

What is claimed is:

1. An assay for identifying amnion and/or chorion cell markers in a blood sample obtained from a pregnant woman comprising:
 - obtaining the blood sample from the pregnant woman; and
 - 5 determining the presence of one or more biomarkers selected from IGF2, IGFBP3, SERPINB10, FBN1, CRYAB, KRT18, PRTG, COL1A2, GPX8, MUC16, KRT5, TSPAN1, UPK1B, CADPS2, LAMC2, AHNK2, EMP1, FN1, MET, PVRL4, A2ML1, DSP, THSD4, KRT17, PDLIM4, COL17A1, DKK3, PLS3, DPYSL3, TPPP3, SHROOM3, THY1, DCN, DIO2, IGFBP2, SPARCL1, NNMT, LPHN3, PEG3, FLT1, NPR3, AOC1, ITGB8, RXFP1, SPOCK1,
 - 10 CYP11A1, COL4A2, CNR1, SEMA3A, SERPINE1, IL1R1, FBLN1, UCHL1, RAI2, TGM2, PRLR, FSTL3, BCAR1, THSD4, FERMT2, PKP2, P4HA2, TEAD1, or AQPEP, in amnion and/or chorion cells in the blood sample or fraction thereof.
2. The assay of claim 1, wherein the presence of amnion and/or chorion cells is indicative of pre-term birth, an associated clinical condition, an increased risk of pre-term birth or an increased
- 15 risk of an associated clinical condition of the pregnant woman, or preeclampsia.
3. The assay of claim 1, wherein the presence of amnion and/or chorion cells is determined by detecting one or more specific amnion and/or chorion cell markers.
4. The assay of claim 3, wherein the specific amnion and/or chorion cell markers are differentially expressed in amnion and/or chorion cells compared to a blood sample or a fraction
- 20 thereof isolated from a pregnant woman.
5. The assay of claim 4, wherein a log₂ fold difference between the expression of the amnion and/or chorion cell marker in amnion and/or chorion cells compared with the expression in a blood sample or fraction thereof is at least 5, at least 10, or at least 15.
6. The assay according to any of the preceding claims, wherein the method comprises the steps
- 25 of:
 - a) providing a blood sample or a fraction thereof isolated from a pregnant woman,
 - b) contacting the sample with (i) a ligand directed to an amnion and/or chorion cell marker or (ii) a hybridization probe comprising at least 10 contiguous nucleotides complementary to a gene encoding the amnion and/or chorion cell marker, and
 - 30 c) detecting the amnion and/or chorion cell marker in the blood sample or fraction thereof of a);

wherein the presence of an amnion and/or chorion cell marker is indicative of pre-term birth or an associated clinical condition or an increased risk of pre-term birth or an associated clinical condition of the pregnant woman.

7. The assay according to any of claims 1 to 6, wherein the amnion and/or chorion cell marker
5 is selected from the group consisting of MUC16, UPK1B, EMP1, PVRL4, THY1, DIO2, LPHN3, FLT1, NPR3, RXFP1, CNR1, PRLR, IGF2, IGFBP3, SERPINB10, FBN1, CRYAB, KRT18, PRTG, COL1A2 and GPX8.
8. The assay according to any of claims 1 to 7, wherein the amnion and/or chorion cell markers
10 are cell membrane markers selected from the group consisting of MUC16, UPK1B, EMP1, PVRL4, THY1, DIO2, LPHN3, FLT1, NPR3, RXFP1, CNR, PRLR, and GPX8.
9. The assay according to any of claims 1 to 8, wherein the amnion cell markers are amnion
membrane cell membrane markers selected from the group consisting of MUC16, UPK1B, EMP1
and PVRL4.
10. The assay according to any of claims 1 to 9, wherein the chorion cell markers are chorion
15 cell membrane markers selected from the group consisting of THY1, DIO2, LPHN3, FLT1, NPR3, RXFP1, CNR1 and PRLR.
11. The assay according to any of claims 1 to 10, wherein the amnion and/or chorion cell
markers are cell markers common between amnion and chorion selected from the group consisting
of IGF2, IGFBP3, SERPINB10, FBN1, CRYAB, KRT18, PRTG, COL1A2 and GPX8.
- 20 12. The assay according to any of claims 1 to 11, wherein the assay further comprises detecting
an epithelial marker, such as a marker selected from the group consisting of CK1, CK2, CK3, CK4,
CK5, CK6, CK7, CK8, CK9, CK10, CK12, CK13, CK14, CK15, CK16, CK17, CK18 and CK19.
13. The assay according to any of claims 1 to 12, wherein the assay further comprises detecting
a mesenchymal marker, such as a marker selected from at least one of: Vimentin.
- 25 14. The assay according to any of claims 1 to 13, wherein the clinical condition associated with
pre-term birth is preeclampsia, pre-term birth, or a tear or rupture of the amniotic membrane.
15. The assay according to any of claims 1 to 14, wherein the assay further comprises:
determining the amount of amnion and/or chorion cells in the blood sample or fraction
thereof, and
30 comparing the amount of amnion and/or chorion cells to a control;

