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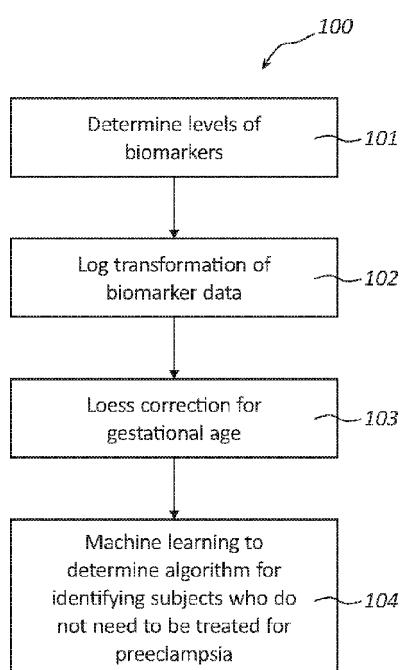
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(54) Title: PREECLAMPSIA BIOMARKERS AND RELATED SYSTEMS AND METHODS



(57) Abstract: Disclosed herein are methods, kits, tests, and systems for detecting, predicting, monitoring, or ruling out preeclampsia in pregnant women. Also provided herein are novel diagnostic markers, methods of data analysis, assay formats, and kits employing such markers to improve one or more characteristics of a test for identifying or ruling out preeclampsia based on biomarkers from patient samples.

FIG. 17



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TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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**PREECLAMPSIA BIOMARKERS AND RELATED SYSTEMS AND METHODS****CROSS REFERENCE**

**[0001]** This application claims the benefit of U.S. Provisional Application No. 62/558,184, filed September 13, 2017 and titled PRECCLAMPSIA MARKERS, which is hereby incorporated by reference in its entirety.

**BACKGROUND OF THE INVENTION**

**[0002]** Preeclampsia is a serious multisystem complication of pregnancy. The incidence of the disorder is generally considered to be between 2% to 8% of all pregnancies, and the disorder carries significant morbidity and mortality risks for both mothers and infants. Preeclampsia is the second largest cause of maternal/fetal deaths, and is responsible for approximately twenty billion dollars in healthcare costs annually. In the United States, approximately one million women present with classical symptoms of preeclampsia (hypertension and/or proteinuria after the 20<sup>th</sup> month of gestation) each year.

**[0003]** The cause(s) and pathogenesis of preeclampsia remain uncertain, and the identification (or ruling out) of preeclampsia using the classical clinical symptoms of the disease is non-ideal. The presentation of classical clinical symptoms can be highly variable, and the symptoms can be indicative of other distinct disorders, such as chronic hypertension, gestational hypertension, temporary high blood pressure, and gestational diabetes. Current laboratories tests (e.g., tests for proteinuria) can be prone to inaccuracies, or are useful for detection of preeclampsia only during relatively late periods in the progression of the disorder. Methods for more reliably determining whether a pregnant woman does or does not have preeclampsia may, among other things, (1) lead to a more timely diagnosis, (2) improve the accuracy of a diagnosis, and/or (3) prevent the unnecessary treatment of women with preeclampsia treatments.

**INCORPORATION BY REFERENCE**

**[0004]** All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0005]** Features of the inventions described herein are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present inventions will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the inventions are utilized, and the accompanying drawings of which:

**[0006]** **Figure 1A** shows a plot of LogWorth vs. effect size from the initial ANOVA-based screening for markers of interest presented in **Example 3**.

**[0007]** **Figure 1B** provides illustrations of data spread for markers for distinguishing between preeclampsia and non-preeclampsia.

**[0008]** **Figure 2** shows scatter plots of the top nine biomarkers identified in **Example 3** split into 4 subcohorts based on the predictive utility of the sFlt1/PlGF ratio for the subcohort (A=nonPreE/true negatives, B=PreE/true positive, C=PreE/false negative, D=nonPreE/false positive).

**[0009]** **Figure 3** shows a four-subcohort analysis that is similar to the four-subcohort analysis of **Figure 2** for the literature-identified candidate analytes Fibronectin, sFlt1, PlGF, and PAPP-A.

**[0010]** **Figure 4** shows a ROC curve and summary statistics for logistic regression model for non-preeclampsia vs preeclampsia built from the top nine predictors identified in a multivariate graded-response-based analysis in **Example 7**.

**[0011]** **Figure 5** shows a ROC curve and summary statistics for logistic regression model built in **Example 7** for non-preeclampsia (nonPreE) vs preeclampsia (PreE) built from sFlt1 and PlGF plus the top 2 predictors identified in **Example 3**.

**[0012]** **Figure 6** shows a system for implementing the methods of the disclosure.

**[0013]** **Figure 7, Figure 8, Figure 9, Figure 10, Figure 11, and Figure 12** show single-plex analysis of additional candidate biomarkers by AlphaScreen™, with the expression level presented by subcohort (A=nonPreE/true negatives, B=PreE/true positive, C=PreE/false negative, D=nonPreE/false positive).

**[0014]** **Figure 13A, Figure 13B, Figure 13C, Figure 13D, Figure 13E, Figure 13F, Figure 13G, Figure 13H, Figure 13I, Figure 13J, and Figure 13K** depict log-transforms of expression levels of the top 11 markers identified for detection of preeclampsia in both preeclampsia and non-preeclampsia samples.

**[0015]** **Figure 14** depicts an exemplary procedure wherein a Loess model is used to perform gestational-age correction of biomarker (PIGF) expression levels.

**[0016]** **Figure 15** depicts a graph of a principal component analysis of non-preeclampsia (-), preeclampsia (+), false positive (O) and false negative (X) samples, showing that false negative samples cluster with non-preeclampsia samples.

**[0017]** **Figure 16** is a diagram showing exemplary functional roles for various markers in the pathophysiology of preeclampsia.

**[0018]** **Figure 17** provides a flow diagram of a method for building biomarker models suitable for identification of preeclampsia.

**[0019]** **Figure 18** lists various antibodies or other antigen-binding agents for use in some embodiments disclosed herein.

**[0020]** **Figure 19** provides a flow diagram for a “stacked” decision structure for ruling out preeclampsia.

**[0021]** **Figure 20** is a figure showing, via color, the extent to which various markers reveal orthogonal information for ruling out preeclampsia.

**[0022]** **Figure 21** is a diagram that shows the relative predictive weights of various individual biomarkers for ruling out preeclampsia.

## DETAILED DESCRIPTION OF THE INVENTION

**[0023]** Detection of preeclampsia using the classic clinical symptoms of the disease is error prone, risking significant adverse outcome for patients and added burden to the healthcare system through misdiagnosis. Measurement of proteinuria is prone to inaccuracies (e.g., false negatives and false positives), preeclampsia complications may occur before proteinuria becomes significant, the clinical presentation of preeclampsia can be highly variable (from severe, rapidly progressing, and early-onset to late-onset and less severe), and the symptoms (hypertension, proteinuria, or both) can be indicative of other distinct disorders that could utilize a less aggressive treatment course (chronic hypertension, gestational hypertension, temporary high blood pressure, and gestational diabetes). Thus, there is significant risk for patients with only suspected preeclampsia to be over treated (e.g., delivered or induced early, thereby unnecessarily putting the infant at risk of preterm birth complications and/or unnecessarily putting the mother at risk of surgical complications), and there is risk for patients with silent or rapidly-progressing preeclampsia to be treated insufficiently aggressively (e.g., putting the infant at risk of intrauterine growth restriction or death, and the

mother at risk of preeclamptic sequelae such as eclampsia seizures, renal or liver damage, pulmonary edema, placental abruption, and coma).

**[0024]** In other words, hypertension and proteinuria merely reflect downstream consequences of the actual preeclampsia disease process. Traditional diagnoses of preeclampsia lead to masking of the disease because the only reliable treatment is delivery. In the interest of improved detection of preeclampsia, research into the dysfunctional angiogenic processes associated with preeclampsia has been undertaken to find better and/or more direct indicators of preeclampsia. One avenue of this research has led to the use of the sFlt1/PIGF ratio in patient serum as a method for identifying preeclampsia (see e.g., Zeisler et al. NEJM 274(2017):13-22 or Verlohren et al. Hypertension. 63(2014):346-52). However, this method only has a maximal sensitivity of 80% and specificity of 78.3%; and thus involves a significant proportion of false negatives and positives, making it of limited use in ruling out a diagnosis of preeclampsia and avoiding the overtreatment/under treatment conundrum.

**[0025]** Accordingly, there is a need for the methods, compositions, systems and kits for improved detection or prediction of preeclampsia in pregnant patients, particularly those that enable the detection or prediction of preeclampsia with a high negative predictive value and/or allow medical professionals to rule out a diagnosis of preeclampsia for an extended period of time.

**[0026]** The disclosure provides for one or more tests with improved characteristics for assessing the risk of preeclampsia in a subject, wherein the test can be used to identify subjects that should not be treated for preeclampsia (e.g., in some instances identifying a subject that shows one or more signs, symptoms, or risk factors of preeclampsia, but should not be treated for preeclampsia). In some embodiments, this test is a multi-marker serum or plasma protein assay. In some embodiments, the test is a multiplexed serum/plasma protein assay. The one or more symptoms associated with preeclampsia can be diabetes (e.g. gestational, type I or type II), higher than normal glucose level, hypertension (e.g., chronic or non-chronic), excessive or sudden weight gain, higher than normal weight, obesity, higher than normal body mass index (BMI), abnormal weight gain, abnormal blood pressure, water retention, hereditary factors, abnormal proteinuria, headache, edema, abnormal protein/creatinine ratio, abnormal platelet count, stress, nulliparity, abnormal Papanicolaou test results (Pap smear), prior preeclampsia episodes (e.g., personal history of PreE), familial history of preeclampsia, preeclampsia in prior pregnancies, renal disease, thrombophilia, or any combination thereof.

**[0027]** The disclosure provides for tests, systems, and methods for assessing a risk of preeclampsia in a subject, such as ruling out a patient as having or needing treatment for preeclampsia. In some embodiments, a test is used to discern whether a patient having one or symptoms or risk factors associated with preeclampsia should be treated for preeclampsia. The one or more symptoms or risk factors associated with preeclampsia can be diabetes (e.g. gestational, type I or type II), higher than normal glucose level, hypertension (e.g., chronic or non-chronic), excessive or sudden weight gain, higher than normal weight, obesity, higher than normal body mass index (BMI), abnormal weight gain, abnormal blood pressure, water retention, hereditary factors, abnormal proteinuria, headache, edema, abnormal protein/creatinine ratio, abnormal platelet count, stress, nulliparity, abnormal Papanicolaou test results (Pap smear), prior preeclampsia episodes (e.g., personal history of PreE), familial history of preeclampsia, preeclampsia in prior pregnancies, renal disease, thrombophilia, or any combination thereof. Stated differently in some embodiments, the tests disclosed herein can be used to identify pregnant women who are symptomatic (and/or have one or more risk factors for preeclampsia), but do not have preeclampsia that is likely to require preterm birth. In some embodiments, the test may be used on asymptomatic patients or patients with little or no risk identified (or identifiable) risk factors.

*Definitions*

**[0028]** As used in the specification and in the claims, the singular form “a,” “an,” and “the” include plural referents unless the context clearly dictates otherwise.

**[0029]** The term “hypertension” refers to abnormally high blood pressure. Hypertension can be identified in any suitable manner, such as by reference to a sitting systolic blood pressure (sSBP) of greater than 140 mmHg or a sitting diastolic blood pressure (sDBP) of greater than 90 mmHg. Hypertension can be further classified into class 1 or class 2 hypertension, with class 1 exhibiting sSBP of 140-149 mmHg or 90-99 mmHg sDBP, and class 2 exhibiting greater than 160 mmHg sSBP or 100 mmHg sDBP. (See, e.g., The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. JAMA 2003;289:2560-71.) Other suitable criteria may be used to identify hypertension, such as having a sitting systolic blood pressure of greater than 130 and/or a sitting diastolic blood pressure of greater than 90 mmHg. Hypertension can also be determined according to the 2017 AHA guidelines (see Whelton et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults,

Journal of the American College of Cardiology (2017), doi: 10.1016/j.jacc.2017.11.006). Such guidelines identify “normal” blood pressure as less than 120/80 mmHg, “elevated” as systolic between 120-129 mmHg and diastolic less than 80 mmHg, “stage 1” as systolic between 120-139 mmHg or diastolic between 80-89 mmHg, “stage 2” as systolic at least 140 mmHg or diastolic at least 90 mmHg, and “hypertensive crisis” as systolic over 180 and/or diastolic over 120.

