Claims

1. An in vitro screening method for assessing whether a subject is at risk to develop or is suffering from ovarian cancer, comprising:

assaying a sample from said subject to determine a concentration of at least one small molecule biomarker, wherein an increase in the concentration of the at least one small molecule biomarker in said sample, when compared to a control sample, is indicative of said subject suffering from or having an increased risk of developing ovarian cancer;

(1) wherein the at least one small molecule biomarker whose increase in concentration is compared to the control is a dihydroxybutyric acid and/or a trihydroxybutyric acid.

2. The method of claim 1, further comprising assaying said sample to determine a concentration of at least one additional small molecule biomarker wherein an increase in concentration of said at least one additional biomarker, when compared to a control sample, is indicative of said subject suffering from or having an increased risk of developing ovarian cancer;

(a) wherein the at least one additional small molecule biomarker whose increase in concentration is compared to the control is a hydroxyacid and/or an adipic acid; and/or

(b) wherein the at least one additional small molecule biomarker whose increase in concentration is compared to the control is a hydroxybutyric acid and/or ketone bodies.

3. The method of claim 2, wherein the assaying step comprises determining the concentration of:

the dihydroxybutyric acid or the trihydroxybutyric acid;

the hydroxyacid or the adipic acid; and/or

the hydroxybutyric acid or ketone bodies.

4. The method of any one of claims 1-3, further comprising measuring a level of one or more of CA-125 and/or HE4 in the sample from the subject, wherein an increased level of one or more of CA-125 and/or HE4 is indicative of the subject having an increased risk of developing or suffering from ovarian cancer when the screening method of any one of claims 1-3 shows increased risk of developing or suffering from ovarian cancer.

5. A method of assessing whether a subject has a decreased survival prognosis for ovarian cancer, comprising:

measuring the level of at least one small molecule biomarker in a sample from the subject, wherein an increase in the level of the at least one small molecule biomarker, relative to the level of the corresponding small molecule biomarker in a control sample, is indicative that the subject has a poor survival prognosis for the ovarian cancer, and wherein the at least one small molecule biomarker is a dihydroxybutyric acid or a trihydroxybutyric acid.

6. An in vitro method for assessing success rate of an ovarian cancer tumor removal in a subject, comprising measuring a concentration of at least one small molecule biomarker in a sample from the subject, wherein a decrease in the concentration of the at least one small molecule biomarker, relative to the concentration of the corresponding small molecule biomarker in a control sample, is indicative that the tumor removal was successful, and

(1) wherein the at least one small molecule biomarker whose decrease in concentration is compared to the control is a dihydroxybutyric acid and/or a trihydroxybutyric acid.

7. The method of claim 6, further comprising measuring a concentration of at least one additional small molecule biomarker from said sample, wherein a decrease in the concentration of said at least one additional small molecule biomarker, when compared to a control sample, is indicative that the tumor removal was successful;

(a) wherein the at least one additional small molecule biomarker whose decrease in concentration is compared to the control is a hydroxyacid and/or an adipic acid; and/or

(b) wherein the at least one additional small molecule biomarker whose decrease in concentration is compared to the control is a hydroxybutyric acid and/or ketone bodies.

8. The method of claim 7, wherein the measuring step comprises determining the level of:

the dihydroxybutyric acid or the trihydroxybutyric acid; and

the hydroxyacid or the adipic acid; and/or

hydroxybutyric acid or ketone bodies.

9. An in vitro method of evaluating effectiveness of an ovarian cancer therapy in a subject, comprising:

assaying a sample from said subject to determine a concentration of at least one first small molecule biomarker and/or a concentration of at least one second small molecule biomarker, wherein a decrease in concentration of the at least one first small molecule biomarker and/or second small molecule biomarker in said sample, when compared to a control sample, is indicative of effectiveness of said ovarian cancer therapy;

(1) wherein the at least one first small molecule biomarker whose concentration is compared to the control is a dihydroxybutyric and/or a trihydroxybutyric acid; and

(a) wherein the at least one second small molecule biomarker whose concentration is compared to the control is a dihydroxyacid and/or an adipic acid; and/or

(b) wherein the at least one second small molecule biomarker whose concentration is compared to the control is a hydroxybutyric acid and/or ketone bodies;

and wherein said increase in at least one of (1), (a), and (b) is indicative of ineffective treatment; and/or

decrease in at least one of (1), (a), and (b) is indicative of effective treatment.

10. The method of claim 9, wherein the ovarian cancer therapy comprises administering a pharmaceutical agent affecting lipid metabolism.

11. An in vitro method of determining concentration of a metabolite in ovarian tissue of a subject, comprising:

assaying a blood sample obtained from the subject to determine a concentration of the metabolite; comparing the concentration of the metabolite with a concentration in a control sample wherein an increase in a level of the metabolite compared to the control sample is indicative that the subject has increased concentration of the metabolite in ovarian tissue; and wherein the metabolite is 3,4-dihydroxybutyric acid, 2,4-dihydroxybutyric acid, and/or 2,3-dihydroxybutyric acid.

