

CLAIMS

1. A method of screening for a fetal trisomy in a pregnant female subject, the method comprising:
 - detecting one or more lipid markers from the subject, wherein the one or more lipid markers is indicative of the risk of a fetal trisomy in the subject; and
 - determining the risk of a fetal trisomy in the pregnant female subject on the basis of the one or more lipid markers detected.
2. The method according to claim 1, wherein the one or more markers is indicative of an increased risk of a fetal trisomy, a low or normal risk of a fetal trisomy, and/or the presence or absence of a fetal trisomy.
3. The method according to claims 1 or 2, wherein the fetal trisomy comprises trisomy 21.
4. The method according to any one of claims 1 to 3, wherein the one or more lipid markers have a size in the range from 200 to 2000 Daltons.
5. The method according to any one of claims 1 to 4, wherein the method comprises determination of the mass of the one or more lipid markers and/or one or more fragments and/or adducts of the one or more lipid markers.
6. The method according to any one of claims 1 to 5, wherein the one or more lipid markers comprise one or more of a phospholipid, a glycerolipid, a glycerophospholipid, a sphingolipid, a ceramide, a sterol, a glycosphingolipid, a dolicol, a lysolipid, a fatty acid, a triacylglyceride, a diacylglycerides, a monacylglycerides, an isoprenoid, a prostanoid, an eicosanoid, a sterol derivatives, a prenol lipid, a saccharolipid, a saturated fatty acid, a long chain saturated fatty acid, an unsaturated fatty acid, a polyunsaturated fatty acid, a long chain polyunsaturated fatty acid, a cholesterol and isomers thereof, a dehydrocholesterol and isomers thereof, a cholesterol esters and isomers thereof, a dehydrocholesterol esters and isomers thereof, a lyso derivative of any of the aforementioned lipid markers, and/or a fragment of any of the aforementioned lipid markers.

7. The method according to any one of claims 1 to 6, wherein the one or more lipid markers comprise one or more phospholipids.
8. The method according to any one of claims 1 to 7, wherein the one or more lipid markers comprise one or more long chain fatty acid groups.
9. The method according to claim 8, wherein the one or more long chain fatty acid groups comprise a long chain polyunsaturated fatty acid group.
10. The method according to claims 8 or 9, wherein the one or more lipid markers comprise one or more long chain fatty acid groups with a chain length of 16 to 22 carbon atoms.
11. The method according to any one of claims 8 to 10, wherein the one or more lipid markers comprise two long chain fatty acid groups.
12. The method according to any one of claims 1 to 11, wherein the method comprises detecting the one or more lipid markers by mass spectrometry.
13. The method according to claim 12, wherein the one or more markers have a mass to charge ratio m/z of 1700 or less.
14. The method according to claims 12 or 13, wherein the one or more lipid markers comprise a lipid with one or more ions with the following assigned m/z : 703.5580, 369.3491, 367.3312, 680.5953, 687.5651, 445.3648, 445.3633, 727.5567, 429.3706, 1202.3250, 431.3875, 429.3726, 844.6007, 688.5950, 890.7703, 1276.3440, 711.5619, 1128.3140, 670.6080, and/or one or more of the aforementioned lipid markers with a mass tolerance of ± 20 ppm, and/or a substantially similar m/z and/or retention time.
15. The method according to claims 12 or 13, wherein the one or more lipid markers comprise a lipid with one or more ions with the following assigned m/z : 340.3576, 355.2511, 363.2531, 390.7783, 399.3453, 404.7929, 407.2269, 408.3136, 427.3771, 429.2121, 447.3448, 447.3460, 461.3620, 469.3597, 471.4063, 473.3184; 478.3545,

481.3239; 489.4134, 506.4412, 530.5135, 544.5071, 551.5172, 555.4646, 558.5448, 568.4784, 579.4305, 603.4949, 604.5660, 607.5640, 618.5444, 626.4976, 640.5345, 640.5699, 647.5577, 676.4879, 684.5594, 700.5542, 728.5875, 740.5176, 744.5807, 772.6135, 780.5458, 788.6118, 798.5637, 817.5510, 816.6401, 820.5947, 826.5947, 832.6303, 834.5978, 850.5523, 860.6632, 864.5363, 876.6591, 902.5855, 904.6889, 904.6932, 920.6888, 928.5873, 948.7143, 964.7115, 992.7408, 1008.7339, 1036.7696, 1052.7680, 1078.9686, 670.6080, and/or one or more of the aforementioned lipid markers with a mass tolerance of ± 20 ppm, and/or a substantially similar m/z .