wherein an amount of amnion and/or chorion cells in the blood sample or fraction thereof is higher than the amount in a control is indicative of pre-term birth or an associated clinical condition or an increased risk of pre-term birth or an associated clinical condition of the pregnant woman.

16. The assay according to claim 15, wherein the amount of amnion and/or chorion cells in a control is a pre-determined value.
17. The assay according to any of claims 1 to 16, wherein the amnion and/or chorion cell marker is detected at a protein level and/or an RNA level.
18. The assay according to any of claims 1 to 7, wherein the blood sample is isolated from the pregnant woman after 20 weeks of gestation.
19. The assay according to any of claims 1 to 18, wherein the amnion and/or chorion cell marker is present in the cell membrane or intracellularly.
20. The assay according to any of claims 1 to 19, wherein the blood sample from a pregnant woman is whole blood.
21. The assay according to any of claims 1 to 20, wherein a treatment is provided to the pregnant woman for minimizing the risk of preterm birth or ameliorating the consequences of pre-term birth, such as hospitalizing the pregnant woman.
22. A method of determining pre-term birth or an associated clinical condition or an increased risk of pre-term birth or an associated clinical condition, the method comprising the steps of:
- a) providing a blood sample or a fraction thereof isolated from a pregnant woman, and
 - b) determining the presence of amnion and/or chorion cells in the blood sample or fraction thereof;
- wherein the presence of amnion and/or chorion cells is indicative of pre-term birth or an associated clinical condition or an increased risk of pre-term birth or an associated clinical condition of the pregnant woman.
23. The method of claim 22, wherein the presence of amnion and/or chorion cells is determined by detecting one or more specific amnion and/or chorion cell markers.
24. The method of claim 23, wherein the specific amnion and/or chorion cell markers are differentially expressed in amnion and/or chorion cells compared to a blood sample or a fraction thereof isolated from the pregnant woman.

25. The method of claim 24, wherein the log₂ fold difference between the expression of the amnion and/or chorion cell marker in amnion and/or chorion cells compared with the expression in a blood sample or fraction thereof is at least 5, at least 10, or at least 15.

26. The method according to any of claims 22 to 25, wherein the method comprises the steps of:

- 5 a) contacting the sample with (i) a ligand directed to an amnion and/or chorion cell marker or (ii) a hybridization probe comprising at least 10 contiguous nucleotides complementary to a gene encoding the amnion and/or chorion cell marker, and
- b) detecting the amnion and/or chorion cell marker in the blood sample or fraction thereof of a);

10 wherein the presence of an amnion and/or chorion cell marker is indicative of pre-term birth or an associated clinical condition or an increased risk of pre-term birth or an associated clinical condition of the pregnant woman.

27. The method according to any of claims 22 to 26, wherein the amnion and/or chorion cell marker is selected from the group consisting of IGF2, IGFBP3, SERPINB10, FBN1, CRYAB,

15 KRT18, PRTG, COL1A2, GPX8, MUC16, KRT5, TSPAN1, UPK1B, CADPS2, LAMC2, AHNAK2, EMP1, FN1, MET, PVRL4, A2ML1, DSP, THSD4, KRT17, PDLIM4, COL17A1, DKK3, PLS3, DPYSL3, TPPP3, SHROOM3, THY1, DCN, DIO2, IGFBP2, SPARCL1, NNMT, LPHN3, PEG3, FLT1, NPR3, AOC1, ITGB8, RXFP1, SPOCK1, CYP11A1, COL4A2, CNR1, SEMA3A, SERPINE1, IL1R1, FBLN1, UCHL1, RAI2, TGM2, PRLR, FSTL3, BCAR1, THSD4,

20 FERMT2, PKP2, P4HA2, TEAD1, and AQPEP.

28. The method according to any of claims 22 to 27, wherein the amnion and/or chorion cell marker is selected from the group consisting of MUC16, UPK1B, EMP1, PVRL4, THY1, DIO2, LPHN3, FLT1, NPR3, RXFP1, CNR1, PRLR, IGF2, IGFBP3, SERPINB10, FBN1, CRYAB, KRT18, PRTG, COL1A2 and GPX8.

