Claims

What is claimed is:

1. A method of estimating de novo lipogenesis in a subject comprising:

measuring in vitro the levels of two or more fatty acid biomarkers in a biological sample wherein the two or more fatty acid biomarkers are selected from the group consisting of the total level of myristic acid (14:0), the total level of myristoleic acid (14:1n5), the total level of palmitate (16:0), the total level of palmitoleate (16:1n7), the total level of sapienic acid (16:1n10), the total level of 18:1n10, the total level of squalene, the total level of 6-octadecenoic acid (18:1n12), the total level of linoleate (18:2n6), the total level of arachidonic acid (20:4n6), the total level of docosaheaenoic acid (22:6n3), the level of myristic acid (14:0) in one or more lipid class, the level of myristoleic acid (14:1n5) in one or more lipid class, the level of palmitate (16:0) in one or more lipid class, the level of palmitoleate (16:1n7) in one or more lipid class, the level of sapienic acid (16:1n10) in one or more lipid class, the level of 18:1n10 in one or more lipid class, the level of squalene in one or more lipid class, the level of 18:1n12 in one or more lipid class, the level of linoleate (18:2n6) in one or more lipid class, the level of arachidonic acid (20:4n6) in one or more lipid class, and the level of docosaheaenoic acid (22:6n3) in one or more lipid class in a sample collected from a subject; and

using a statistical model comprised of the measured levels of the two or more fatty acid biomarkers to generate a de novo lipogenesis index score to estimate the de novo lipogenesis in the subject.

2. The method of claim 1, wherein the fatty acid biomarkers comprise the total levels of palmitate (16:0), palmitoleate (16:1n7) and linoleate (18:2n6) in blood.

3. The method of claim 2, wherein the fatty acid biomarkers further comprise the total levels of myristic acid (14:0), and (14:1n5) in blood.

4. The method of claim 3, wherein the fatty acid biomarkers further comprise the total levels of arachidonic acid (20:4n6) and docosaheaenoic acid (22:6n3) in blood.

5. The method of claim 1, wherein the biological sample is selected from the group consisting of a sebum sample, a skin sample, an epidermal sample, and a skin cell sample and wherein the two or more biomarkers are selected from the group consisting of 16:0, 16:1n7, 16:1n10, 18:1n10, 18:1n12, 14:0, 14:1n5, 18:2n6, 20:4n6, squalene, and 22:6n3 and combinations thereof.

6. The method of claim 1, wherein the fatty acid biomarkers are measured in one or more individual lipid classes selected from the group consisting of triacylglycerides, phosphatidylcholine, and cholesteryl esters.

7. The method of claim 4, wherein the fatty acid biomarkers are measured after separating the fatty acids from their backbone.

8. The method of claim 4, wherein the fatty acid biomarkers are measured as an intact complex lipid species.

9. The method of claim 1, wherein the fatty acid biomarkers are measured in total blood lipids.

10. The method of claim 1, wherein the fatty acid biomarkers are expressed as a proportion of total fatty acids.

11. The method of claim 10, wherein the proportion is in mole%.

12. The method of claim 1, wherein the mathematical model is a linear combination of the measured level of each biomarker in the model whereby positive markers have positive coefficients and negative markers have negative coefficients.

13. The method of claim 1, wherein the mathematical model comprises a ratio of a positive marker to a negative marker.

14. The method of claim 13, wherein the ratio consists of the sum of positive markers to the sum of negative markers.

15. The method of claim 1, wherein the de novo lipogenesis index score is calculated by using one of the following models:

(i) DNL= a(16:0) + b(16:1n7) - c(18:2n6)

(ii) DNL = (a(16:0) + b(16:1n7)) / c(18:2n6)

(iii) DNL = a(16:0) + b(16:1n7) - c(18:2n6) + d(14:0) + e(14:1n5)

(iv) DNL = a(16:0) + b(16:1n7) - c(18:2n6) + d(14:0) + e(14:1n5)-f(20:4n6) – g(22:6n3)

(v) DNL = a(16:0) + b(16:1n10) - c(18:2n6), or

(vi) DNL = a(16:0) + b(16:1n10) - c(squalene),

wherein a, b, c, d, e, f, g, are constant numbers; (16:0), (16:1n7), 18:2n6), (14:0), (14:1n5), (20:4n6), (22:6n3), (16:1n10) and squalene, which are measured values of the biomarker analyte; and DNL is the predicted de novo lipogenesis index score.

