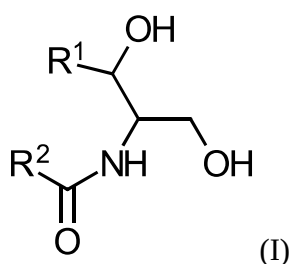


CLAIMS

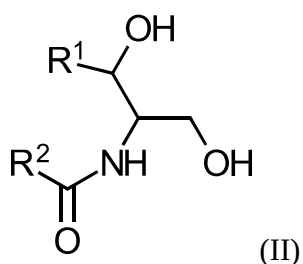
1. A method for determining whether a human subject is at risk to develop one or more cardiovascular (CV) complications, wherein the method comprises

(a) determining in a biological sample obtained from the human subject the concentration of at least one ceramide of Formula I:



wherein R^1 is a mono-unsaturated alkyl chain having 13 carbon atoms or a saturated, mono-unsaturated or di-unsaturated alkyl chain having 15 carbon atoms, and wherein R^2 is a saturated alkyl chain having 21-25 carbon atoms, and wherein the biological sample is a blood sample, blood serum sample, a blood plasma sample, or a lipoprotein fraction obtained therefrom;

(b) determining in the biological sample obtained from the human subject the concentration of at least one ceramide of Formula (II):



wherein R^1 is a linear mono-unsaturated alkyl chain having 13 carbon atoms or a saturated, mono-unsaturated or di-unsaturated alkyl chain having 15 carbon atoms, and wherein

R² is a saturated alkyl chain having 15 or 17 carbon atoms, a mono-unsaturated alkyl chain having 21-23 carbon atoms, or a di-unsaturated alkyl chain having 23 or 25 carbon atoms;

(c) comparing the concentration of the at least one ceramide of Formula I and the concentration of the at least one ceramide of Formula II to a control sample; and

(d) determining that the subject has an increased risk of developing one or more CV complications, if the biological sample contains a decreased concentration of the at least one ceramide of Formula I and an increased concentration of the at least one ceramide of Formula II, as compared to the control sample,

wherein the method further comprises spiking the biological sample with at least one isotope-labelled ceramide of Formula I and at least one isotope-labelled ceramide of Formula II prior to determining the concentration of the at least one ceramide of Formula I and the at least one ceramide of Formula II and

wherein the CV complications are selected from the group consisting of at least one of acute myocardial infarction, acute coronary syndrome, stroke and cardiovascular death.

2. The method of claim 1, wherein the concentrations of the at least one ceramide of Formula (I) and the at least one ceramide of Formula (II) are determined using mass spectrometry.

3. The method of claim 2, wherein the concentrations of the at least one ceramide of Formula (I) and the at least one ceramide of Formula (II) are determined using a mass spectrometry instrument coupled to a direct sample infusion method or to a high performance separation method.

4. The method of claim 1, wherein concentrations of at least 2 or at least 3 ceramides of Formula (I) are determined.

5. The method of claim 1, wherein concentrations of at least 2 or at least 3 ceramides of Formula (II) are determined.

6. The method of claim 1, wherein the subject has an increased risk of developing one or more CV complications, if the biological sample contains an increased Z value as compared to the control sample, according to the following equation: $Z = (\text{ceramide of Formula I})^a / (\text{ceramide of Formula II})^b$, wherein a and b are real numbers.

7. The method of claim 1, wherein the concentrations of the following ceramides of Formula (II) are determined: Cer(d18:1/16:0), Cer(d18:1/18:0), and Cer(d18:1/24:1).

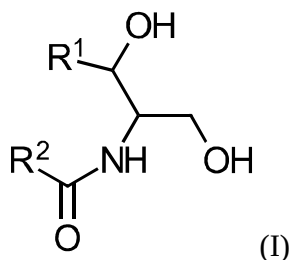
8. The method of claim 7, wherein the concentration of the following ceramide of Formula (I) is determined: Cer(d18:1/24:0).

9. The method of claim 1, further comprising a step of extracting lipids from the biological sample prior to determining the concentration of the at least one ceramide of Formula I and the at least one ceramide of Formula II.