**[0030]** As used herein, the term “proteinuria” is defined as the presence of abnormal protein in the urine. A number of indicator dyes and reagents can be used to measure proteinuria semi-quantitatively (e.g., bromophenol blue). In some embodiments, concentrations of protein in urine can be determined by a semi quantitative “dipstick” analysis and graded as negative, trace (10-20 mg/dL), 1+ (~30 mg/dL), 2+ (~100 mg/dL), 3+ (~300 mg/dL), or 4+ (~1,000 mg/dL), with 2+ commonly being used as the threshold for problematic proteinuria. In an alternative scheme, concentrations of protein in urine can also be measured per 24 hour urine collection, in which greater than or equal to 300 mg protein indicates proteinuria. In an alternative scheme, concentrations of protein in urine can be measured in a spot urine sample, in which 30 mg of protein per deciliter or greater indicates proteinuria. In yet an alternative scheme, proteinuria can also be expressed as the protein/creatinine ratio (Pr/Cr) in urine, in which a Pr/Cr ratio of  $\geq 0.3$  is indicative of problematic proteinuria.

**[0031]** As used herein, the term “antibody or fragments thereof” is used in the broadest sense and specifically encompasses intact monoclonal antibodies, polyclonal antibodies, multispecific antibodies (e.g. bispecific antibodies) formed from at least two intact antibodies, and antibody fragments. Antibody fragments comprise a portion of an intact antibody that retains antigen-binding activity; examples include Fab, Fab', F(ab)<sub>2</sub>, F(abc)<sub>2</sub>, and Fv fragments as well as diabodies, linear antibodies, scFvs, and multispecific antibodies formed from antibody fragments.

**[0032]** As used herein, the term “aptamer” refers to an oligonucleotide that is capable of forming a complex with an intended target substance. Such complex formation is target-specific in the sense that other materials which may accompany the target do not complex to the aptamer. It is recognized that complex formation and affinity are a matter of degree; however, in this context, “target-specific” means that the aptamer binds to target with a much higher degree of affinity than it binds to contaminating or “off-target” materials.

**[0033]** As used herein, the term “preeclampsia” (or “PreE”) refers to a pregnancy-specific disorder involving multiple organ systems thought to originate from abnormal placentation,

dysfunctional trophoblast development, defective placental angiogenesis, and a heightened systemic inflammatory response in the mother. Preeclampsia, when untreated, can progress to eclampsia, HELLP syndrome, hemorrhagic or ischemic stroke, liver damage, acute kidney injury, and acute respiratory distress syndrome (ARDS). Thus, while preeclampsia frequently presents with symptoms such as hypertension and proteinuria, it is distinct from simple vascular tension disorders and kidney dysfunction (as evidenced by the non-overlapping set of complications that result when it is untreated), and symptoms reflective of vascular tension disorders and kidney dysfunction on their own therefore have less than ideal predictive/diagnostic value for preeclampsia. Further information on the pathophysiology of preeclampsia can be found, e.g., in Phipps et al. Clin J Am Soc Nephrol 11(2016):1102–1113. In some embodiments, a traditional diagnosis of preeclampsia is made when hypertension and proteinuria as defined above are detected at the same time. In other embodiments (see American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. Obstet Gynecol.122(2013):1122-31, which is explicitly incorporated by reference herein) a traditional diagnosis of preeclampsia is made upon simultaneous detection of hypertension (blood pressure greater than or equal to 140 mmHg systolic or greater than or equal to 90 mmHg diastolic on two occasions at least 4 hours apart after 20 weeks gestation in a woman with a previously normal blood pressure, or blood pressure with greater than equal to 160 mmHg systolic or greater than or equal to 110 mmHg diastolic within a short interval of minutes) and proteinuria (greater than or equal to 300 mg per 24-hour urine collection either measured or extrapolated, or protein creatinine ratio greater than or equal to 0.3, or a dipstick reading of 1+) or upon new onset hypertension in the absence of proteinuria when (a) blood platelet count is less than 100,000 per milliliter, (b) serum creatinine is greater than 1.1 mg/dL or double baseline for the patient, or (c) blood concentration of liver transaminases is twice normal or greater). In some cases, preeclampsia is made without a diagnosis of proteinuria, for instance where evidence of other end-stage organ damage is present.

**[0034]** The term “subject” can include human or non-human animals. Thus, the methods and described herein are applicable to both human and veterinary disease and animal models. Preferred subjects are “patients,” i.e., living humans that are receiving medical care for a disease or condition. This includes persons with no defined illness who are being investigated for signs of pathology.

**[0035]** The term “FRET pair” refers to a pair of dye molecules where one of the dye molecules absorbs light (the acceptor or quencher dye) at a wavelength at which the other emits light (the donor dye) and the two dyes are spatially separated by a distance that permits energy transfer, with the disclosed embodiments generally being within about 100 angstroms, such as within about 50, 20 or 10 angstroms of each other (for example, because they are bonded to the same substrate moiety). Excitation of the donor dye leads to excitation of the acceptor dye through the FRET mechanism, and a lower level of fluorescence is observed from the donor dye. The efficiency of FRET depends on the distance between the dyes, the quantum yield of the donor dye, the fluorescence lifetime of the donor dye, and the overlap of the donor's emission spectrum and the acceptor's absorption spectrum.

**[0036]** The term “photosensitizer” refers to a photoactivatable compound, or a biological precursor of a photoactivatable compound, that produces a reactive species (for e.g., oxygen) having a photochemical effect on a biomolecule.

**[0037]** The term “oxygen-sensitive dye” refers a fluorescent dye that changes its fluorescence intensity or emission maximum after binding to molecular oxygen (such dyes are used for FOCI assays), or a chemiluminescent dye that emits light after binding to molecular oxygen (such dyes are used for LOCI assays).

**[0038]** The term “affimer” as used herein refers to small, highly stable proteins that bind to a target molecule with similar specificity and affinity to that of antibodies.

**[0039]** The term “unnecessary treatment of preeclampsia” can refer to treatments for preeclampsia that would be, statistically speaking, unjustified when a practitioner takes into account the results of a test or procedure described herein, such as a test based on the determination of an amount of concentration of various protein biomarkers. Such unnecessary treatment can include preterm induction based on one or more symptoms or risk factors for preeclampsia.

#### *Subjects*

**[0040]** In some embodiments, the methods, compositions, systems and kits provided herein are used for detecting or predicting a condition in a pregnant human subject at any stage in pregnancy. In other embodiments, the pregnant human subject is post- the 20<sup>th</sup> week of gestation. In other embodiments, the pregnant human subject is post-first or -second trimester of pregnancy. In some embodiments, the pregnant human subject is post-21st, 22nd, 23rd, 24th, 25th, 26th, 27th, 28th, 29th, 30th, 31st, 32nd, 33rd, 34th, 35th, 36th, 37th, 38th, 39th, 40th, 41st, or 42nd week of gestation.

**[0041]** The methods, compositions, systems and kits are suitable for detecting or predicting a condition of the pregnant subject such as preeclampsia (PreE) or non-preeclampsia (NonPreE). In some embodiments, preeclampsia is further divided into very early-onset (before 25 weeks gestation), early-onset (before 34 weeks gestation) and late-onset (after 34 weeks gestation) preeclampsia. Typically, when the pregnant patient does not exhibit hypertensive or renal symptoms, the patient is considered NonPreE. Further, when the pregnant patient exhibits only hypertensive symptoms alone without signs of proteinuria, the patient is generally only suspected to have preeclampsia. However, as the measurement of proteinuria is prone to inaccuracies (e.g., false negatives and false positives), preeclampsia complications may occur before proteinuria becomes significant, the clinical presentation of preeclampsia can be highly variable (from severe, rapidly progressing, and early-onset to late-onset and less severe), and the symptoms (hypertension, proteinuria, or both) can be indicative of other distinct disorders that could utilize a different treatment course. Thus, there is significant risk for patients with only suspected preeclampsia to be unnecessarily treated (e.g., delivered/induced early putting the infant at risk of preterm birth complications or the mother at risk of surgical complications), and there is risk for patients with silent or rapidly-progressing preeclampsia to be treated insufficiently aggressively (e.g., putting the infant at risk of intrauterine growth restriction or death, and the mother at risk of preeclampsia sequelae such as eclampsia seizures, renal or liver damage, pulmonary edema, placental abruption, and coma).

**[0042]** A subject therefore can be a pregnant female that has no known risk factors, or has one or more at-risk factors for a condition such as PreE. In some instances, hypertension and/or proteinuria can indicate a subject at risk of preeclampsia. In some instances, a subject at risk of preeclampsia can have a urine protein content measured as 2+ (100 mg/dL) or greater by dipstick assay, greater than or equal to 300 mg per 24 hour urine collection, 30 mg of protein per deciliter or greater in a spot urine sample, or a Pr/Cr ratio in urine of  $\geq 30$  mg per millimole. In some instances, a subject at risk of preeclampsia can have a sitting systolic blood pressure (sSBP) of greater than 140 mmHg or a sitting diastolic blood pressure (sDBP) of greater than 90 mmHg or both. In some instances, sFlt1/PIGF ratio can be used to identify subject at risk of preeclampsia (see, e.g., Zeisler et al. NEJM 274(2017):13-22 or Verlohren et al. Hypertension. 63(2014):346-52). In some instances both hypertension and proteinuria can be used to identify a subject at risk of preeclampsia. In some instances new onset hypertension in combination with one or more symptoms selected from (a) blood platelet

count is less than 100,000 per milliliter, (b) serum creatinine is greater than 1.1 mg/dL or double baseline for the patient, or (c) blood concentration of liver transaminases is twice normal or greater can be used to identify a subject at risk of preeclampsia.

*Samples*

**[0043]** Methods for detecting molecules (e.g., nucleic acids, proteins, etc.) in a pregnant subject in order to detect, diagnose, monitor, predict, or evaluate the status or outcome of the pregnancy are described in this disclosure. In some cases, the molecules are circulating molecules (e.g. unbound to cells and freely circulating in bodily fluids such as blood, blood plasma or blood serum). In some cases, the molecules are expressed in the cytoplasm of blood, endothelial, or organ cells. In some cases, the molecules are expressed on the surface of blood, endothelial, or organ cells.

**[0044]** The methods, kits, and systems disclosed herein can be used to classify one or more samples from one or more subjects. A sample can be any material containing tissues, cells, nucleic acids, genes, gene fragments, expression products, proteins, polypeptides, exosomes, gene expression products, or gene expression product fragments of a subject to be tested. A sample can include but is not limited to, tissue, cells, plasma, serum, or any other biological material from cells or derived from cells of an individual. The sample can be a heterogeneous or homogeneous population of cells or tissues. The sample can be a fluid that is acellular or depleted of cells (e.g., plasma or serum). In some cases, the sample is from a single patient. In some cases, the method comprises analyzing multiple samples at once, e.g., via massively parallel multiplex expression analysis on protein arrays or the like.

**[0045]** The sample is preferably a bodily fluid. The bodily fluid can be saliva, urine, blood, and/or amniotic fluid. The sample can be a fraction of any of these fluids, such as plasma, serum or exosomes (exemplary exosome isolation techniques can be found, e.g. in Li et al. Theranostics. 7(2017): 789–804). In preferred embodiments, the sample is a blood sample, plasma sample, or serum sample.

**[0046]** The sample may be obtained using any method that can provide a sample suitable for the analytical methods described herein. The sample may be obtained by a non-invasive method such as a throat swab, buccal swab, bronchial lavage, urine collection, scraping of the cervix, cervicovaginal sample secretion collection (e.g. with an ophthalmic sponge such as a Weck-Cel sponge), saliva collection, or feces collection. The sample may be obtained by a minimally-invasive method such as a blood draw. The sample may be obtained by venipuncture.

**[0047]** As used herein “obtaining a sample” includes obtaining a sample directly or indirectly. In some embodiments, the sample is taken from the subject by the same party (e.g. a testing laboratory) that subsequently acquires biomarker data from the sample. In some embodiments, the sample is received (e.g. by a testing laboratory) from another entity that collected it from the subject (e.g. a physician, nurse, phlebotomist, or medical caregiver). In some embodiments, the sample is taken from the subject by a medical professional under direction of a separate entity (e.g. a testing laboratory) and subsequently provided to said entity (e.g. the testing laboratory). In some embodiments, the sample is taken by the subject or the subject’s caregiver at home and subsequently provided to the party that acquires biomarker data from the sample (e.g. a testing laboratory). A variety of kits suitable for self or home collection of biological samples have been described commercially and in the literature; see e.g., US20170023446A1 and US4777964A.

*Sample Data*

**[0048]** The methods, kits, and systems disclosed herein may comprise data pertaining to one or more samples or uses thereof. The data can be representative of an amount or concentration of one or more biomarkers, such as various proteins described herein. Stated differently, the data can be expression level data of proteins or polypeptides. The expression level data of biomarkers described herein can be determined by protein array, proteomics, expression proteomics, mass spectrometry (e.g., liquid chromatography-mass spectrometry (LC-MS), multiple reaction monitoring (MRM), selected reaction monitoring (SRM), scheduled MRM, scheduled SRM), 2D PAGE, 3D PAGE, electrophoresis, proteomic chip, proteomic microarray, Edman degradation, direct or indirect ELISA, immunosorbent assay, immuno-PCR (see, e.g., Sano et al. *Science*. 258(1992):120-2.), proximity extension assay (see, e.g., Thorsen et al. *Journal of Translational Medicine*. 11(2013):253, US20130288249A1, US9777315B2), Luminex assay, or homogenous assays such as ALPHAscreen (see, e.g., Application Note. *Nature Methods* 5, (2008), US5898005A, US5861319A), time-resolved fluorescence resonance energy transfer (TR-FRET see e.g., US20130203068A1 and WO1998015830A2), time-resolved fluorescence (TRF), fluorescent oxygen channeling immunoassay (FOCI), or luminescent oxygen channeling immunoassay (LOCIT<sup>TM</sup>; see e.g. Ullman et al. *Proc Natl Acad Sci U S A*. 91(1994):5426-5430 or Ullman et al. *Clin Chem*. 1996 Sep;42(9):1518-26 for exemplary methods and reagents).