16. A method of assessing the disease status of an individual having a disease by using a ~~DNL~~ de novo lipogenesis index score~~Score~~, the method comprising

measuring in vitro the levels of one or more fatty acid biomarkers in a biological sample in a sample collected from a subject: and

using a statistical model comprised of the measured levels of the one or more fatty acid biomarkers to generate a de novo lipogenesis index score for use in assessing the disease status of the individual.

17. The method of claim 16, wherein the disease is diabetes.

18. The method of claim 16, wherein the disease is a diabetic process selected from the group consisting of hepatic steatosis and insulin sensitivity.

19. A method of assessing liver health of an individual having liver impairment using a ~~DNL~~ de novo lipogenesis index ~~Score~~score, the method comprising

measuring in vitro the levels of one or more fatty acid biomarkers in a biological sample in a sample collected from a subject: and

using a statistical model comprised of the measured levels of the one or more fatty acid biomarkers to generate a de novo lipogenesis index score for use in assessing liver health of the individual.

20. The method of claim 19, wherein the liver impairment is selected from the group consisting of steatosis and hepatic insulin resistance.

21. ~~A~~ The method of claim 15, wherein the de novo lipogenesis index score is used for staging hepatic disorders ~~using a DNL Score as described herein~~.

22. The method of claim 21, wherein the hepatic disorder is selected from the group consisting of NASH and NAFLD.

23. ~~A~~ The method of claim 1, wherein the de novo lipogenesis index score is used to predict~~ing~~ a progression of weight gain from normal to obesity ~~as described herein~~.

24. ~~A~~ The method of claim 1, wherein the de novo lipogenesis index score is used to monitor~~ing~~ the response to a therapeutic agent on de novo lipogenesis and associated disease conditions ~~as described herein~~.

25. The method of claim 24, wherein the therapeutic agent is a small molecule inhibitor.

26. ~~A~~ The method of claim 1, wherein the de novo lipogenesis index score is used to ~~determining~~ determine the efficacy of a therapeutic agent to inhibit de novo lipogenesis ~~as described herein~~.

27. The method of claim 26, wherein the therapeutic agent is selected from the group consisting of acetyl-CoA carboxylase (ACC), fatty acid synthase (FAS), stearoyl-CoA desaturase (SCD), elongates (ELOVL), and diacylglycerol:CoA acyltransferase (DGAT) inhibitors.

~~28. Methods related to de novo lipogenesis as described herein.~~

29. The method of claim 1, wherein the sebum de novo lipogenesis index score is calculated by using one of the following models:

(i) Sebum DNL1 = ~~0.0398~~a(16:0) + ~~0.0455~~b(16:1n10) – ~~1.398~~c(18:2n6), or

(ii) Sebum DNL2 = ~~0.0398~~a(16:0) + ~~0.0455~~b(16:1n10) – ~~0.0113~~c(squalene),

wherein a, b, c are constant numbers, wherein (16:0), (16:1n10), (18:2n6) and squalene are measured values of said biomarker analyte~~.~~; and wherein DNL is the predicted sebum de novo lipogenesis index score.