12. The method of any one of claims 1-11, wherein the method comprises determining the concentration of 2, 3, 4, 5, 6, 7, 8, 9, 10 or more small molecule biomarkers.

13. The method of any one of claims 1-12, wherein the biomarker concentration is determined by using mass spectrometry, nuclear magnetic resonance spectroscopy, fluorescence spectroscopy or dual polarisation interferometry, an immunoassay, enzymatic assay, colorimetric assay, fluorometric assay, a rapid test, a breath test and/or with a binding moiety capable of specifically binding the biomarker.

14. The method of any one of claims 1-10, 12 or 13, wherein the at least one small molecule biomarker whose increase in concentration is compared to the control is the dihydroxybutyric acid and/or trihydroxybutyric acid, and the dihydroxybutyric acid is 2,4-dihydroxybutyric acid, 3,4-dihydroxybutyric acid, and/or 2,3-dihydroxybutyric acid, and/or the trihydroxybutyric acid is 2,3,4-trihydroxybutyric acid.

15. The method of any one of claims 1-14, wherein the ovarian cancer is early stage ovarian cancer.

16. The method of claim 2, wherein the at least one additional small molecule biomarker whose increase in concentration is compared to the control is the hydroxyacid or ketone bodies, wherein the hydroxyacid is 4-hydroxyphenyllactic acid and/or 3-hydroxyisovaleric acid, and wherein the ketone bodies are acetone or acetoacetic acid.

17. The method of claim 2, wherein the at least one additional small molecule biomarker whose increase in concentration is compared to the control is the hydroxybutyric acid, wherein the hydroxybutyric acid is 3-hydroxybutyric acid and/or 2-hydroxybutyric acid.

18. The method of claim 1, further comprising assaying said sample to determine a concentration of at least one additional small molecule biomarker, wherein an increase or decrease in concentration of said at least one additional biomarker, when compared to a control sample, is indicative of said subject suffering from or having an increased risk of developing ovarian cancer;

(a) wherein the at least one additional small molecule biomarker whose decrease in concentration is compared to the control is a sphingomyelin;

(b) wherein the at least one additional small molecule biomarker whose increase in concentration is compared to the control is a long chain triglyceride having acyl side chains comprising at least 54 carbon atoms in total; and/or

(c) wherein the at least one additional small molecule biomarker whose decrease in concentration is compared to the control is a triglyceride having acyl side chains comprising less than 54 carbon atoms in total.

19. The method of claim 5, further comprising assaying said sample to determine a concentration of at least one additional small molecule biomarker, wherein an increase or decrease in the concentration of said at least one additional biomarker, when compared to a control sample, is indicative of said subject having a poor survival prognosis for ovarian cancer, and

(a) wherein the at least one additional small molecule biomarker whose increase in concentration is compared to the control is a hydroxyacid, an adipic acid, a hydroxybutyric acid, and/or ketone bodies;

(b) wherein the at least one additional small molecule biomarker whose decrease in concentration is compared to the control is a sphingomyelin.

20. The method of claim 6, further comprising assaying said sample to determine a concentration of at least one additional small molecule biomarker, wherein an increase or decrease in the concentration of said at least one additional biomarker, when compared to a control sample, is indicative that the tumor removal was successful;

(a) wherein the at least one additional small molecule biomarker whose increase in concentration is compared to the control is a sphingomyelin;

(b) wherein the at least one additional small molecule biomarker whose decrease in concentration is compared to the control is a long chain triglyceride having acyl side chains comprising at least 54 carbon atoms in total; and/or

(c) wherein the at least one additional small molecule biomarker whose increase in concentration is compared to the control is a triglyceride having acyl side chains comprising less than 54 carbon atoms in total.

21. The method of claim 9, further comprising assaying said sample to determine a concentration of at least one additional small molecule biomarker, wherein an increase or decrease in the concentration of said at least one additional biomarker, when compared to a control sample, is indicative of effectiveness of said ovarian cancer therapy;

(a) wherein the at least one additional small molecule biomarker whose concentration is compared to the control is a sphingomyelin;

(b) wherein the at least one additional small molecule biomarker whose concentration is compared to the control is a long chain triglyceride having acyl side chains comprising at least 54 carbon atoms in total; and/or

(c) wherein the at least one additional small molecule biomarker whose concentration is compared to the control is a triglyceride having acyl side chains comprising less than 54 carbon atoms in total;

and wherein said decrease in at least one of (a) and (c), or said increase in (b) is indicative of ineffective treatment; and/or said increase in at least one of (a) and (c), or said decrease in (b) is indicative of effective treatment.

22. The method of claim 11, further comprising assaying said sample to determine a concentration of at least one additional metabolite, wherein the at least one additional metabolite is 3-hydroxybutyric acid, 2-hydroxybutyric acid, SM(d18:1/21:0), SM(d18:1/14:0), adipic acid, 4-hydroxyphenyllactic acid and/or 3-hydroxyisovaleric acid.