**[0049]** In some embodiments, the compositions, methods and devices described herein make use of labeled molecules in various sandwich, competitive, or non-competitive assay formats

to determine expression levels of biomarkers described herein. Such methods generate a signal that is related to the presence or amount of one or more of the proteins described herein. Suitable assay formats also include chromatographic, mass spectrographic, and protein "blotting" methods. Additionally, certain methods and devices, such as biosensors, optical immunoassays, immunosorbent assays, and enzyme immunoassays, may be employed to determine the presence or amount of analytes without the need for a labeled molecule. Examples of enzyme immunoassays (EIA) include chemiluminescent enzyme immunoassay, electrochemiluminescence immunoassay (ECLIA), and enzyme-linked immunosorbent assay (ELISA), which are further described by Kuhle, Jens, et al. "Comparison of three analytical platforms for quantification of the neurofilament light chain in blood samples: ELISA, electrochemiluminescence immunoassay and Simoa." Clinical Chemistry and Laboratory Medicine (CCLM) 54.10 (2016): 1655-1661. Robotic instrumentation for performing these immunoassays are commercially available including, but not limited to Abbott AXSYM®, IMx®, or Commander® systems; Biolog 24i® or CLC480 systems; Beckman Coulter ACCESS®, ACCESS 2®, or Unicel Dxl 600 / 800 systems; bioMerieux VIDAS® or mini-VIDAS® systems; Chimera Biotec GmbH Imperacer® assay; Dade Behring STRATUS® system; DiaSorin LIAISON XL® or ETI-Max 300 systems; Dynex Agility® system; Gold Standard Diagnostics Thunderbolt® analyzer; Gyrolab xPlore/xPand® system; Hudson Robotics ELISA Workstation; Ortho Clinical Diagnostics Vitros® ECL or 3600 systems; Hamiltorn Robotics ELISA NIMBUS or STARlet systems; Luminex xMAP® system; PerkinElmer ALPHAscreen® or AlphaLISA®; Phadia Laboratory System 100E, 250, 1000, 2500, or 5000; Quanterix SIMOA® system; Quidel Sofia®2 POC systems; Radiometer AQT90 Flex system; Roche Diagnostics ElecSys® 2010, Cobas® 4000/6000/8000 Analyzers, or Integra® 400 Plus; c111, c311, c501, c502 family of analyzers; Seikisui Diagnostics FastPack® IP automated system; Siemens Dimension Vista® 1500 System, DPC Immulite 1000/2000 system, or DCA Vantage® Analyzer; Singulex Single Molecule Counting (SMC™) assay; Stratus® CS Acute Care Diagnostic System; Sysmex Eurolyser®; ThermoFisher MGC 240 Benchtop Analyzer; Tosoh Bioscience AIA®-360 or AIA-600II systems; UniCel Dxl 860i Synchron Access Clinical System, UniCel DxC 680i Synchron Access Clinical System, Access/ Access 2 Immunoassay System, 600 Access Immunoassay System, 600i Synchron Access Clinical System, Dxl 800 Access Immunoassay System, DxC 880i Synchron Access Clinical System; and Vital Diagnostics PathFast® point-of-care chemiluminescence immunoassay analyzer. But any suitable immunoassay may be utilized,

for example, enzyme-linked immunoassays (ELISA), radioimmunoassays (RIAs), competitive binding assays, and the like.

**[0050]** Other exemplary analytical systems include assay systems, such as, for example, optical systems containing one or more sources of radiation and/or one or more detectors. Such systems may use, for example, a light source that illuminates and a sample and a detector configured to detect light that is emitted by the sample (e.g., fluorescence spectroscopy), optical density (e.g., the portion of light that passes through the sample), and/or light that is diffracted by sample (e.g., diffraction optics). An analytical system may use, for example, ELISA (enzyme-linked immunosorbent assay). An analytical system may use, for example, LOCI (luminescent oxygen channeling), FOCI (fluorescent oxygen channeling), or ALPHAscreen. An analytical technique may involve incubating and/or diluting a sample before or during the analysis/assaying of the sample.

**[0051]** In some embodiments, the compositions, methods and devices described herein make use of fluorescent oxygen channeling immunoassay (FOCI) compositions and methods. FOCI is generally described in U.S. Patent Nos. 5,807,675; 5,616,719; and 7,635,571, the entire contents of which are expressly incorporated herein by reference. In some embodiments, a first analyte-binding agent that is capable of binding to an analyte and comprises a photosensitizer is used in combination with a second analyte-binding agent comprising a fluorogenic dye. In some embodiments, the photosensitizer of the first analyte-binding agent generates singlet oxygen in an excited state thereby causing the fluorogenic dye of the second analyte-binding agent to emit fluorescence upon reacting with the singlet oxygen. In some embodiments, the emitted fluorescence can be detected to, e.g., determine the presence and/or absence of the analyte and/or to quantitate and/or analyze the analyte in a sample. In some embodiments, the first and the second analyte-binding agents bind to the same region (e.g., epitope) of the analyte (e.g., a protein). For example, in some embodiments, the first and the second analyte-binding agents comprise the same type of analyte-binding moiety or reagent (e.g., the same antibody). In some embodiments, the first and the second analyte-binding agents bind to separate regions (e.g., epitopes) of the analyte (e.g., a protein). In some embodiments, the first and the second analyte-binding agents bind to the separate regions of the analyte (e.g., a protein) that do not spatially overlap. In some embodiments, the first analyte-binding agent and the second analyte-binding agent are configured such that when both analyte-binding agents are bound to the analyte, the singlet oxygen generated by photosensitizer of the first analyte-binding agent is in close proximity to

the fluorogenic dye of the second analyte-binding agent. In some embodiments, the first and/or second analyte binding agent(s) is an antigen-binding agent (e.g., an antibody). In some embodiments, the first and/or second analyte binding agent(s) is an affimer. In some embodiments, the first and/or second analyte binding agent(s) is an antigen-binding agent is an aptamer. In some embodiments, both the photosensitizer and fluorogenic dye are provided in the form of beads.

**[0052]** In some cases, arrays can use different probes (e.g., antibodies, scFvs, Fab fragments) attached to different particles or beads. In such arrays, the identity of which probe is attached to which particle or beads may be determinable from an encoding system. The probes can be antibodies or antigen-binding fragments or derivatives thereof.

**[0053]** The data pertaining to the sample can be compared to data pertaining to one or more control samples. In some cases, control samples can be samples from the same patient at different times. In some cases, the one or more control samples can comprise one or more samples from healthy subjects, unhealthy subjects, or a combination thereof. The one or more control samples can comprise one or more samples from healthy subjects, subjects suffering from pregnancy-associated conditions other than preeclampsia, subjects suffering chronic conditions along with pregnancy associated conditions, or subjects suffering from chronic conditions alone.

**[0054]** In some instances, the expression level data for various samples is used to develop or train an algorithm or classifier provided herein. In some instances, where the subject is a patient, such as a pregnant female; gene expression levels are measured in a sample from the patient and a classifier or algorithm (e.g., trained algorithm) is applied to the resulting data in order to detect, predict, monitor, rule out, or estimate the risk of a pregnancy-associated condition such as preeclampsia.

**[0055]** In some cases, analysis of expression levels initially provides a measurement of the expression level of each of several individual biomarkers. The expression level can be absolute in terms of a concentration of a biomarker, or relative in terms of a relative concentration of an expression product of interest to another biomarker in the sample. For example, relative expression levels of proteins can be expressed with respect to the expression level of a house-keeping or structural protein in the sample. Relative expression levels can also be determined by simultaneously analyzing differentially labeled samples bound to the same array. Expression levels can also be expressed in arbitrary units, for example, related to signal intensity.

*Classifiers and classifier probe sets*

**[0056]** Disclosed herein is the use of a classification system comprising one or more classifiers. In some instances, the classifier is a 2-way classifier. In some instances, a two-way classifier can classify a sample from a pregnant patient into one of two classes comprising preeclampsia (PreE) and non-preeclampsia (nonPreE). In some instances, the classifier may be used classify a subject as not needing treatment for preeclampsia. In some instances, a multi-way classifier may be used (e.g., preeclampsia, non-preeclampsia, and indeterminate).

**[0057]** Classifiers and/or classifier probe sets (e.g., antibody sets) can be used to either rule-in or rule-out a sample as from a patient to be treated for preeclampsia. For example, a classifier can be used to classify a sample as being from a healthy subject. Alternatively, a classifier can be used to classify a sample as being from an unhealthy subject. Alternatively, or additionally, classifiers can be used to either rule-in or rule-out a sample as being from a subject who should be treated for preeclampsia.

*Data Analysis Systems and Methods*

**[0058]** The methods, kits, and systems disclosed herein can comprise algorithms or uses thereof. The one or more algorithms can be used to classify one or more samples from one or more subjects. The one or more algorithms can be applied to data from one or more samples. The data can comprise biomarker expression data.

**[0059]** The methods disclosed herein can comprise assigning a classification to one or more samples from one or more subjects. Assigning the classification to the sample can comprise applying an algorithm to the expression level. In some cases, the gene expression levels are inputted to a data analysis system comprising a trained algorithm for classifying the sample as one of the conditions comprising preeclampsia, eclampsia, non-preeclampsia, chronic hypertension, gestational hypertension, or HELLP (Hemolysis, Elevated Liver enzymes, and Low Platelet count—see e.g., Weinstein et al. Am J Obstet Gynecol. 142(1982):159-67) syndrome. In some embodiments the algorithm can, as part of its execution, calculate an index for a sample and compare the sample index to a threshold value; the predefined relationship can be indicative of a likelihood of the sample belonging to a particular classification.

**[0060]** The algorithm can provide a record of its output including a classification of a sample and/or a confidence level. In some instances, the output of the algorithm can be the

possibility of the subject of having a condition comprising preeclampsia, eclampsia, chronic hypertension, gestational hypertension, or HELLP syndrome.

**[0061]** A data analysis system can be a trained algorithm. The algorithm can comprise a linear classifier. In some instances, the linear classifier comprises one or more of linear discriminant analysis, Fisher's linear discriminant, Naïve Bayes classifier, Logistic regression, Perceptron, Support vector machine, or a combination thereof. The linear classifier can be a support vector machine (SVM) algorithm. The algorithm can comprise a two-way classifier. The two-way classifier can comprise one or more decision tree, random forest, Bayesian network, support vector machine, neural network, or logistic regression algorithms.

**[0062]** The algorithm can comprise one or more linear discriminant analysis (LDA), Basic perceptron, Elastic Net, logistic regression, (Kernel) Support Vector Machines (SVM), Diagonal Linear Discriminant Analysis (DLDA), Golub Classifier, Parzen-based, (kernel) Fisher Discriminant Classifier, k-nearest neighbor, Iterative RELIEF, Classification Tree, Maximum Likelihood Classifier, Random Forest, Nearest Centroid, Prediction Analysis of Microarrays (PAM), k-medians clustering, Fuzzy C-Means Clustering, Gaussian mixture models, graded response (GR), Gradient Boosting Method (GBM), Elastic-net logistic regression, logistic regression, or a combination thereof. The algorithm can comprise a Diagonal Linear Discriminant Analysis (DLDA) algorithm. The algorithm can comprise a Nearest Centroid algorithm. The algorithm can comprise a Random Forest algorithm. In some embodiments, for discrimination of preeclampsia and non-preeclampsia, the performance of logistic regression, random forest, and gradient boosting method (GBM) is superior to that of linear discriminant analysis (LDA), neural network, and support vector machine (SVM).

#### *Biomarkers/Gene Expression Products*

**[0063]** The term "biomarker" refers to a measurable indicator of some biological state or condition. In some instances, a biomarker can be a substance found in a subject, a quantity of the substance, or some other indicator. For example, a biomarker can be the amount of a protein and/or other gene expression products in a sample. In some embodiments, a biomarker is a full-length, unmodified protein. In other embodiments, a biomarker is an alternatively spliced, post-translationally cleaved, or post-translationally chemically modified (e.g., methylated, phosphorylated, glycosylated, formylated, etc) protein.

**[0064]** The methods, compositions and systems as described here also relate to the use of biomarker panels and/or gene expression products for purposes of identification, diagnosis, classification, treatment or to otherwise characterize various conditions of pregnant patients comprising NonPreE, PreE, chronic hypertension, gestational hypertension, or HELLP syndrome. Sets of biomarkers and/or gene expression products useful for classifying biological samples are provided, as well as methods of obtaining such sets of biomarkers. Often, the pattern of levels of gene expression biomarkers in a panel (also known as a signature) is determined from one or more reference samples and then used to evaluate the signature of the same panel of biomarkers in a test sample, such as by a measure of similarity between the test sample signature and the reference sample signature.