~~30. A method of estimating de novo lipogenesis in a subject comprising:~~

~~measuring the level(s) of one or more fatty acid biomarkers in a biological sample wherein the one or more fatty acid biomarkers are selected from the group consisting of the total level of myristic acid (14:0), the total level of myristoleic acid (14:1n5), the total level of palmitate (16:0), the total level of palmitoleate (16:1n7), the total level of sapienic acid (16:1n10), the total level of 18:1n10, the total level of~~

~~squalene, the total level of 6-octadecenoic acid (18:1n12), the total level of linoleate~~ (18:2n6), the total level of arachidonic acid (20:4n6), the total level of docosaheaenoic acid (22:6n3), the level of myristic acid (14:0) in one or more lipid class, the level of myristoleic acid (14:1n5) in one or more lipid class, the level of palmitate (16:0) in one or more lipid class, the level of palmitoleate (16:1n7) in one or more lipid class, the level of sapienic acid (16:1n10) in one or more lipid class, the level of 18:1n10 in one or more lipid class, the level of squalene in one or more lipid class, the level of 18:1n12 in one or more lipid class, the level of linoleate (18:2n6) in one or more lipid class, the level of arachidonic acid (20:4n6) in one or more lipid class, and the level of docosaheaenoic acid (22:6n3) in one or more lipid class in a sample collected from a subject; and

using a statistical model comprised of the measured levels of the one or more fatty acid biomarkers to generate a de novo lipogenesis index to estimate the de novo lipogenesis in the subject.

31. The method of claim 30, wherein the fatty acid biomarkers comprise the total levels of palmitate (16:0), palmitoleate (16:1n7) and linoleate (18:2n6) in blood.

32. The method of claim 31, wherein the fatty acid biomarkers further comprise the total levels of myristic acid (14:0), and (14:1n5) in blood.

33. The method of claim 32, wherein the fatty acid biomarkers further comprise the total levels of arachidonic acid (20:4n6) and docosaheaenoic acid (22:6n3) in blood.

34. The method of claim 30, wherein the biological sample is selected from the group consisting of a skin sample, an epidermal sample, and a skin cell sample and wherein the one or more biomarkers are selected from the group consisting of 16:0, 16:1n7, 16:1n10, 18:1n10, 18:1n12, 14:0, 14:1n5, 18:2n6, 20:4n6, squalene, and 22:6n3 and combinations thereof.

35. The method of claim 30, wherein the fatty acid biomarkers are measured in one or more individual lipid classes selected from the group consisting of triacylglycerides, phosphatidylcholine, and cholesteryl esters.

~~36. The method of claim 35, wherein the fatty acid biomarkers are measured after~~ separating the fatty acids from their backbone.

37. The method of claim 35, wherein the fatty acid biomarkers are measured as an intact complex lipid species.

38. The method of claim 30, wherein the fatty acid biomarkers are measured in total blood lipids.

39. The method of claim 30, wherein the fatty acid biomarkers are expressed as a proportion of total fatty acids.

40. The method of claim 39, wherein the proportion is in mole %.

41. The method of claim 30, wherein the mathematical model is a linear combination of the measured level of each biomarker in the model whereby positive markers have positive coefficients and negative markers have negative coefficients.

42. The method of claim 30, wherein the mathematical model comprises a ratio of a positive marker to a negative marker.

43. The method of claim 42, wherein the ratio consists of the sum of positive markers to the sum of negative markers.

44. The method of claim 30, wherein the de novo lipogenesis index score is calculated by using one of the following models:

(i) DNL= a(16:0) + b(16:1n7) - c(18:2n6), or

(ii) DNL = (a(16:0) + b(16:1n7)) / c(18:2n6)

(iii) DNL = a(16:0) + b(16:1n7) - c(18:2n6) + d(14:0) + e(14:1n5)

(iv) DNL = a(16:0) + b(16:1n7) - c(18:2n6) + d(14:0) + e(14:1n5)-f(20:4n6) – g(22:6n3)

(v) DNL = a(16:0) + b(16:1n10) - c(18:2n6), or

~~(vi) DNL = a(16:0) + b(16:1n10) - c(squalene) wherein a, b, c, d, e, f, g, are~~ constant numbers; (16:0), (16:1n7), 18:2n6), (14:0), (14:1n5), (20:4n6), (22:6n3), (16:1n10) and squalene, are measured values of the biomarker analyte; and DNL is the predicted de novo lipogenesis index score..

