagnostic procedures that could have been avoided. Furthermore, mammography has about 22% of false negative rate in women under 50, and sometimes cannot accurately distinguish between benign and malignant tumours, causing delay of more than two months for timely treatment of the patients. Thus, based on the issues identified above, there is a need for minimally invasive methods of detection of breast cancer in subjects, from healthy individuals or subjects with benign breast lesions.

SUMMARY

[0003] In one aspect, the present disclosure refers to a method of determining if a subject is suffering from or is at the risk of developing breast cancer, the method comprising: measuring in a sample obtained from a subject thought to be suffering from or being at the risk of developing breast cancer the expression level of at least two or more miRNAs selected from the group consisting of miR-451a, miR-195-5p, miR-126-5p, miR-423-3p, miR-192-5p, miR-17-5p, miR-125b-5p, miR-660-5p, miR-25-3p, miR-143-3p, miR-363-3p and miR-338-3p in the sample; wherein differential or unchanged expression level of said miRNA in the sample, as compared to a control, determines the subject is suffering from, or is at risk of developing breast cancer. In one example, the present disclosure refers to a method of determining if a subject is suffering from or is at the risk of developing breast cancer, the method comprising: receiving a sample that is to be obtained from a subject thought to be suffering from or at the risk of developing breast cancer; measuring the expression level of at least two or more miRNAs selected from the group consisting of

miR-451a, miR-195-5p, miR-126-5p, miR-423-3p, miR-192-5p, miR-17-5p, miR-125b-5p, miR-660-5p, miR-25-3p, miR-143-3p, miR-363-3p and miR-338-3p in the sample; wherein differential or unchanged expression level of said miRNA in the sample, as compared to a control, determines the subject is suffering from, or is at risk of developing breast cancer.

[0004] In another aspect, the present disclosure refers to a use of an anti-breast cancer compound in the manufacture of a medicament for treating breast cancer, wherein the use comprises: measuring in a sample obtained from a subject thought to be suffering from or being at the risk of developing breast cancer the expression level of at least two or more miRNAs selected from the group consisting of miR-451a, miR-195-5p, miR-126-5p, miR-423-3p, miR-192-5p, miR-17-5p, miR-125b-5p, miR-660-5p, miR-25-3p, miR-143-3p, miR-363-3p and miR-338-3p in the sample, wherein differential or unchanged expression level of said miRNA in the sample, as compared to a control, determines the subject is suffering from, or is at risk of developing breast cancer; and wherein the subject determined to be suffering from, or is at risk of developing breast cancer is to be treated with the anti-breast cancer compound. In another example, the present disclosure refers to the use of an anti-breast cancer compound in the manufacture of a medicament for treating breast cancer, wherein the use comprises: measuring in a sample obtained from a subject thought to be suffering from or being at the risk of developing breast cancer the expression level of at least two or more miRNAs selected from the group consisting of miR-451a, miR-195-5p, miR-126-5p, miR-423-3p, miR-192-5p, miR-17-5p, miR-125b-

CLAIMS

What is claimed is:

1. A method of determining if a subject is suffering from or is at the risk of developing breast cancer, the method comprising:

measuring in a sample obtained from a subject thought to be suffering from or being at the risk of developing breast cancer the expression level of at least two or more miRNAs selected from the group consisting of miR-451a, miR-195-5p, miR-126-5p, miR-423-3p, miR-192-5p, miR-17-5p, miR-125b-5p, miR-660-5p, miR-25-3p, miR-143-3p, miR-363-3p and miR-338-3p in the sample;

wherein differential or unchanged expression level of said miRNA in the sample, as compared to a control, determines the subject is suffering from, or is at risk of developing breast cancer.

2. Use of an anti-breast cancer compound in the manufacture of a medicament for treating breast cancer, wherein the use comprises:

measuring in a sample obtained from a subject thought to be suffering from or being at the risk of developing breast cancer the expression level of at least two or more miRNAs selected from the group consisting of miR-451a, miR-195-5p, miR-126-5p, miR-423-3p, miR-192-5p, miR-17-5p, miR-125b-5p, miR-660-5p, miR-25-3p, miR-143-3p, miR-363-3p and miR-338-3p in the sample,

wherein differential or unchanged expression level of said miRNA in the sample, as compared to a control, determines the subject is suffering from, or is at risk of developing breast cancer; and

wherein the subject determined to be suffering from, or is at risk of developing breast cancer is to be treated with the anti-breast cancer compound.