**[0065]** In some embodiments, the methods, compositions, and systems described herein may involve the detection of one or more biomarker belonging to a particular functional class of biomarkers with a connection to one or more pathophysiological features of preeclampsia (see **FIG. 16**, which shows various pathophysiological features or preeclampsia). While **Figure 16** shows various pathophysiological features, and associated biomarkers, that are thought to be associated with preeclampsia, numerous other methods for describing the pathophysiology and relationship between the markers is possible. For instance, KIM-1, CD274, and decorin can be considered as kidney damage associated proteins. Similarly, sFlt1, endoglin, pappalysin 2, and decorin can be considered as angiogenesis-associated proteins. A person of skill in the art will recognize that various other classification schemes could be similarly used.

**[0066]** Without wishing to be limited by theory, preeclampsia is thought to originate in abnormal trophoblast invasion, which results in incomplete spiral artery remodeling and hypoperfusion of the placenta, and that this hypoperfusion of the placenta triggers dysfunction in multiple body systems causing the signs and symptoms of preeclampsia. Such dysfunctional systems can include, as a result of placental hypoperfusion, angiogenesis and endothelial function, as evidenced e.g. by imbalances in pro-and-anti-angiogenic factors, many of which are released by the placenta in response to the abnormal physiology of preeclampsia, and which disrupt vascular homeostasis in the mother's body. SFLT1 (Soluble FMS-like tyrosine kinase 1, a tyrosine-protein kinase that acts as a cell-surface receptor for VEGFA, VEGFB and PIGF and decreases towards term, and plays an essential role in the development of embryonic vasculature), PIgf (Placental growth factor, a proangiogenic protein peaking at 30 weeks of gestation that stimulates endothelial cell growth, proliferation,

and migration), DCN (Decorin, which is a functional component of the extracellular matrix and plays a role in tissue repair and regulation of cell adhesion and migration by binding to ECM molecules), ENG (Endoglin, which in its soluble form, sENG is a powerful antiangiogenic molecule, and acts by inhibiting TGF- $\beta$ 1 binding), and FGF21 (Fibroblast growth factor 21, which has been demonstrated to be expressed in placental syncytiotrophoblasts, and is both an adipokine and a regulator of glucose transport) are considered to be markers of angiogenesis dysfunction in preeclampsia. Another such dysfunctional system is oxygen signaling, which results from hypoperfusion of the placenta, and leads to upregulation of oxidative stress factors. KIM-1 (Kidney Injury Molecule-1) is considered to be a marker of dysfunction in oxygen signaling in preeclampsia, as its expression is known to increase in response to local hypoxia/ischemia in proximal renal tubule cells. Another such dysfunctional system is altered immune response, which may result from inflammation of placental tissues as a result of their hypoperfusion. CLEC4A (C-type Lectin domain family member A, which maintains the balance of polarization of naïve Th cells into Th1 and Th2 effector cells), TFF2 (Trefoil factor 2, which is upregulated on mucosal surfaces during inflammation), and CD274/PD-L1 (cluster of differentiation 274 or programmed-death ligand 1) are considered to be markers of the dysfunctional immune response in preeclampsia. These systems are thought to interact and amplify each other, resulting in the widespread maternal vascular dysfunction and organ damage that can result from preeclampsia.

**[0067]** The methods herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers recited in the following table (Table A).

**Table A: High Priority Biomarkers for Identifying or Ruling Out Preeclampsia**

	<i>Biomarker</i>
<b>1</b>	PIGF
<b>2</b>	SFLT.1
<b>3</b>	KIM1
<b>4</b>	CLEC4A

**[0068]** The methods herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers recited in the following table (Table B).

**Table B: High Priority Biomarkers for Identifying or Ruling Out Preeclampsia**

	<i>Biomarker</i>
<b>5</b>	FGF21
<b>6</b>	ENDOGLIN
<b>7</b>	DECORIN
<b>8</b>	CD274

9	HGF
10	TFF2
11	PAPP.A2

**[0069]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from (e.g., based on analysis from) one or more biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from two or more biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from three or more biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one biomarker selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from two biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from three biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from four biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from five biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from all the biomarkers identified in Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than 3 biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than 4 biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than 5 biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than 6 biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than 7 biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than 8 biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g.

preeclampsia) from no more than 9 biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than 10 biomarkers selected from Table A and Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than 11 biomarkers selected from Table A and Table B.

**[0070]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers selected from Table A and one or more biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 2 or more biomarkers selected from Table A and one or more biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 or more biomarkers selected from Table A and one or more biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 4 biomarkers selected from Table A and one or more biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and one or more biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and two or more biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and three or more biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and four or more biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and five or more biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and six or more biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and one biomarker selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and two biomarkers selected from Table B. In some cases,

the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and three biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and four biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and five biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and six biomarkers selected from Table B. In some cases, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from 3 biomarkers selected from Table A and seven biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than one biomarker selected from Table A and no more than 2 biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than two biomarkers selected from Table A and no more than 2 biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than three biomarkers selected from Table A and no more than 2 biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than one biomarker selected from Table A and no more than 3 biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than two biomarkers selected from Table A and no more than 3 biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than three biomarkers selected from Table A and no more than 3 biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than one biomarker selected from Table A and no more than 3 biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than one biomarker selected from Table A and no more than 4 biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g.

preeclampsia) from no more than two biomarkers selected from Table A and no more than 4 biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than three biomarkers selected from Table A and no more than 4 biomarkers selected from Table B. The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from no more than one biomarker selected from Table A and no more than 4 biomarkers selected from Table B.

**[0071]** In some embodiments, the methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from a panel of markers comprising sFLT-1, PIgf, FGF21, CLEC4a, endoglin, CD274, and decorin.

**[0072]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from (e.g., based on analysis from) sFlt.1, PIgf, KIM1, and CLEC4A; sFlt.1, PIgf, KIM1, CLEC4A, and FGF21; sFlt.1, PIgf, KIM1, CLEC4A, and CD274; sFlt.1, PIgf, KIM1, CLEC4A, and ENDOGLIN; sFlt.1, PIgf, KIM1, CLEC4A, and DECORIN; sFlt.1, PIgf, KIM1, CLEC4A, FGF21, and ENDOGLIN; sFlt.1, PIgf, KIM1, CLEC4A, FGF21, and CD274; sFlt.1, PIgf, KIM1, CLEC4A, ENDOGLIN, and CD274; sFlt.1, PIgf, KIM1, CLEC4A, ENDOGLIN, and DECORIN; sFlt.1, PIgf, KIM1, CLEC4A, FGF21, ENDOGLIN, and CD274; sFlt.1, PIgf, KIM1, CLEC4A, FGF21, ENDOGLIN, CD274, and DECORIN; PIgf, KIM1, CLEC4A, and ENDOGLIN; PIgf, KIM1, CLEC4A, ENDOGLIN, and DECORIN; sFlt.1, PIgf, KIM1, TFF2, FGF21, and DECORIN; sFlt.1, PIgf, KIM1, CLEC4A, CD274, and ENDOGLIN; or HGF, SYND1, CLEC4A, sFlt.1, PIgf, KIM1, CLEC4A, and FGF21.

**[0073]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from (e.g., based on analysis from) the following sets of four biomarkers optionally in combination with PIgf: SFLT1, KIM1, CLEC4A, FGF21; SFLT1, KIM1, CLEC4A, endoglin; SFLT1, KIM1, CLEC4A, decorin; SFLT1, KIM1, CLEC4A, CD274; SFLT1, KIM1, CLEC4A, HGF; SFLT1, KIM1, CLEC4A, TFF2; SFLT1, KIM1, CLEC4A, PAPP.A2; SFLT1, KIM1, FGF21, endoglin; SFLT1, KIM1, FGF21, decorin; SFLT1, KIM1, FGF21, CD274; SFLT1, KIM1, FGF21, HGF; SFLT1, KIM1, FGF21, TFF2; SFLT1, KIM1, FGF21, PAPP.A2; SFLT1, KIM1, endoglin, decorin; SFLT1, KIM1, endoglin, CD274; SFLT1, KIM1, endoglin, HGF; SFLT1, KIM1, endoglin, TFF2; SFLT1, KIM1, endoglin, PAPP.A2; SFLT1, KIM1, decorin, CD274; SFLT1, KIM1, decorin, HGF; SFLT1, KIM1, decorin, TFF2; SFLT1, KIM1, decorin, PAPP.A2; SFLT1, KIM1, CD274, HGF; SFLT1, KIM1, CD274, TFF2; SFLT1, KIM1, CD274, PAPP.A2; SFLT1, KIM1, HGF, TFF2;

SFLT1, KIM1, HGF, PAPP.A2; SFLT1, KIM1, TFF2, PAPP.A2; SFLT1, CLEC4A, FGF21, endoglin; SFLT1, CLEC4A, FGF21, decorin; SFLT1, CLEC4A, FGF21, CD274; SFLT1, CLEC4A, FGF21, HGF; SFLT1, CLEC4A, FGF21, TFF2; SFLT1, CLEC4A, FGF21, PAPP.A2; SFLT1, CLEC4A, endoglin, decorin; SFLT1, CLEC4A, endoglin, CD274; SFLT1, CLEC4A, endoglin, HGF; SFLT1, CLEC4A, endoglin, TFF2; SFLT1, CLEC4A, endoglin, PAPP.A2; SFLT1, CLEC4A, decorin, CD274; SFLT1, CLEC4A, decorin, HGF; SFLT1, CLEC4A, decorin, TFF2; SFLT1, CLEC4A, decorin, PAPP.A2; SFLT1, CLEC4A, CD274, HGF; SFLT1, CLEC4A, CD274, TFF2; SFLT1, CLEC4A, CD274, PAPP.A2; SFLT1, CLEC4A, HGF, TFF2; SFLT1, FGF21, endoglin, decorin; SFLT1, FGF21, endoglin, CD274; SFLT1, FGF21, endoglin, HGF; SFLT1, FGF21, endoglin, TFF2; SFLT1, FGF21, endoglin, PAPP.A2; SFLT1, FGF21, decorin, CD274; SFLT1, FGF21, decorin, HGF; SFLT1, FGF21, decorin, TFF2; SFLT1, FGF21, decorin, PAPP.A2; SFLT1, FGF21, CD274, HGF; SFLT1, FGF21, CD274, TFF2; SFLT1, FGF21, CD274, PAPP.A2; SFLT1, FGF21, HGF, TFF2; SFLT1, FGF21, HGF, PAPP.A2; SFLT1, FGF21, TFF2, PAPP.A2; SFLT1, endoglin, decorin, CD274; SFLT1, endoglin, decorin, HGF; SFLT1, endoglin, decorin, TFF2; SFLT1, endoglin, decorin, PAPP.A2; SFLT1, endoglin, CD274, HGF; SFLT1, endoglin, CD274, TFF2; SFLT1, endoglin, CD274, PAPP.A2; SFLT1, endoglin, HGF, TFF2; SFLT1, endoglin, HGF, PAPP.A2; SFLT1, endoglin, TFF2, PAPP.A2; SFLT1, decorin, CD274, HGF; SFLT1, decorin, CD274, TFF2; SFLT1, decorin, CD274, PAPP.A2; SFLT1, decorin, HGF, TFF2; SFLT1, decorin, HGF, PAPP.A2; SFLT1, decorin, TFF2, PAPP.A2; SFLT1, CD274, HGF, TFF2; SFLT1, CD274, HGF, PAPP.A2; SFLT1, CD274, TFF2, PAPP.A2; SFLT1, HGF, TFF2, PAPP.A2; KIM1, CLEC4A, FGF21, endoglin; KIM1, CLEC4A, FGF21, decorin; KIM1, CLEC4A, FGF21, CD274; KIM1, CLEC4A, FGF21, HGF; KIM1, CLEC4A, FGF21, TFF2; KIM1, CLEC4A, FGF21, PAPP.A2; KIM1, CLEC4A, endoglin, decorin; KIM1, CLEC4A, endoglin, CD274; KIM1, CLEC4A, endoglin, HGF; KIM1, CLEC4A, endoglin, TFF2; KIM1, CLEC4A, endoglin, PAPP.A2; KIM1, CLEC4A, decorin, CD274; KIM1, CLEC4A, decorin, HGF; KIM1, CLEC4A, decorin, TFF2; KIM1, CLEC4A, decorin, PAPP.A2; KIM1, CLEC4A, CD274, HGF; KIM1, CLEC4A, CD274, TFF2; KIM1, CLEC4A, HGF, PAPP.A2; KIM1, CLEC4A, TFF2, PAPP.A2; KIM1, FGF21, endoglin, decorin; KIM1, FGF21, endoglin, CD274; KIM1, FGF21, endoglin, HGF; KIM1, FGF21, endoglin, TFF2; KIM1, FGF21, endoglin, PAPP.A2; KIM1, FGF21, decorin, CD274; KIM1, FGF21, decorin,