45. The method of claim 30, wherein the sebum de novo lipogenesis index score is calculated by using one of the following models:

(i) Sebum DNL1 = 0.0398(16:0) + 0.0455(16:1n10) – 1.398(18:2n6), or

(ii) Sebum DNL2 = 0.0398(16:0) + 0.0455(16:1n10) – 0.0113(squalene)

wherein (16:0), (16:1n10), (18:2n6) and squalene are the measured values of said biomarker analyte.

Claims

What is claimed is:

1. A method of estimating de novo lipogenesis in a subject comprising:

measuring in vitro the levels of two or more fatty acid biomarkers in a biological sample wherein the two or more fatty acid biomarkers are selected from the group consisting of the total level of myristic acid (14:0), the total level of myristoleic acid (14:1n5), the total level of palmitate (16:0), the total level of palmitoleate (16:1n7), the total level of sapienic acid (16:1n10), the total level of 18:1n10, the total level of squalene, the total level of 6-octadecenoic acid (18:1n12), the total level of linoleate (18:2n6), the total level of arachidonic acid (20:4n6), the total level of docosaheaenoic acid (22:6n3), the level of myristic acid (14:0) in one or more lipid class, the level of myristoleic acid (14:1n5) in one or more lipid class, the level of palmitate (16:0) in one or more lipid class, the level of palmitoleate (16:1n7) in one or more lipid class, the level of sapienic acid (16:1n10) in one or more lipid class, the level of 18:1n10 in one or more lipid class, the level of squalene in one or more lipid class, the level of 18:1n12 in one or more lipid class, the level of linoleate (18:2n6) in one or more lipid class, the level of arachidonic acid (20:4n6) in one or more lipid class, and the level of docosaheaenoic acid (22:6n3) in one or more lipid class in a sample collected from a subject; and

using a statistical model comprised of the measured levels of the two or more fatty acid biomarkers to generate a de novo lipogenesis index score to estimate the de novo lipogenesis in the subject.

2. The method of claim 1, wherein the fatty acid biomarkers comprise the total levels of palmitate (16:0), palmitoleate (16:1n7) and linoleate (18:2n6) in blood.

3. The method of claim 2, wherein the fatty acid biomarkers further comprise the total levels of myristic acid (14:0), and (14:1n5) in blood.

4. The method of claim 3, wherein the fatty acid biomarkers further comprise the total levels of arachidonic acid (20:4n6) and docosaheaenoic acid (22:6n3) in blood.

5. The method of claim 1, wherein the biological sample is selected from the group consisting of a sebum sample, a skin sample, an epidermal sample, and a skin cell sample and wherein the two or more biomarkers are selected from the group consisting of 16:0, 16:1n7, 16:1n10, 18:1n10, 18:1n12, 14:0, 14:1n5, 18:2n6, 20:4n6, squalene, and 22:6n3 and combinations thereof.

6. The method of claim 1, wherein the fatty acid biomarkers are measured in one or more individual lipid classes selected from the group consisting of triacylglycerides, phosphatidylcholine, and cholesteryl esters.

7. The method of claim 4, wherein the fatty acid biomarkers are measured after separating the fatty acids from their backbone.

8. The method of claim 4, wherein the fatty acid biomarkers are measured as an intact complex lipid species.

9. The method of claim 1, wherein the fatty acid biomarkers are measured in total blood lipids.

10. The method of claim 1, wherein the fatty acid biomarkers are expressed as a proportion of total fatty acids.

11. The method of claim 10, wherein the proportion is in mole%.

12. The method of claim 1, wherein the mathematical model is a linear combination of the measured level of each biomarker in the model whereby positive markers have positive coefficients and negative markers have negative coefficients.