3. The method of claim 1, or the use of claim 2, further comprises measuring at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, or 12 miRNAs.

4. The method of claim 1, or the use of claim 2, wherein the two or more miRNAs comprise or consist of miR-451a, miR-195-5p, miR-125b-5p, miR-660-5p, miR-25-3p, miR-143-3p, miR-363-3p, and miR-338-3p.

5. The method or use of any one of the preceding claims, wherein the two or more miRNAs comprise or consist of miR-451a, miR-195-5p, miR-126-5p, miR-423-3p, miR-192-5p, and miR-17-5p.

6. The method or use of any one of the preceding claims, wherein, if present, the following miRNAs are upregulated: miR-451a, miR-195-5p, miR-125b-5p, miR-126-5p, miR-660-5p, miR-25-3p, miR-143-3p, and miR-363-3p.

7. The method or use of any one of the preceding claims, wherein, if present, miR-338-3p is downregulated.

8. The method or use of any one of the preceding claims, wherein, if present, the following miRNAs are unchanged: miR-423-3p, miR-192-5p, and miR-17-5p.

9. A method for determining whether a breast lesion in a subject is malignant or benign, the method comprising:

measuring the expression level of at least two or more miRNA selected from the group consisting of miR-451a, miR-195-5p, miR-126-5p, miR-423-3p, miR-192-5p, miR-17-5p, miR-125b-5p, miR-660-5p, miR-25-3p, miR-143-3p, miR-363-3p and miR-338-3p in a sample that is to be obtained from the subject,

wherein differential expression or unchanged miRNA expression level of said miRNAs in the sample, as compared to a control, determines the lesion is benign or malignant.

10. The method of claim 9, wherein the method comprises measuring at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, or 12 miRNAs.

11. The method of claims 9 or 10, wherein the at least two or more miRNAs comprise or consist of miR-451a, miR-195-5p, miR-125b-5p, miR-660-5p, miR-25-3p, miR-143-3p, miR-363-3p, and miR-338-3p.

12. The method of any one of claims 9-11, wherein the at least two or more miRNAs comprise or consist of miR-451a, miR-195-5p, miR-126-5p, miR-423-3p, miR-192-5p, and miR-17-5p.

13. The method of any one of the claims 9-12, wherein, if present, the following miRNA are upregulated: miR-451a, miR-195-5p, miR-125b-5p, miR-126-5p, miR-660-5p, miR-25-3p, miR-143-3p, and miR-363-3p.

14. The method of any one of claims 9-13, wherein, if present, miR-338-3p is downregulated.

15. The method of any one of claims 9-14, wherein, if present, the following miRNA are unchanged: miR-423-3p, miR-192-5p, and miR-17-5p.

16. The method or use according to any one of the preceding claims, wherein the control is a cancer-free subject.

17. The method or use according to any one of the preceding claims, wherein the control is a subject with benign breast lesions.

18. The method or use according to any one of claims 1-16, wherein the control is a subject with normal mammogram results.

19. The method or use of any one the preceding claims, wherein the expression level of the miRNA is any one of concentration, log(concentration), Ct value, Ct/Cq value, or two to the power of Ct/Cq value.

20. The method or use of any one of the preceding claims, wherein expression level of the miRNA is determined by Real-Time Quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR).

21. The method or use of any one of the preceding claims, wherein the sample is a tissue sample or bodily fluid sample.

22. The method or use of claim 21, wherein the bodily fluid is selected from the group consisting of cellular and non-cellular components of a liquid biopsy, amniotic fluid, bronchial lavage, cerebrospinal fluid, interstitial fluid, peritoneal fluids, pleural fluid, saliva, seminal fluid, urine, tears, peripheral blood, whole blood, plasma, and serum.

23. The method or use of any one of the preceding claims, wherein the subject has had an abnormal mammogram result.

24. The method or use of any one of claims 9-23, wherein the method or use includes a step of obtaining a predictive score based on the miRNA selected a mathematical model selected from linear model, logistic regression, support vector machine algorithm, logistic regression algorithm, multinomial logistic regression algorithm, Fisher's linear discriminant algorithm, quadratic classifier algorithm, perceptron algorithm, k-nearest neighbours algorithm, artificial neural network algorithm, random forests algorithm, decision tree algorithm, naive Bayes algorithm, adaptive Bayes network algorithm, and ensemble learning method combining multiple learning algorithms.

25. A kit comprising a combination of primers suitable for detecting the two or more miRNA as defined in the method or use of any one of claims 1 to 24.