16. The method according to any one of claims 12 to 15, wherein the one or more lipid markers comprise, for one or more of each of the assigned m/z and/or retention times, a cholesterol and isomers thereof, a dehydrocholesterol and isomers thereof, a cholesterol ester and isomers thereof and a dehydrocholesterol esters and isomers thereof.

17. The method according to any one of claims 12 to 16, wherein the method comprises using an isotopically labelled lipid as a reference marker to quantify relative amounts of the one or more lipid markers.

18. The method according to any one of claims 1 to 17, wherein the method comprises comparing one or more of the lipid markers with one or more following:

- (i) one or more markers known to be indicative of an increased risk of a fetal trisomy;
- (ii) one or more markers known to be indicative of a decreased risk of a fetal trisomy;
- (iii) one or more markers known to be indicative of the presence of a fetus with a fetal trisomy in a pregnant female subject;
- (ii) one or more markers known to be indicative of a fetus without a fetal trisomy in a pregnant female subject.

19. The method according to any one of claims 1 to 18, wherein the detecting of the one or more lipid markers comprises detecting the presence and/or level of the one or more lipid markers.

20. The method according to claim 19, wherein the level of the one or more markers is altered.
21. The method according to claim 20, wherein an increased level of one or more of the lipid markers is indicative of an increased risk of a fetal trisomy.
22. The method according to claims 20 or 21, wherein a decreased level of one or more of the lipid markers is indicative of an increased risk of a fetal trisomy.
23. The method according to any one of claims 20 to 22, wherein an increased level of one or more of the lipid markers is indicative of a decreased risk of a fetal trisomy.
24. The method according to any one of claims 20 to 23, wherein a decreased level of one or more of the lipid markers is indicative of a decreased risk of a fetal trisomy.
25. The method according to any one of claims 1 to 24, wherein the method comprises detecting the one or more lipid markers in the first trimester of pregnancy.
26. The method according to any one of claims 1 to 25, wherein the method comprises obtaining a biological sample from the subject.
27. The method according to claim 26, wherein the biological sample comprises one or more of blood, plasma and serum.
28. The method according to claims 26 or 27, wherein the method comprises processing the biological sample to allow detection of the one or more lipid markers in the biological sample.
29. The method according to any one of claims 26 to 28, wherein the method comprises exposing the biological sample, and/or a processed form, an extract, a derivative, a component or a fraction thereof to a substantially organic solvent and isolating the organic fraction.

30. The method according to claim 29, wherein an isotopically labelled lipid is added prior to and/or after extraction with an organic solvent.
31. The method according to claim 30, wherein the isotopically labelled lipid is an isotopically labelled form of a naturally occurring lipid.
32. The method according to any one of claims 1 to 31, wherein the one or more lipid markers comprise at least two markers.
33. The method according to any one of claims 1 to 32, wherein the method comprises using a computer processor means to process data associated with the presence and/or level of the one or more lipid markers to generate a likelihood and/or risk of the presence or absence of a fetal trisomy.
34. The method according to any one of claims 1 to 33, wherein the method is used to identify the presence or absence of a fetal trisomy, to identify a fetal trisomy in the subject, to exclude the presence of a fetal trisomy in the subject, to identify an increased risk of a fetal trisomy, and/or to identify a low or normal risk of a fetal trisomy.
35. A method of screening for a fetal trisomy in a pregnant female subject, the method comprising:
detecting one or more lipid markers from the subject, wherein the one or more lipid markers is indicative of the risk of a fetal trisomy in the subject; and
determining the presence or absence of a fetal trisomy in the pregnant female subject on the basis of the one or more lipid markers detected.
36. A method of screening for a fetal trisomy in a pregnant female subject, the method comprising:
processing a biological sample from the subject to allow detection of lipid markers;
detecting one or more lipid markers in the processed sample indicative of the risk of a fetal trisomy in the subject; and
determining the risk of a fetal trisomy in the pregnant female subject on the basis of the one or more lipid markers detected.

37. A method of screening for a fetal trisomy in a pregnant female subject, the method comprising:

- processing a biological sample from the subject to allow detection of lipid markers by mass spectrometry;
- detecting by mass spectrometry one or more lipid markers in the processed sample indicative of the risk of a fetal trisomy in the subject; and
- determining the risk of a fetal trisomy in the pregnant female subject on the basis of the one or more lipid markers detected.

38. A mass spectrographic method of screening for a fetal trisomy in a pregnant female subject, the method comprising:

- processing a biological sample from the subject to allow detection of lipid markers;
- detecting by mass spectrometry one or more lipid markers in the processed sample indicative of the risk of a fetal trisomy in the subject; and
- determining the risk of a fetal trisomy in the pregnant female subject on the basis of the one or more lipid markers detected.

