

CLAIMS

WHAT IS CLAIMED IS:

1. A method, such as a laboratory method, for detecting and/or quantifying a plurality of proteins in a sample from a pregnant human female, the method comprising:
contacting a biological sample from a pregnant human female with a plurality of probes, wherein the plurality of probes comprises probes with specific affinity for four or more proteins, and wherein the four or more proteins comprise:
 - (a) placental growth factor;
 - (b) one or more angiogenesis-associated proteins selected from the group consisting of soluble fms-like tyrosine kinase 1 (sFlt1), endoglin, pappalysin 2 (PAPP-A2), and decorin; and
 - (c) one or more kidney damage associated-proteins selected from the group consisting of (1) kidney injury molecule-1 (KIM1), (2) programmed cell death 1 ligand 1 (CD274), and decorin; and
 - (d) one or more proteins selected from the group consisting of C-type lectin domain family 4 member A (CLEC4A), fibroblast growth factor 21 (FGF21), trefoil factor 2 (TFF2), and hepatocyte growth factor (HGF).detecting the presence and/or quantity of the four or more proteins based on binding of the plurality of different probes to corresponding proteins; and
determining the presence or absence of preeclampsia based on the presence and/or quantity of the four or more proteins.
2. The method of claim 1, wherein the four or more proteins comprise PlGF, sFlt1, KIM1, and endoglin.
3. The method of any one of claims 1-2, wherein the biological sample has been collected from the pregnant human female after gestational week 20.
4. The method of any one of claims 1-2, wherein the biological sample has been collected from the pregnant female prior to gestational week 30.
5. The method of any one of claims 1-4, wherein the biological sample is a urine, blood, amniotic fluid, exosome, plasma, or serum sample.
6. The method of claim 5, wherein the biological sample is from blood of the pregnant human female.
7. The method of any one of claims 1–6, wherein the amount or concentration of no more than 20proteins is determined.

8. The method of any one of claims 1–6, wherein one or more of the plurality of different probes are antibodies or antibody fragments or wherein each of the plurality of different probes are antibodies or antibody fragments.

9. The method of any one of claims 1–7, wherein the plurality of probes contact the biological sample or a fraction thereof in a single reaction vessel or wherein the plurality of probes contact the biological sample or a fraction thereof in separate reaction vessels for each protein of the four or more proteins.

10. The method of any one of claims 1–8, further comprising a second plurality of probes, wherein the second plurality of probes comprises probes with specific affinity for the four or more proteins, wherein the second plurality of probes binds to its corresponding protein at an epitope that differs from the epitope to which each of the first plurality of probes binds.

11. The method of claim 10, wherein coincident binding of at least one pair of the first and the second plurality of probes to the same protein molecules in the sample is detected by a luminescent oxygen channeling immunoassay (LOCI), a time-resolved fluorescence resonance energy transfer (TR-FRET) assay, an amplified luminescent proximity homogenous assay, an enzyme-linked immunosorbent assay, a proximity extension assay, or a lateral flow assay.

12. The method of any one of claims 1-2 or 5-11, wherein the biological sample has been obtained from the pregnant female after gestational week 28.

13. The method of any one of claims 1-2 or 5-11, wherein the biological sample has been obtained from the pregnant female after gestational week 30.

14. The method of any one of claims 1-13, further comprising applying a classifier algorithm to an expression profile of the four or more proteins, wherein the classifier algorithm calculates an index; and

comparing the index to a reference value to determine whether to avoid the unnecessary treatment of preeclampsia.

15. The method of any one of claims 1-14, further comprising making a clinical or therapeutic decision regarding treatment of the pregnant human female based on said determination.

16. The method of any one of claims 1-15, wherein the method determines the absence of preeclampsia and the clinical decision is to avoid unnecessary treatment of preeclampsia.

17. A method of classifying a sample as being from a pre-eclampsia or non-preeclampsia subject, wherein said method is implemented on a digital processing device comprising an operating system configured to implement a trained algorithm for classifying the sample, the method comprising:

receiving expression level data derived from a sample from a pregnant human female,
and

executing the algorithm to classify the sample as being from a pre-eclampsia or non-preeclampsia subject,

wherein the data has been derived by a method comprising:

i) contacting a biological sample from the pregnant human female with a first plurality of probes, wherein the first plurality of probes comprises probes with specific affinity for four or more proteins and wherein the four or more proteins comprise:

(a) placental growth factor (PlGF);

(b) one or more angiogenesis-associated proteins selected from the group consisting of soluble fms-like tyrosine kinase 1 (sFlt1), endoglin, pappalysin 2 (PAPP-A2), and decorin;

(c) one or more kidney damage associated-proteins selected from the group consisting of (1) kidney injury molecule-1 (KIM1), (2) programmed cell death 1 ligand 1 (CD274), and decorin; and

(d) one or more proteins selected from the group consisting of C-type lectin domain family 4 member A (CLEC4A), fibroblast growth factor 21 (FGF21), trefoil factor 2 (TFF2), and hepatocyte growth factor (HGF); and

ii) detecting the quantity of the four or more proteins based on binding of the first plurality of different probes to corresponding proteins.

18. A computer-implemented method of assessing the likelihood that a pregnant subject has or will develop preeclampsia within a specified period of time, comprising:

receiving, at a computer, expression level data derived from a plasma or serum sample from the pregnant subject;

applying, by the computer, a classifier algorithm to the expression level data derived from the pregnant subject using a classification rule or class probability equation; and
using, by the computer, the classification rule or class probability equation to output a classification for the sample, wherein the classification classifies the sample as having

a probability of having preeclampsia with a negative predictive value of greater than 80%, wherein the pregnant subject has hypertension or proteinuria;

wherein the data has been derived by a method comprising:

i) contacting a biological sample from the pregnant human female with a first plurality of probes, wherein the first plurality of probes comprises probes with specific affinity for four or more proteins and wherein the four or more proteins comprise:

(a) placental growth factor (PlGF);

(b) one or more angiogenesis-associated proteins selected from the group consisting of soluble fms-like tyrosine kinase 1 (sFlt1), endoglin, pappalysin 2 (PAPP-A2), and decorin;

(c) one or more kidney damage associated-proteins selected from the group consisting of (1) kidney injury molecule-1 (KIM1), (2) programmed cell death 1 ligand 1 (CD274), and decorin; and

(d) one or more proteins selected from the group consisting of C-type lectin domain family 4 member A (CLEC4A), fibroblast growth factor 21 (FGF21), trefoil factor 2 (TFF2), and hepatocyte growth factor (HGF); and

ii) detecting the quantity of the four or more proteins based on binding of the first plurality of different probes to corresponding proteins.