HGF; KIM1, FGF21, decorin, TFF2; KIM1, FGF21, decorin, PAPP.A2; KIM1, FGF21, CD274, HGF; KIM1, FGF21, CD274, TFF2; KIM1, FGF21, CD274, PAPP.A2; KIM1, FGF21, HGF, TFF2; KIM1, FGF21, HGF, PAPP.A2; KIM1, FGF21, TFF2, PAPP.A2; KIM1, endoglin, decorin, CD274; KIM1, endoglin, decorin, HGF; KIM1, endoglin, decorin, TFF2; KIM1, endoglin, decorin, PAPP.A2; KIM1, endoglin, CD274, HGF; KIM1, endoglin, CD274, TFF2; KIM1, endoglin, CD274, PAPP.A2; KIM1, endoglin, HGF, TFF2; KIM1, endoglin, HGF, PAPP.A2; KIM1, endoglin, TFF2, PAPP.A2; KIM1, decorin, CD274, HGF; KIM1, decorin, CD274, TFF2; KIM1, decorin, CD274, PAPP.A2; KIM1, decorin, HGF, TFF2; KIM1, decorin, HGF, PAPP.A2; KIM1, decorin, TFF2, PAPP.A2; KIM1, CD274, HGF, TFF2; KIM1, CD274, HGF, PAPP.A2; KIM1, CD274, TFF2, PAPP.A2; KIM1, HGF, TFF2, PAPP.A2; CLEC4A, FGF21, endoglin, decorin; CLEC4A, FGF21, endoglin, CD274; CLEC4A, FGF21, endoglin, HGF; CLEC4A, FGF21, endoglin, TFF2; CLEC4A, FGF21, endoglin, PAPP.A2; CLEC4A, FGF21, decorin, CD274; CLEC4A, FGF21, decorin, HGF; CLEC4A, FGF21, decorin, TFF2; CLEC4A, FGF21, decorin, PAPP.A2; CLEC4A, FGF21, CD274, HGF; CLEC4A, FGF21, CD274, TFF2; CLEC4A, FGF21, CD274, PAPP.A2; CLEC4A, FGF21, HGF, TFF2; CLEC4A, FGF21, HGF, PAPP.A2; CLEC4A, FGF21, TFF2, PAPP.A2; CLEC4A, endoglin, decorin, CD274; CLEC4A, endoglin, decorin, HGF; CLEC4A, endoglin, decorin, TFF2; CLEC4A, endoglin, decorin, PAPP.A2; CLEC4A, endoglin, CD274, HGF; CLEC4A, endoglin, CD274, TFF2; CLEC4A, endoglin, CD274, PAPP.A2; CLEC4A, endoglin, HGF, TFF2; CLEC4A, endoglin, HGF, PAPP.A2; CLEC4A, endoglin, TFF2, PAPP.A2; CLEC4A, decorin, CD274, HGF; CLEC4A, decorin, CD274, TFF2; CLEC4A, decorin, CD274, PAPP.A2; CLEC4A, decorin, HGF, TFF2; CLEC4A, decorin, HGF, PAPP.A2; CLEC4A, decorin, TFF2, PAPP.A2; CLEC4A, CD274, HGF, PAPP.A2; CLEC4A, CD274, TFF2, PAPP.A2; CLEC4A, HGF, TFF2, PAPP.A2; FGF21, endoglin, decorin, CD274; FGF21, endoglin, decorin, HGF; FGF21, endoglin, decorin, TFF2; FGF21, endoglin, decorin, PAPP.A2; FGF21, endoglin, CD274, HGF; FGF21, endoglin, CD274, TFF2; FGF21, endoglin, CD274, PAPP.A2; FGF21, endoglin, HGF, TFF2; FGF21, endoglin, HGF, PAPP.A2; FGF21, endoglin, TFF2, PAPP.A2; FGF21, decorin, CD274, HGF; FGF21, decorin, CD274, TFF2; FGF21, decorin, HGF, TFF2; FGF21, decorin, HGF, PAPP.A2; FGF21, decorin, TFF2, PAPP.A2; FGF21, CD274, HGF, TFF2; FGF21, CD274, HGF, PAPP.A2; FGF21, CD274, TFF2, PAPP.A2; FGF21, HGF, TFF2, PAPP.A2; endoglin, decorin, CD274, HGF; endoglin, decorin, CD274, TFF2; endoglin, decorin, CD274, PAPP.A2; endoglin,

decorin, HGF, TFF2; endoglin, decorin, HGF, PAPP.A2; endoglin, decorin, TFF2, PAPP.A2; endoglin, CD274, HGF, TFF2; endoglin, CD274, HGF, PAPP.A2; endoglin, CD274, TFF2, PAPP.A2; endoglin, HGF, TFF2, PAPP.A2; decorin, CD274, HGF, TFF2; decorin, CD274, HGF, PAPP.A2; decorin, CD274, TFF2, PAPP.A2; or decorin, HGF, TFF2, PAPP.A2; CD274, HGF, TFF2, PAPP.A2

**[0074]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from (e.g., based on analysis from) the following sets of three biomarkers optionally in combination with PlGF: SFLT1, KIM1, CLEC4A; SFLT1, KIM1, FGF21; SFLT1, KIM1, endoglin; SFLT1, KIM1, decorin; SFLT1, KIM1, CD274; SFLT1, KIM1, HGF; SFLT1, KIM1, TFF2; SFLT1, KIM1, PAPP.A2; SFLT1, CLEC4A, FGF21; SFLT1, CLEC4A, endoglin; SFLT1, CLEC4A, decorin; SFLT1, CLEC4A, CD274; SFLT1, CLEC4A, HGF; SFLT1, CLEC4A, TFF2; SFLT1, CLEC4A, PAPP.A2; SFLT1, FGF21, endoglin; SFLT1, FGF21, decorin; SFLT1, FGF21, CD274; SFLT1, FGF21, HGF; SFLT1, FGF21, TFF2; SFLT1, FGF21, PAPP.A2; SFLT1, endoglin, decorin; SFLT1, endoglin, CD274; SFLT1, endoglin, HGF; SFLT1, endoglin, TFF2; SFLT1, endoglin, PAPP.A2; SFLT1, decorin, CD274; SFLT1, decorin, HGF; SFLT1, decorin, TFF2; SFLT1, decorin, PAPP.A2; SFLT1, CD274, HGF; SFLT1, CD274, TFF2; SFLT1, CD274, PAPP.A2; SFLT1, HGF, TFF2; SFLT1, HGF, PAPP.A2; SFLT1, TFF2, PAPP.A2; KIM1, CLEC4A, FGF21; KIM1, CLEC4A, endoglin; KIM1, CLEC4A, decorin; KIM1, CLEC4A, CD274; KIM1, CLEC4A, HGF; KIM1, CLEC4A, TFF2; KIM1, CLEC4A, PAPP.A2; KIM1, FGF21, endoglin; KIM1, FGF21, decorin; KIM1, FGF21, CD274; KIM1, FGF21, HGF; KIM1, FGF21, TFF2; KIM1, FGF21, PAPP.A2; KIM1, endoglin, decorin; KIM1, endoglin, CD274; KIM1, endoglin, HGF; KIM1, endoglin, TFF2; KIM1, endoglin, PAPP.A2; KIM1, decorin, CD274; KIM1, decorin, HGF; KIM1, decorin, TFF2; KIM1, decorin, PAPP.A2; KIM1, CD274, HGF; KIM1, CD274, TFF2; KIM1, CD274, PAPP.A2; KIM1, HGF, TFF2; KIM1, HGF, PAPP.A2; KIM1, TFF2, PAPP.A2; CLEC4A, FGF21, endoglin; CLEC4A, FGF21, decorin; CLEC4A, FGF21, CD274; CLEC4A, FGF21, PAPP.A2; CLEC4A, endoglin, decorin; CLEC4A, endoglin, CD274; CLEC4A, endoglin, HGF; CLEC4A, endoglin, TFF2; CLEC4A, endoglin, PAPP.A2; CLEC4A, decorin, CD274; CLEC4A, decorin, HGF; CLEC4A, decorin, TFF2; CLEC4A, decorin, PAPP.A2; CLEC4A, CD274, HGF; CLEC4A, CD274, TFF2; CLEC4A, CD274, PAPP.A2; CLEC4A, HGF, TFF2; CLEC4A, HGF, PAPP.A2; CLEC4A, TFF2, PAPP.A2; FGF21, endoglin, decorin; FGF21, endoglin, CD274; FGF21, endoglin, HGF; FGF21,

endoglin, TFF2; FGF21, endoglin, PAPP.A2; FGF21, decorin, CD274; FGF21, decorin, HGF; FGF21, decorin, TFF2; FGF21, decorin, PAPP.A2; FGF21, CD274, HGF; FGF21, CD274, TFF2; FGF21, CD274, PAPP.A2; FGF21, HGF, TFF2; FGF21, HGF, PAPP.A2; FGF21, TFF2, PAPP.A2; endoglin, decorin, CD274; endoglin, decorin, HGF; endoglin, decorin, TFF2; endoglin, decorin, PAPP.A2; endoglin, CD274, HGF; endoglin, CD274, TFF2; endoglin, CD274, PAPP.A2; endoglin, HGF, TFF2; endoglin, HGF, PAPP.A2; endoglin, TFF2, PAPP.A2; decorin, CD274, HGF; decorin, CD274, TFF2; decorin, CD274, PAPP.A2; decorin, HGF, TFF2; decorin, HGF, PAPP.A2; decorin, TFF2, PAPP.A2; CD274, HGF, TFF2; CD274, HGF, PAPP.A2; CD274, TFF2, PAPP.A2; or HGF, TFF2, PAPP.A2.

**[0075]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from (e.g., based on analysis from) the following sets of three biomarkers optionally in combination with PIgf: SFLT1, KIM1; SFLT1, CLEC4A; SFLT1, FGF21; SFLT1, endoglin; SFLT1, decorin; SFLT1, CD274; SFLT1, HGF; SFLT1, TFF2; SFLT1, PAPP.A2; KIM1, CLEC4A; KIM1, FGF21; KIM1, endoglin; KIM1, decorin; KIM1, CD274; KIM1, HGF; KIM1, TFF2; KIM1, PAPP.A2; CLEC4A, FGF21; CLEC4A, endoglin; CLEC4A, decorin; CLEC4A, CD274; CLEC4A, HGF; CLEC4A, TFF2; CLEC4A, PAPP.A2; FGF21, endoglin; FGF21, decorin; FGF21, CD274; FGF21, HGF; FGF21, TFF2; FGF21, PAPP.A2; endoglin, decorin; endoglin, CD274; endoglin, HGF; endoglin, TFF2; endoglin, PAPP.A2; decorin, CD274; decorin, HGF; decorin, TFF2; decorin, PAPP.A2; CD274, HGF; CD274, TFF2; CD274, PAPP.A2; HGF, TFF2; HGF, PAPP.A2; TFF2, PAPP.A2.

**[0076]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from (e.g., based on analysis from) the following sets of biomarkers: PIgf, sFLT1, KIM1; PIgf, sFLT1, CLEC4A; PIgf, sFLT1, FGF21; PIgf, sFLT1, Decorin; PIgf, sFLT1, CD274; PIgf, sFLT1, HGF; PIgf, sFLT1, TFF2; PIgf, sFLT1, PAPP-A2; PIgf, Endoglin, KIM1; PIgf, Endoglin, CLEC4A; PIgf, Endoglin, FGF21; PIgf, Endoglin, Decorin; PIgf, Endoglin, CD274; PIgf, Endoglin, HGF; PIgf, Endoglin, TFF2; PIgf, Endoglin, PAPP-A2; PIgf, KIM1, CLEC4A; PIgf, KIM1, FGF21; PIgf, KIM1, Decorin; PIgf, KIM1, CD274; PIgf, KIM1, HGF; PIgf, KIM1, TFF2; PIgf, KIM1, PAPP-A2; PIgf, CLEC4A, FGF21; PIgf, CLEC4A, Decorin; PIgf, CLEC4A, CD274; PIgf, CLEC4A, HGF; PIgf, CLEC4A, TFF2; PIgf, CLEC4A, PAPP-A2; PIgf, CD274, CLEC4A; PIgf, CD274, FGF21; PIgf, CD274, HGF; PIgf, CD274, TFF2; PIgf, CD274, PAPP-A2; PIgf, Decorin, CLEC4A; PIgf, Decorin, FGF21; PIgf, Decorin, HGF; PIgf,

Decorin, TFF2; PIgf, Decorin, PAPP-A2; PIgf, FGF21, TFF2, Decorin; PIgf, FGF21, TFF2, CD274; PIgf, FGF21, TFF2, HGF; PIgf, FGF21, TFF2; PIgf, FGF21, TFF2, PAPP-A2; PIgf, Endoglin, PAPP-A2, DECORIN, KIM1; PIgf, Endoglin, PAPP-A2, DECORIN, CLEC4A; PIgf, Endoglin, PAPP-A2, DECORIN, FGF21; PIgf, Endoglin, PAPP-A2, DECORIN, CD274; PIgf, Endoglin, PAPP-A2, DECORIN, HGF; PIgf, Endoglin, PAPP-A2, DECORIN, TFF2.