39. A method of screening for a fetal trisomy in a pregnant female subject, the method comprising:

- detecting one or more lipid markers from the subject, wherein the one or more lipid markers is indicative of the risk of a fetal trisomy in the subject;
- using a computer processor means to process data associated with the presence and/or level of the one or more lipid markers detected to generate a likelihood and/or risk of the presence or absence of a fetal trisomy; and
- determining the risk of a fetal trisomy in the pregnant female subject on the basis of the likelihood and/or risk generated.

40. A computer-readable medium encoded with programming instructions executable by a computer processor means to allow the computer processor means to receive data associated with the presence and/or level of one or more lipid markers indicative of the risk of a fetal trisomy in a subject and process the data to generate a likelihood and/or risk of the presence or absence of a fetal trisomy in the subject.

41. A computer processor means comprising a computer-readable medium according to claim 40.

42. Use of a mass spectrometer to detect one or more lipid markers from a biological sample of a pregnant female subject, wherein the one or more lipid markers are indicative of the risk of a fetal trisomy in a pregnant female.

43. A method of identifying the presence or absence of a fetal trisomy in a pregnant female subject, the method comprising:

detecting one or more lipid markers from the subject, wherein the one or more lipid markers is indicative of risk of a fetal trisomy in the subject; and
identifying the presence or absence of a fetal trisomy in the pregnant female subject on the basis of the one or more lipid markers detected.

44. A method of identifying the presence or absence of a fetal trisomy in a pregnant female subject, the method comprising:

processing a biological sample from the subject to allow detection of lipid markers;
detecting one or more lipid markers in the processed sample indicative of the risk of a fetal trisomy in the subject; and
identifying the presence or absence of a fetal trisomy in the pregnant female subject on the basis of the one or more lipid markers detected.

45. A method of identifying the presence or absence of a fetal trisomy in a pregnant female subject, the method comprising:

processing a biological sample from the subject to allow detection of lipid markers by mass spectrometry;
detecting by mass spectrometry one or more lipid markers in the processed sample indicative of the risk of a fetal trisomy in the subject; and
identifying the presence or absence of a fetal trisomy in the pregnant female subject on the basis of the one or more lipid markers detected.

46. A mass spectrographic method of identifying the presence or absence of a fetal

trisomy in a pregnant female subject, the method comprising:

processing a biological sample from the subject to allow detection of lipid markers;
detecting one or more lipid markers in the processed sample indicative of the risk of a fetal trisomy in the subject; and
identifying the presence or absence of a fetal trisomy in the pregnant female subject on the basis of the one or more lipid markers detected.

47. A method of identifying the presence or absence of a fetal trisomy in a pregnant female subject, the method comprising:

detecting one or more lipid markers from the subject, wherein the one or more lipid markers is indicative of the risk of a fetal trisomy in the subject; and
using a computer processor means to process data associated with the presence and/or level of the one or more lipid markers to generate a likelihood and/or risk of the presence or absence of a fetal trisomy; and
identifying the presence or absence of a fetal trisomy in the pregnant female subject on the basis of the likelihood and/or risk generated.

48. A method of determining the risk of a pregnant female subject carrying a fetus with a trisomy, the method comprising:

detecting one or more lipid markers from the subject, wherein the one or more markers is indicative of the risk of a fetal trisomy in the subject; and
determining the risk of the subject carrying a fetus with a trisomy on the basis of the one or more lipid markers detected.

49. A method according to claim 48, wherein the determining of the risk comprises a computer processor means to process data associated with the presence and/or level of the one or more lipid markers.

50. The method according to claims 48 or 49, wherein the determining of the risk comprises a multiple of mean analysis of the one or more of lipid markers to determine a likelihood ratio for the risk.

51. A kit for performing the method of any one of claims 1 to 38 or 43 to 50.

52. A method of identifying one or more lipid markers indicative of the risk of a fetal trisomy, the method comprising:

identifying one or more lipid markers which are differentially present between a pregnant female subject having a fetal trisomy and a pregnant female subject without a fetal trisomy; and

identifying the one or more lipid markers as one or more lipid markers indicative of the risk of a fetal trisomy.

53. A method of identifying one or more lipid markers indicative of the presence or absence a fetal trisomy, the method comprising:

identifying one or more lipid markers which are differentially present between a pregnant female subject having a fetal trisomy and a pregnant female subject without a fetal trisomy; and

identifying the one or more lipid markers as one or more lipid markers indicative of the presence or absence of a fetal trisomy.

54. A method of identifying one or more lipid markers indicative of the risk of a fetal trisomy, the method comprising identifying a plurality of lipid markers which in combination are indicative of the risk of a fetal trisomy.