13. The method of claim 1, wherein the mathematical model comprises a ratio of a positive marker to a negative marker.

14. The method of claim 13, wherein the ratio consists of the sum of positive markers to the sum of negative markers.

15. The method of claim 1, wherein the de novo lipogenesis index score is calculated by using one of the following models:

(i) DNL= a(16:0) + b(16:1n7) - c(18:2n6)

(ii) DNL = (a(16:0) + b(16:1n7)) / c(18:2n6)

(iii) DNL = a(16:0) + b(16:1n7) - c(18:2n6) + d(14:0) + e(14:1n5)

(iv) DNL = a(16:0) + b(16:1n7) - c(18:2n6) + d(14:0) + e(14:1n5)-f(20:4n6) – g(22:6n3)

(v) DNL = a(16:0) + b(16:1n10) - c(18:2n6), or

(vi) DNL = a(16:0) + b(16:1n10) - c(squalene),

wherein a, b, c, d, e, f, g, are constant numbers; (16:0), (16:1n7), 18:2n6), (14:0), (14:1n5), (20:4n6), (22:6n3), (16:1n10) and squalene, which are measured values of the biomarker analyte; and DNL is the predicted de novo lipogenesis index score.

16. A method of assessing the disease status of an individual having a disease by using a de novo lipogenesis index score, the method comprising

measuring in vitro the levels of one or more fatty acid biomarkers in a biological sample in a sample collected from a subject; and

using a statistical model comprised of the measured levels of the one or more fatty acid biomarkers to generate a de novo lipogenesis index score for use in assessing the disease status of the individual.

17. The method of claim 16, wherein the disease is diabetes.

18. The method of claim 16, wherein the disease is a diabetic process selected from the group consisting of hepatic steatosis and insulin sensitivity.

19. A method of assessing liver health of an individual having liver impairment using a de novo lipogenesis index score, the method comprising

measuring in vitro the levels of one or more fatty acid biomarkers in a biological sample in a sample collected from a subject; and

using a statistical model comprised of the measured levels of the one or more fatty acid biomarkers to generate a de novo lipogenesis index score for use in assessing liver health of the individual.

20. The method of claim 19, wherein the liver impairment is selected from the group consisting of steatosis and hepatic insulin resistance.

21. The method of claim 15, wherein the de novo lipogenesis index score is used for staging hepatic disorders.

22. The method of claim 21, wherein the hepatic disorder is selected from the group consisting of NASH and NAFLD.

23. The method of claim 1, wherein the de novo lipogenesis index score is used to predict a progression of weight gain from normal to obesity.

24. The method of claim 1, wherein the de novo lipogenesis index score is used to monitor the response to a therapeutic agent on de novo lipogenesis and associated disease conditions.

25. The method of claim 24, wherein the therapeutic agent is a small molecule inhibitor.

26. The method of claim 1, wherein the de novo lipogenesis index score is used to determine the efficacy of a therapeutic agent to inhibit de novo lipogenesis.

27. The method of claim 26, wherein the therapeutic agent is selected from the group consisting of acetyl-CoA carboxylase (ACC), fatty acid synthase (FAS), stearoyl-CoA desaturase (SCD), elongates (ELOVL), and diacylglycerol:CoA acyltransferase (DGAT) inhibitors.

29. The method of claim 1, wherein the sebum de novo lipogenesis index score is calculated by using one of the following models:

(i) Sebum DNL1 = a(16:0) + b(16:1n10) – c(18:2n6), or

(ii) Sebum DNL2 = a(16:0) + b(16:1n10) – c(squalene),

wherein a, b, c are constant numbers, wherein (16:0), (16:1n10), (18:2n6) and squalene are measured values of said biomarker analyte; and wherein DNL is the predicted sebum de novo lipogenesis index score.