[0077] The methods provided herein can comprise identifying or ruling out a condition from one or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2 (chemokine C-C motif ligand 2), CD134 (cluster of differentiation 134), DCN, HGF (hepatocyte growth factor), NOS3 (nitric oxide synthase 3), PIgf, CD274, CDCP1 (cub domain containing protein 1), FGF-21, TGF $\alpha$  (transforming growth factor alpha), UPA (urokinase-type plasminogen activator), CLEC4A, CLEC4C (C-type lectin domain family 4 member C), ZBTB16 (Zinc Finger And BTB Domain Containing 16), APLP1 (Amyloid Beta Precursor Like Protein 1), DPP7 (Dipeptidyl Peptidase 7), GRAP2 (GRB2 Related Adaptor Protein 2), ITGB7 (Integrin Subunit Beta 7), PAG1 (Phosphoprotein Membrane Anchor With Glycosphingolipid Microdomains 1), TFF2, AMN (Amnion Associated Transmembrane Protein), CAPG (Capping Actin Protein, Gelsolin Like), CLEC1A5, FES (Tyrosine-protein kinase Fes/Fps), KIM1, PGF (Placental Growth Factor), ERBB4 (Erb-B2 Receptor Tyrosine Kinase 4), GPNMB (Glycoprotein Nmb), PPY (Pancreatic Polypeptide), or SYND1 (Syndecan 1), and any combination thereof (“Group 1”). In some cases, preeclampsia of a pregnant patient can be detected from one or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from two or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from three or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4,

GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from four or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from five or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from six or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from seven or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from eight or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from nine or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from ten or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any

combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from eleven or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from twelve or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from thirteen or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from fourteen or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from fifteen or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from sixteen or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from seventeen or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof.

thereof. In some cases, preeclampsia of a pregnant patient can be detected from eighteen or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from nineteen or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than twenty biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than nineteen biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eighteen biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than seventeen biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than sixteen biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof.

any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than fifteen biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than fourteen biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than thirteen biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than twelve biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eleven biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than ten biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than nine biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof.

any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eight biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than seven biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than six biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than five biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than four biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than three biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 biomarkers selected from Table 2, Table 3, Table 4, Table 5, CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16,

APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof.

**[0078]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof (“Group 2”). In some cases, preeclampsia of a pregnant patient can be detected from one or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from two or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from three or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from four or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from five or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from six or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from seven or more biomarkers selected from Table 2, Table 3, Table 4, Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from eight or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from nine or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from ten or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from eleven or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from twelve or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from thirteen or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from fourteen or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be

detected from fifteen or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from sixteen or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from seventeen or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from eighteen or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from nineteen or more biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than twenty biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than nineteen biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eighteen biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than seventeen biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than sixteen biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than fifteen biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than fourteen biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than thirteen biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than twelve biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eleven biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than ten biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than nine

biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eight biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than seven biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than six biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than five biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than four biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than three biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 biomarkers selected from Table 2, Table 3, Table 4, or Table 5, and any combination thereof.

**[0079]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof (“Group 3”). In some cases, preeclampsia of a pregnant patient can be detected from one or more biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from two or more biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from three or more biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from four or more biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from five or more biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from six or more biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from seven or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from eight or more biomarkers selected from Table 2, Table 3, or Table 4, and

any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from nine or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from ten or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from eleven or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from twelve or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from thirteen or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from fourteen or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from fifteen or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from sixteen or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from seventeen or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from eighteen or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from nineteen or more biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than twenty biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than nineteen biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eighteen biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than seventeen biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than sixteen biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than fifteen biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof.

combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than fourteen biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than thirteen biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than twelve biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eleven biomarkers selected from Table 2, Table 3, or Table 4, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than ten biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than nine biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eight biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than seven biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than six biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than five biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than four biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than three biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 biomarkers selected from Table 2, Table 3, or Table 5, and any combination thereof.

**[0080]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers selected from Table 2 or Table 5, and any combination thereof (“Group 4”). In some cases, preeclampsia of a pregnant patient can be detected from one or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from two or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases,

preeclampsia of a pregnant patient can be detected from three or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from four or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from five or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from six or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from seven or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from eight or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from nine or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from ten or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from 11, 12, 13, 14, 15, 16, 17, 18, or 19 or more biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than 20, 19, 18, 17, 16, 15, 14, 13, 12, or 11 biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than ten biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than nine biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eight biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than seven biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than six biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than five biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than four biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than three biomarkers selected from Table 2 or Table 5, and any combination thereof. In some cases,

preeclampsia of a pregnant patient can be detected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 biomarkers selected from Table 2 or Table 5, and any combination thereof.

**[0081]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof (“Group 5”). In some cases, preeclampsia of a pregnant patient can be detected from one or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from two or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from three or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from four or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from five or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from six or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof.

or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from seven or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from eight or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from nine or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from ten or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from 11, 12, 13, 14, 15, 16, 17, 18, or 19 or more biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than 20, 19, 18, 17, 16, 15, 14, 13, 12, or 11 biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than ten biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than nine biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PIgf, CD274, CDCP1,

FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than eight biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than seven biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than six biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than five biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than four biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from no more than three biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof. In some cases, preeclampsia of a pregnant patient can be detected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 biomarkers selected from CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG,

CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, or SYND1, and any combination thereof.

**[0082]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from one or more biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from two or more biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from three or more biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from four or more biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from five or more biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from six or more biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from nine biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from no more than eight biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from no more than seven biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from no more than six biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from no more than five biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from no more than four biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from no more than three biomarkers selected from Table 5. In some cases, preeclampsia of a pregnant patient can be detected from 1, 2, 3, 4, 5, 6, 7, 8, or 9 biomarkers selected from Table 5.

**[0083]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from one or more biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from two or more biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from three or more biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from four or more biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from five or more biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from six or more biomarkers selected from Table 2. In some cases,

preeclampsia of a pregnant patient can be detected from nine biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from no more than eight biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from no more than seven biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from no more than six biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from no more than five biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from no more than four biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from no more than three biomarkers selected from Table 2. In some cases, preeclampsia of a pregnant patient can be detected from 1, 2, 3, 4, 5, 6, 7, 8, or 9 biomarkers selected from Table 2.

**[0084]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from one or more biomarkers selected from 4. In some cases, preeclampsia of a pregnant patient can be detected from two or more biomarkers selected from 4. In some cases, preeclampsia of a pregnant patient can be detected from three or more biomarkers selected from 4. In some cases, preeclampsia of a pregnant patient can be detected from four or more biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from five or more biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from six or more biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from seven or more biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from eight or more biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from nine or more biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from ten or more biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from 11, 12, 13, 14, 15, 16, 17, 18, or 19 or more biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from no more than 20, 19, 18, 17, 16, 15, 14, 13, 12, or 11 biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from no more than ten biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from no more than nine biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected

from no more than eight biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from no more than seven biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from no more than six biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from no more than five biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from no more than four biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from no more than three biomarkers selected from Table 3. In some cases, preeclampsia of a pregnant patient can be detected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 biomarkers selected from Table 3.

**[0085]** The methods provided herein can comprise identifying or ruling out a condition (e.g. preeclampsia) from one or more biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from one or more biomarkers selected from 5. In some cases, preeclampsia of a pregnant patient can be detected from two or more biomarkers selected from 5. In some cases, preeclampsia of a pregnant patient can be detected from three or more biomarkers selected from 5. In some cases, preeclampsia of a pregnant patient can be detected from four or more biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from five or more biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from six or more biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from seven or more biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from eight or more biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from nine or more biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from ten or more biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from 11, 12, 13, 14, 15, 16, 17, 18, or 19 or more biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from no more than ten biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from no more than nine biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from no more than eight biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from no more than seven biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected

from no more than six biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from no more than five biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from no more than four biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from no more than three biomarkers selected from Table 4. In some cases, preeclampsia of a pregnant patient can be detected from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 biomarkers selected from Table 4.

**[0086]** In some embodiments, the methods provided herein can comprise detecting a condition (such as preeclampsia) from one or more biomarkers selected from (a) known preeclampsia candidate biomarkers reported in the literature (such as PAPP-A, sFlt1, PIgf, or Fibronectin), (b) preeclampsia biomarkers specifically identified herein (such as those selected from Group 1, Group 2, Group 3, Group 4, Group 5, Table 2, Table 3, Table 4, or Table 5), or (c) any combination of (a) and (b). In other embodiments, the methods provided herein can comprise detecting a condition (such as preeclampsia) from two or more, three or more, four or more, five or more, six or more, or seven or more biomarkers selected from (a), (b), or (c). In other embodiments, the methods provided herein can comprise detecting a condition (such as preeclampsia) from no more than ten, no more than 9, no more than 8, no more than 7, no more than 6, no more than 5, no more than 4, or no more than 3 biomarkers selected from (a), (b), or (c). In other embodiments, the methods provided herein can comprise detecting a condition (such as preeclampsia) from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 biomarkers selected from (a), (b), or (c).

#### *Clinical/Therapeutic Applications*

**[0087]** The methods, compositions, systems and kits provided herein can be used to detect, diagnose, predict or monitor a condition of a pregnant patient. In some instances, the methods, compositions, systems and kits described herein provide information to a medical practitioner that can be useful in making a clinical therapeutic decision. Clinical and therapeutic decisions can include decisions to: continue with a particular therapy, modify a particular therapy, alter the dosage of a particular therapy, stop or terminate a particular therapy, altering the frequency of a therapy, introduce a new therapy, introduce a new therapy to be used in combination with a current therapy, or any combination of the above. In some instances, medical action taken may comprise watchful waiting or the administration of one or more additional diagnostic tests of the same or different nature. In some cases, a clinical decision may be made to not induce labor, or to proceed with ambulant monitoring of the

subject. In some cases, the methods provided herein can be applied in an experimental setting, e.g., clinical trial. In some instances, the methods provided herein can be used to monitor a pregnant patient who is being treated with an experimental agent such as an angiogenic/antiangiogenic drug, compound, or therapeutic cell type. In some instances, the methods provided herein can be useful to determine whether a subject can be administered an experimental agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, therapeutic cell, small molecule, or other drug candidate) to reduce the risk of preeclampsia. Thus, the methods described herein can be useful in determining if a subject can be effectively treated with an experimental agent and for monitoring the subject for risk of preeclampsia.

*Detecting/Diagnosing a Condition of a Pregnant Patient*

**[0088]** The methods, compositions, systems and kits provided herein are particularly useful for detecting, diagnosing, or ruling out a condition of a pregnant patient such as a condition the pregnant patient has at the time of testing. An exemplary condition that can be detected, diagnosed, or ruled out with the present method includes preeclampsia. The methods, compositions, systems, and kits provided herein can also be useful, in combination with other standard clinical data collected for pregnant patients, for ruling in or ruling out a diagnosis of preeclampsia, hypertension, gestational hypertension, or HELLP syndrome. The methods provided herein are particularly useful for pregnant patients who have exhibited one or more new-onset symptoms associated with preeclampsia prior to testing (e.g., hypertension, proteinuria, low platelet count, elevated serum creatinine levels, elevated liver enzymes, pulmonary edema, or cerebral/visual symptoms), such that the patients are suspected of having preeclampsia.

**[0089]** In some embodiments, the methods, compositions, systems and kits provided herein can rule out a diagnosis of preeclampsia for a specified number of days in the future. In some instances, the specified number of days in the future is 1 to 30 days. In some instances the specified number of days in the future is at least 1 day. In some instances the specified number of days in the future is at most 30 days. In some instances the specified number of days in the future is 1 day to 5 days, 1 day to 10 days, 1 day to 30 days, 5 days to 10 days, 5 days to 30 days, or 10 days to 30 days. In some instances the specified number of days in the future is 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, or 30 days. In some preferred embodiments, the specified number of days in the future is 5 days to 10 days. In other preferred embodiments, the specified number of days

in the future is 5, 6, 7, 8, 9, or 10 days. In some embodiments, the methods, compositions, systems and kits provided herein can rule-out mothers for hospital admission and preterm delivery. In some embodiments, the methods, compositions, systems and kits provided herein can rule out a diagnosis of preeclampsia for a specified number of weeks in the future. In some instances the specified number of weeks is at least 1 week. In some instances the specified number of weeks is at least 2 weeks. In some instances the specified number of weeks is at least 3 weeks. In some instances the specified number of weeks is at least 4 weeks. In some instances the specified number of weeks is at least 5 weeks. In some instances the specified number of weeks is at least 6 weeks. In some instances the specified number of weeks is at most 1 week. In some instances the specified number of weeks is at most 2 weeks. In some instances the specified number of weeks is at most 3 weeks. In some instances the specified number of weeks is at most 4 weeks. In some instances the specified number of weeks is at most 5 weeks. In some instances the specified number of weeks is at most 6 weeks.