25 29. The method according to any of claims 22 to 28, wherein the amnion and/or chorion cell markers are membrane cell markers selected from the group consisting of MUC16, UPK1B, EMP1, PVRL4, THY1, DIO2, LPHN3, FLT1, NPR3, RXFP1, CNR, PRLR, and GPX8.

30. The method according to any of claims 22 to 29, wherein the amnion cell markers are amnion cell membrane markers selected from the group consisting of MUC16, UPK1B, EMP1 and

30 PVRL4.

31. The method according to any of claims 22 to 30, wherein the chorion cell markers are chorion cell membrane markers selected from the group consisting of THY1, DIO2, LPHN3, FLT1, NPR3, RXFP1, CNR1 and PRLR.
32. The method according to any of claims 22 to 31, wherein the amnion and/or chorion cell
5 marker are cell markers common between amnion and chorion is selected from the group consisting of IGF2, IGFBP3, SERPINB10, FBN1, CRYAB, KRT18, PRTG, COL1A2 and GPX8.
33. The method according to any of claims 22 to 32, wherein the method further comprises detecting an epithelial marker, such as a marker selected from the group consisting of CK1, CK2, CK3, CK4, CK5, CK6, CK7, CK8, CK9, CK10, , CK12, CK13, CK14, CK15, CK16, CK17, CK18
10 and CK19 and/or a mesenchymal marker selected from at least one of: Vimentin.
34. The method according to any of claims 22 to 33, wherein the method further comprises:
- a) determining the amount of amnion and/or chorion cells in the blood sample or fraction thereof, and
 - b) comparing the amount of amnion and/or chorion cells to a pregnant women who is at a same
15 gestational age, but not at a high risk of pre-term birth;
- wherein an amount of amnion and/or chorion cells in the blood sample or fraction thereof higher than the amount in a control is indicative of pre-term birth or an associated clinical condition or an increased risk of pre-term birth or an associated clinical condition of the pregnant woman.
35. The method according to claim 34, wherein the amount of amnion and/or chorion cells in a
20 control is a pre-determined value.
36. The method according to any of claims 22 to 35, wherein the amnion and/or chorion cell marker is detected at the protein level and/or the RNA level.
37. The method according to any of claims 22 to 36, wherein the blood sample is isolated from the pregnant woman after 20 weeks of gestation.
- 25 38. The method according to any of claims 22 to 37, wherein the amnion and/or chorion cell marker is present on the cell membrane or intracellularly.
39. The method according to any of claims 22 to 38, wherein the blood sample from a pregnant woman is whole blood.
40. The method according to any of claims 22 to 39, wherein a treatment is provided to the
30 pregnant woman for minimizing the risk of preterm birth or ameliorating the consequences of pre-term birth, such as hospitalizing the individual.

41. A kit comprising one or more agents for the detection of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 49, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63 or all the markers in Table 1 and/or table 2, on amnion and/or chorion cells in a blood sample or fraction thereof.
- 5 42. A method of determining pre-term birth or an associated clinical condition or an increased risk of pre-term birth or an associated clinical condition, the method comprising the steps of:
- a) obtaining a blood sample or a fraction thereof isolated from a pregnant woman, and
 - b) determining the presence of amnion and/or chorion cells in the blood sample or
 - 10 fraction thereof;
 - c) isolating the amnion and/or chorion cells in the blood sample or fraction thereof;
 - d) determining the RNA sequence of the isolated amnion/chorion cells;
 - e) comparing a gene expression profile of the isolated amnion/chorion cells to a pregnant women who is at a same gestational age, but not at a high risk of pre-term birth;
 - 15 wherein the gene expression profile is indicative of pre-term birth or an associated clinical condition or an increased risk of pre-term birth or an associated clinical condition of the pregnant woman.
43. The method according to claim 42, wherein the clinical condition associated with pre-term birth is preeclampsia.
- 20 44. The method according to claims 42 or 43, wherein the method further comprises detecting a maternal marker, such as a marker selected from the group consisting of CD14 and CD45.
45. Amnion and/or chorion specific markers for use in diagnosing risk of premature birth.