10. The method of claim 1, wherein the isotope of the at least one isotope-labelled ceramide is deuterium.

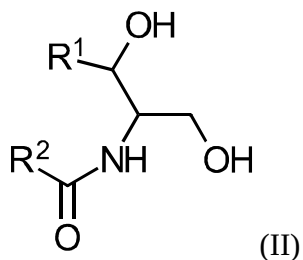
11. A method for determining whether a human subject is at risk to develop one or more cardiovascular (CV) complications, wherein the method comprises:

(a) determining in a biological sample obtained from the human subject the concentration of at least one ceramide of Formula I:



wherein R^1 is a mono-unsaturated alkyl chain having 13 carbon atoms or a saturated, mono-unsaturated or di-unsaturated alkyl chain having 15 carbon atoms, and wherein R^2 is a saturated alkyl chain having 21-25 carbon atoms, and wherein the biological sample is a blood sample, blood serum sample, a blood plasma sample, or a lipoprotein fraction obtained therefrom;

(b) determining in the biological sample obtained from the human subject the concentration of at least one ceramide of Formula (II):



wherein R^1 is a linear mono-unsaturated alkyl chain having 13 carbon atoms or a saturated, mono-unsaturated or di-unsaturated alkyl chain having 15 carbon atoms, and wherein R^2 is a saturated alkyl chain having 15 or 17 carbon atoms, a mono-unsaturated alkyl chain having 21-23 carbon atoms, or a di-unsaturated alkyl chain having 23 or 25 carbon atoms;

(c) comparing the concentration of the at least one ceramide of Formula I and the concentration of the at least one ceramide of Formula II to a control sample; and

(d) determining that the subject has an increased risk of developing one or more CV complications, if the biological sample contains a decreased concentration of the at least one

ceramide of Formula I and an increased concentration of the at least one ceramide of Formula II, as compared to the control sample,

wherein the method further comprises spiking the biological sample with at least one isotope-labelled ceramide of Formula I and at least one isotope-labelled ceramide of Formula II prior to determining the concentration of the at least one ceramide of Formula I and the at least one ceramide of Formula II,

wherein the CV complications are selected from the group consisting of at least one of acute myocardial infarction, acute coronary syndrome, stroke and cardiovascular death and

wherein the concentrations of the at least one ceramide of Formula (I) and the at least one ceramide of Formula (II) are determined using mass spectrometry.

12. The method of claim 1, wherein the human subject is undergoing a lipid-lowering drug treatment.

13. The method of claim 12, wherein the lipid-lowering drug treatment is a statin treatment.

14. The method of claim 11, wherein the concentrations of the at least one ceramide of Formula (I) and the at least one ceramide of Formula (II) are determined using a mass spectrometry instrument coupled to a direct sample infusion method or to a high performance separation method.

15. The method of claim 11, wherein concentrations of at least 2 or at least 3 ceramides of Formula (I) are determined.

16. The method of claim 11, wherein concentrations of at least 2 or at least 3 ceramides of Formula (II) are determined.

17. The method of claim 11, wherein the subject has an increased risk of developing one or more CV complications, if the biological sample contains an increased Z value as compared to the control sample, according to the following equation: $Z = (\text{ceramide of Formula I})^a / (\text{ceramide of Formula II})^b$, wherein a and b are real numbers.

18. The method of claim 11, wherein the concentrations of the following ceramides of Formula (II) are determined: Cer(d18:1/16:0), Cer(d18:1/18:0), and Cer(d18:1/24:1).

19. The method of claim 18, wherein the concentration of the following ceramide of Formula (I) is determined: Cer(d18:1/24:0).

20. The method of claim 11, further comprising a step of extracting lipids from the biological sample prior to determining the concentration of the at least one ceramide of Formula I and the at least one ceramide of Formula II.

21. The method of claim 11, wherein the human subject is undergoing a lipid-lowering drug treatment.

22. The method of claim 21, wherein the lipid-lowering drug treatment is a statin treatment.

23. The method of claim 11, wherein the isotope of the at least one isotope-labelled ceramide is deuterium.