**[0090]** In some embodiments, the methods, compositions, systems and kits provided herein can rule out a diagnosis of preeclampsia for a specified number of weeks in the future with a particular PPV. In some cases the positive predictive value (PPV) is at least about 30%, 31%, 32%, 33%, 34%, 35%, 36%, 37%, 38%, 39%, 40%, 41%, 42%, 43%, 44%, 45%, 46%, 47%, 48%, 49%, 50%, 51%, 52%, 53%, 54%, 55%, 56%, or 57%, or any range in between these values.

**[0091]** In some embodiments, the methods, compositions, systems and kits provided herein can rule out a diagnosis of preeclampsia for a specified number of weeks in the future with a particular NPV. The NPV can be at least about 80%, 81 %, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 95.2%, 95.5%, 95.7%, 96%, 96.2%, 96.5%, 96.7%, 97%, 97.2%, 97.5%, 97.7%, 98%, 98.2%, 98.5%, 98.7%, 99%, 99.2%, 99.5%, 99.7%, or 99.9%, or any range in between these values.

**[0092]** In some embodiments, the methods, compositions, systems and kits provided herein can rule out a diagnosis of preeclampsia for a specified number of weeks in the future with a particular AUC. In some cases, the AUC of can be at least about 50%, 53%, 55%, 57%, 60%, 63%, 65%, 67%, 70%, 72%, 75%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3 %, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or any range in between these values.

**[0093]** In some embodiments, the methods, compositions, systems and kits provided herein can rule out a diagnosis of preeclampsia for a specified number of weeks in the future with a particular AUP. The AUP can be at least about 50%, 53%, 55%, 57%, 60%, 63%, 65%, 67%, 70%, 72%, 75%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3 %, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or any range in between these values.

**[0094]** The diagnosis, detection, or ruling out of a condition of the pregnant patient can be particularly useful in limiting the number of unnecessary invasive medical interventions that are administered to the patient, and/or indicating alternative less-invasive therapeutic interventions such as pharmacological therapies (anticonvulsants, antihypertensives, central alpha agonists, alpha-blockers, beta-blockers, calcium-channel blockers, vasodilators, cyclooxygenase inhibitors). For example, the methods provided herein can limit, delay, or eliminate the use of preterm cesarean delivery or labor induction in patients suspected of having preeclampsia via high-confidence ruling out of a diagnosis of preeclampsia in the pregnant patient (e.g., via a high negative predictive value of the methods, compositions, systems, and kits provided herein).

**[0095]** In a further embodiment, the methods, compositions, systems and kits provided herein can be used alone or in combination with other standard diagnosis methods currently used to detect, diagnose, or rule out a condition of a pregnant patient, such as but not limited to blood pressure measurement, urine protein measurement, blood platelet counting, serum creatinine level measurement, creatinine clearance measurement, urine protein/creatinine ratio measurement, serum transaminase level measurement, serum LDH level measurement, serum bilirubin level measurement, or Doppler ultrasound indices (e.g., uterine artery indices). For example, hypertension in a pregnant patient can be indicative of conditions such as chronic hypertension, gestational hypertension, or preeclampsia; ruling out the diagnosis of preeclampsia via the methods, compositions, systems and kits provided herein allows for the patient to be correctly diagnosed with chronic hypertension or gestational hypertension.

#### *Predicting a Condition of a Pregnant Patient*

**[0096]** In some embodiments, the methods provided herein can predict preeclampsia prior to actual onset of the condition or symptoms associated with the condition (e.g., hypertension or proteinuria). In some instances, the methods provided herein can predict preeclampsia or other disorders in a pregnant patient at least 1 day, 1 week, 2 weeks, 3 weeks, 1 month, 2 months prior to onset of the condition or symptoms associated with the condition. In other

instances, the methods provided herein can predict preeclampsia or other disorders in a pregnant patient at least 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 or 31 days prior to onset. In other instances, the methods provided herein can predict preeclampsia or other disorders in a pregnant patient at least 1, 2, 3, or 4 months prior to onset.

*Monitoring a Condition of a Pregnant Patient*

**[0097]** Provided herein are methods, systems, kits and compositions for monitoring a condition of a pregnant patient. Often, the monitoring is conducted by serial testing, such as serial non-invasive tests, serial minimally-invasive tests (e.g., blood draws), or some combination thereof. Preferably, the monitoring is conducted by administering serial non-invasive tests or serial minimally-invasive tests (e.g., blood draws).

**[0098]** In some instances, the pregnant patient is monitored as needed (e.g., on an as-needed basis) using the methods described herein. Additionally or alternatively the pregnant patient can be monitored weekly, monthly, or at any pre-specified intervals. In some instances, the pregnant patient is monitored at least once every 24 hours. In some instances the pregnant patient is monitored at least once every 1 day to 30 days. In some instances the pregnant patient is monitored at least once every at least 1 day. In some instances the pregnant patient is monitored at least once every at most 30 days. In some instances the pregnant patient is monitored at least (optionally on average) once every 1 day to 5 days, 1 day to 10 days, 1 day to 15 days, 1 day to 20 days, 1 day to 25 days, 1 day to 30 days, 5 days to 10 days, 5 days to 15 days, 5 days to 20 days, 5 days to 25 days, 5 days to 30 days, 10 days to 15 days, 10 days to 20 days, 10 days to 25 days, 10 days to 30 days, 15 days to 20 days, 15 days to 25 days, 15 days to 30 days, 20 days to 25 days, 20 days to 30 days, or 25 days to 30 days. In some instances the pregnant patient is monitored at least once every 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 28, 29, 30 or 31 days. In some instances, the pregnant patient is monitored at least once every 1, 2, or 3 months. In some instances, the pregnant patient is monitored via the methods described herein no more frequently than one week, 10 days, two weeks, three weeks, or one month. In other words, the predictive value of the some of the methods described herein can be of clinical use for at least one week, at least 10 days, at least two week, at least three weeks, or at least one month.

**[0099]** In some instances, biomarker expression levels in the patients can be measured, for example, within, one week, two weeks, three weeks, or four weeks after detection of one or more symptoms associated with preeclampsia (e.g., hypertension or proteinuria). In some

methods, biomarker expression levels are determined at regular intervals, e.g., every 1 week, 2 weeks, 3 weeks, 1 month, 2 months or 3 months post-conception, after the beginning of the 2<sup>nd</sup> trimester, after the beginning of the 3<sup>rd</sup> trimester, or after week 20 of the pregnancy, either indefinitely, or until evidence of a condition is observed. In some methods, biomarker expression levels are determined at regular intervals after week 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, or 42 weeks. Where evidence of a condition is observed, the frequency of monitoring is sometimes increased. In some methods, baseline values of expression levels are determined in a subject before detection of one or more symptoms associated with preeclampsia (e.g., hypertension or proteinuria) in combination with determining expression levels after onset of symptoms.

*Therapeutic Decisions/Regimens*

**[0100]** The results of diagnosing, predicting, ruling out, or monitoring a condition of the pregnant patient can be useful for informing a clinical or therapeutic decision such as determining or monitoring a therapeutic regimen.

**[0101]** In some embodiments, an entity that acquires sample data and/or classifies a sample from a patient as having preeclampsia is other than the physician, caregiver, or medical institution performing the treatment. In some embodiments, the entity acquiring sample data (e.g. levels of two or more proteins from Tables A, B, 2, 3, 4, and 5), calculating an index based (at least in part) on the levels of the plurality of the protein biomarkers, and/or determining risk of preeclampsia is a third-party testing service. Thus, in some embodiments, determining or monitoring a therapeutic regimen first comprises receiving information from a third-party testing service, which can comprise, for example (but not limited to), classification of a sample as being at risk or not of preeclampsia, risk of a pregnant patient having preeclampsia, levels of a plurality of protein biomarkers from the sample associated with preeclampsia (e.g. levels of two or more proteins from Tables A, B, 2, 3, 4, and 5), or the likelihood a pregnant patient will deliver preterm.

**[0102]** In some embodiments, an entity that acquires sample data, determines the risk of preterm birth of the patient from the sample, and/or classifies a sample from a patient as having a significant risk of preterm birth is the same entity that performing the treatment.

**[0103]** In some instances, determining a therapeutic regimen can comprise administering a therapeutic drug. In some instances, determining a therapeutic regimen comprises modifying, continuing, initiating or stopping a therapeutic regimen. In some instances, determining a therapeutic regimen comprises treating the disease or condition (e.g., preeclampsia,

eclampsia, gestational hypertension, hypertension, or HELLP syndrome). In some instances, the therapy is an anti-hypertensive therapy. In some instances, the therapy is an anti-cyclooxygenase (COX) therapy. In some instances, the therapy is an anti-convulsant therapy.

**[0104]** Modifying the therapeutic regimen can comprise terminating a therapy. Modifying the therapeutic regimen can comprise altering a dosage of a therapy. Modifying the therapeutic regimen can comprise altering a frequency of a therapy. Modifying the therapeutic regimen can comprise administering a different therapy. In some instances, the results of diagnosing, predicting, or monitoring a condition of the pregnant patient can be useful for informing a therapeutic decision such as caesarean delivery. Other examples of therapeutic decisions can be cervical ripening and/or labor induction. Examples of agents that can be used for cervical ripening and/or labor induction include prostaglandins, misoprostol, mifepristone, relaxin, and oxytocin. Other examples of therapeutic decisions can be cesarean delivery.

**[0105]** Examples of a therapeutic regimen can include administering compounds or agents having anti-hypertensive properties (e.g., central alpha agonists such as methyldopa, vasodilators such as clonidine, diazoxide, hydralazine and prazosin, calcium-channel blockers such as nifedipine and verapamil, alpha-blockers such as labetalol, or beta-blockers such as oxprenolol), compounds or agents having anti-cyclooxygenase activity (e.g., acetylsalicylic acid), or compounds having anti-convulsant activity (e.g., phenytoin or magnesium sulfate). These compounds can be used alone or in combination.

**[0106]** In some cases, modifying the therapeutic regimen can comprise proceeding with treatment of said pregnant human in a manner that avoids unnecessary treatment of preeclampsia. For instance, in some embodiments, managing the pregnant human subject identified not as at risk for preeclampsia comprises ambulant monitoring, or refraining from the administration of any drug for treating preeclampsia. In some instances, in patients that are identified as not patients that should not be treated for preeclampsia, antihypertensive drugs (rather than delivery) may be prescribed and/or administered to the patient.

*Sensitivity, Specificity, NPV, PPV, AUC, AUP, and Accuracy*

**[0107]** The methods, kits, and systems disclosed herein for use in identifying, classifying (or ruling out a classification) or characterizing a sample can be characterized by having a specificity of at least about 80% using the methods disclosed herein. In some embodiments, the specificity of the methods is at least about 85%. In some embodiments, the specificity of the methods is at least about 90%. In some embodiments, the specificity of the methods is at least about 95%. The specificity of the method can be at least about 80%, 81%, 82%, 83%,

84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, or any range in between these values.

**[0108]** In some embodiments, the present invention provides a method of identifying, classifying (or ruling out a classification) or characterizing a sample that gives a sensitivity of at least about 80% using the methods disclosed herein. In some embodiments, the sensitivity of the methods is at least 85%. In some embodiments, the sensitivity of the methods is at least 90%. In some embodiments, the sensitivity of the methods is at least 95%. The sensitivity of the method can be at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, or any range in between these values.

**[0109]** The methods, kits and systems disclosed herein can improve upon the accuracy of current methods of monitoring or predicting a status or outcome of a pregnancy (e.g. preeclampsia) or identifying or ruling out a classification of a sample. The accuracy of the methods, kits, and systems disclosed herein can be at least about 50%, 53%, 55%, 57%, 60%, 63%, 65%, 67%, 70%, 72%, 75%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3 %, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or any range in between these values.

**[0110]** The methods, kits, and systems for use in identifying, classifying (or ruling out a classification) or characterizing a sample can be characterized by having a negative predictive value (NPV) greater than or equal to 90%. The NPV can be at least about 80%, 81 %, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 95.2%, 95.5%, 95.7%, 96%, 96.2%, 96.5%, 96.7%, 97%, 97.2%, 97.5%, 97.7%, 98%, 98.2%, 98.5%, 98.7%, 99%, 99.2%, 99.5%, 99.7%, or 99.9%, or any range in between these values. The NPV can be greater than or equal to 95%. The NPV can be greater than or equal to 96%. The NPV can be greater than or equal to 97%. The NPV can be greater than or equal to 98%.

**[0111]** The methods, kits, and/or systems disclosed herein for use in identifying, classifying (or ruling out a classification) or characterizing a sample(e.g. for preeclampsia) can be characterized by having a positive predictive value (PPV) of at least about 30%, 31%, 32%, 33%, 34%, 35%, 36%, 37%, 38%, 39%, 40%, 41%, 42%, 43%, 44%, 45%, 46%, 47%, 48%, 49%, 50%, 51%, 52%, 53%, 54%, 55%, 56%, or 57%, or any range in between these values using the methods disclosed herein.

**[0112]** The methods, kits and systems disclosed herein can improve upon the AUC of current methods of monitoring or predicting a status or outcome of a pregnancy (e.g. preeclampsia)

or identifying or ruling out a classification of a sample. The AUC of the methods, kits, and systems disclosed herein can be at least about 50%, 53%, 55%, 57%, 60%, 63%, 65%, 67%, 70%, 72%, 75%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3 %, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or any range in between these values.

**[0113]** The methods, kits and systems disclosed herein can improve upon the AUP of current methods of monitoring or predicting a status or outcome of a pregnancy (e.g. preeclampsia) or identifying or ruling out a classification of a sample. The AUP of the methods, kits, and systems disclosed herein can be at least about 50%, 53%, 55%, 57%, 60%, 63%, 65%, 67%, 70%, 72%, 75%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3 %, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or any range in between these values.

**[0114]** The methods, kits, and systems disclosed herein for use in diagnosing, prognosing, and/or monitoring a status or outcome of a pregnancy in a subject in need thereof can be characterized by having an accuracy of at least about 80%, 82%, 85%, 87%, 90%, 92%, 95%, or 97% or any range in between these values.

**[0115]** The methods, kits, and systems disclosed herein for use in diagnosing, prognosing, and/or monitoring a status or outcome of a pregnancy in a subject in need thereof can be characterized by having a specificity of at least about 80%, 82%, 85%, 87%, 90%, 92%, 95%, or 97%, or any range in between these values.

**[0116]** The methods, kits, and systems disclosed herein for use in diagnosing, prognosing, and/or monitoring a status or outcome of a pregnancy in a subject in need thereof can be characterized by having a sensitivity of at least about 80%, 82%, 85%, 87%, 90%, 92%, 95%, or 97%, or any range in between these values.

**[0117]** The methods, kits, and systems disclosed herein for use in diagnosing, prognosing, and/or monitoring a status or outcome of a pregnancy in a subject in need thereof can be characterized by having a negative predictive value (NPV) greater than or equal to 90%. The NPV can be at least about 90%, 91%, 92%, 93%, 94%, 95%, 95.2%, 95.5%, 95.7%, 96%, 96.2%, 96.5%, 96.7%, 97%, 97.2%, 97.5%, 97.7%, 98%, 98.2%, 98.5%, 98.7%, 99%, 99.2%, 99.5%, 99.7%, or 99.9%, or any range in between these values. The NPV can be greater than or equal to 95%. The NPV can be greater than or equal to 96%. The NPV can be greater than or equal to 97%. The NPV can be greater than or equal to 98%.

**[0118]** The methods, kits, and systems disclosed herein for use in diagnosing, prognosing, and/or monitoring a status or outcome of a pregnancy in a subject in need thereof can be characterized by having a positive predictive value (PPV) of at least about 80%. In some embodiments, the methods, kits, and systems disclosed herein for use in diagnosing, prognosing, and/or monitoring a status or outcome of a pregnancy in a subject in need thereof can be characterized by having a positive predictive value (PPV) of at least about 85%. In some embodiments, the methods, kits, and systems disclosed herein for use in diagnosing, prognosing, and/or monitoring a status or outcome of a pregnancy in a subject in need thereof can be characterized by having a positive predictive value (PPV) of at least about 90%. The PPV can be at least about 80%, 85%, 90%, 95%, 95.2%, 95.5%, 95.7%, 96%, 96.2%, 96.5%, 96.7%, 97%, 97.2%, 97.5%, 97.7%, 98%, 98.2%, 98.5%, 98.7%, 99%, 99.2%, 99.5%, 99.7%, or 99.9%, or any range in between these values. The PPV can be greater than or equal to 95%. The PPV can be greater than or equal to 98%.

**[0119]** In some embodiments, disclosure provides a test for confirming preeclampsia in a subject, preferably a pregnant subject, wherein the test is able to discern subjects not having preeclampsia but having one or more symptoms associated with preeclampsia from subjects having preeclampsia with an NPV of at least about 90%, 91%, 92%, 93%, 94%, 95%, 95.2%, 95.5%, 95.7%, 96%, 96.2%, 96.5%, 96.7%, 97%, 97.2%, 97.5%, 97.7%, 98%, 98.2%, 98.5%, 98.7%, 99%, 99.2%, 99.5%, 99.7%, or 99.9%, or any range in between these values. The one or more symptoms associated with preeclampsia can be diabetes (e.g. gestational, type I or type II), higher than normal glucose level, hypertension (e.g. chronic or non-chronic), excessive or sudden weight gain, higher than normal weight, obesity, higher than normal body mass index (BMI), abnormal weight gain, abnormal blood pressure, water retention, hereditary factors, abnormal proteinuria, headache, edema, abnormal protein/creatinine ratio, abnormal platelet count, stress, nulliparity, abnormal Papanicolaou test results (Pap smear), prior preeclampsia episodes (e.g., personal history of PreE), familial history of preeclampsia, preeclampsia in prior pregnancies, renal disease, thrombophilia, or any combination thereof. Gestational age may also be used in tests, such as tests for ruling out preeclampsia.

**[0120]** In some embodiments, disclosure provides for a method, kit, system, or test that has a sensitivity of at least 79% and a specificity of at least 94%. In some embodiments, a method, kit, system, or test has a sensitivity of at least 82% and a specificity of at least 80%. In some

embodiments, a method, kit, system of test has a sensitivity of at least 90% and a specificity of at least 80%.

*Computer program*

**[0121]** The methods, kits, and systems disclosed herein can include at least one computer program, or use of the same. A computer program can include a sequence of instructions, executable in the digital processing device's CPU (i.e. processor), written to perform a specified task. Computer readable instructions can be implemented as program modules, such as functions, objects, Application Programming Interfaces (APIs), data structures, and the like, that perform particular tasks or implement particular abstract data types. In light of the disclosure provided herein, those of skill in the art will recognize that a computer program can be written in various versions of various languages.

**[0122]** The functionality of the computer readable instructions can be combined or distributed as desired in various environments. The computer program will normally provide a sequence of instructions from one location or a plurality of locations.

**[0123]** Further disclosed herein are systems for classifying (or ruling out a classification) one or more samples and uses thereof. The system can comprise (a) a digital processing device comprising an operating system configured to perform executable instructions and a memory device; (b) a computer program including instructions executable by the digital processing device to classify a sample from a subject comprising: (i) a first software module configured to receive a biomarker expression profile of one or more biomarkers from the sample from the subject; (ii) a second software module configured to analyze the biomarker expression profile from the subject; and (iii) a third software module configured to classify the sample from the subject based on a classification system. In some embodiments, the classification system comprises two classes. In other embodiments, the classification system comprises two or more classes. At least two of the classes can be selected from preeclampsia, non-preeclampsia (e.g., for at least a period of time), normal pregnancy, complicated pregnancy, and gestational hypertension. Analyzing the biomarker expression profile from the subject can comprise applying an algorithm. Analyzing the biomarker expression profile can comprise normalizing the biomarker expression profile from the subject.

**[0124]** **Figure 6** shows a computer system (also "system" herein) 401 programmed or otherwise configured for implementing the methods of the disclosure, such as producing a selector set and/or for data analysis. The system 401 includes a central processing unit (CPU, also "processor" and "computer processor" herein) 405, which can be a single core or multi

core processor, or a plurality of processors for parallel processing. The system 401 also includes memory 410 (e.g., random-access memory, read-only memory, flash memory), electronic storage unit 415 (e.g., hard disk), communications interface 420 (e.g., network adapter) for communicating with one or more other systems, and peripheral devices 425, such as cache, other memory, data storage and/or electronic display adapters. The memory 410, storage unit 415, interface 420 and peripheral devices 425 are in communication with the CPU 405 through a communications bus (solid lines), such as a motherboard. The storage unit 415 can be a data storage unit (or data repository) for storing data. The system 401 is operatively coupled to a computer network (“network”) 430 with the aid of the communications interface 420. The network 430 can be the Internet, an internet and/or extranet, or an intranet and/or extranet that is in communication with the Internet. The network 430 in some instances is a telecommunication and/or data network. The network 430 can include one or more computer servers, which can enable distributed computing, such as cloud computing. The network 430 in some instances, with the aid of the system 401, can implement a peer-to-peer network, which can enable devices coupled to the system 401 to behave as a client or a server.

**[0125]** The system 401 is in communication with a processing system 435. The processing system 435 can be configured to implement the methods disclosed herein. In some examples, the processing system 435 is a microfluidic qPCR system. In other examples, the processing system 435 is an ALPHA screen or other plate reader. In other examples, the processing system 435 is a FACS sorter or analyzer. The processing system 435 can be in communication with the system 401 through the network 430, or by direct (e.g., wired, wireless) connection. In some embodiments, raw data from the processing system (e.g. a biomarker expression profile) is uploaded through the network to the system for processing (e.g. sample classification or determination of a probability of a certain classification). This data transfer may be direct (e.g. FTP, TCP, or other direct network connection between the processing system 435 and the system 401), or indirect (e.g. transfer to a cloud storage system which can be accessed by the system 401).

**[0126]** Methods as described herein can be implemented by way of machine (or computer processor) executable code (or software) stored on an electronic storage location of the system 401, such as, for example, on the memory 410 or electronic storage unit 415. During use, the code can be executed by the processor 405. In some examples, the code can be retrieved from the storage unit 415 and stored on the memory 410 for ready access by the

processor 405. In some situations, the electronic storage unit 415 can be precluded, and machine-executable instructions are stored on memory 410.

*Digital processing device*

**[0127]** The methods, kits, and systems disclosed herein can include a digital processing device, or use of the same. In further embodiments, the digital processing device includes one or more hardware central processing units (CPU) that carry out the device's functions. In still further embodiments, the digital processing device further comprises an operating system configured to perform executable instructions. In some embodiments, the digital processing device is optionally connected a computer network. In further embodiments, the digital processing device is optionally connected to the Internet such that it accesses the World Wide Web. In still further embodiments, the digital processing device is optionally connected to a cloud computing infrastructure. In other embodiments, the digital processing device is optionally connected to an intranet. In other embodiments, the digital processing device is optionally connected to a data storage device.

**[0128]** In accordance with the description herein, suitable digital processing devices include, by way of non-limiting examples, server computers, desktop computers, laptop computers, notebook computers, sub-notebook computers, netbook computers, netpad computers, set-top computers, handheld computers, Internet appliances, mobile smartphones, tablet computers, personal digital assistants, video game consoles, and vehicles. Those of skill in the art will recognize that many smartphones are suitable for use in the system described herein. Those of skill in the art will also recognize that select televisions, video players, and digital music players with optional computer network connectivity are suitable for use in the system described herein. Suitable tablet computers include those with booklet, slate, and convertible configurations, known to those of skill in the art.

**[0129]** The digital processing device will normally include an operating system configured to perform executable instructions. The operating system is, for example, software, including programs and data, which manages the device's hardware and provides services for execution of applications. Those of skill in the art will recognize that suitable server operating systems include, by way of non-limiting examples, FreeBSD, OpenBSD, NetBSD®, Linux, Apple® Mac OS X Server®, Oracle® Solaris®, Windows Server®, and Novell® NetWare®. Those of skill in the art will recognize that suitable personal computer operating systems include, by way of non-limiting examples, Microsoft® Windows®, Apple® Mac OS X®, UNIX®, and UNIX-like operating systems such as GNU/Linux®. In some embodiments, the operating

system is provided by cloud computing. Those of skill in the art will also recognize that suitable mobile smart phone operating systems include, by way of non-limiting examples, Nokia® Symbian® OS, Apple® iOS®, Research In Motion® BlackBerry OS®, Google® Android®, Microsoft® Windows Phone® OS, Microsoft® Windows Mobile® OS, Linux®, and Palm® WebOS®.

**[0130]** The device generally includes a storage and/or memory device. The storage and/or memory device is one or more physical apparatuses used to store data or programs on a temporary or permanent basis. In some embodiments, the device is volatile memory and requires power to maintain stored information. In some embodiments, the device is non-volatile memory and retains stored information when the digital processing device is not powered. In further embodiments, the non-volatile memory comprises flash memory. In some embodiments, the non-volatile memory comprises dynamic random-access memory (DRAM). In some embodiments, the non-volatile memory comprises ferroelectric random access memory (FRAM). In some embodiments, the non-volatile memory comprises phase-change random access memory (PRAM). In other embodiments, the device is a storage device including, by way of non-limiting examples, CD-ROMs, DVDs, flash memory devices, magnetic disk drives, magnetic tapes drives, optical disk drives, and cloud computing based storage. In further embodiments, the storage and/or memory device is a combination of devices such as those disclosed herein.

**[0131]** A display to send visual information to a user will normally be initialized. Examples of displays include a cathode ray tube (CRT, a liquid crystal display (LCD), a thin film transistor liquid crystal display (TFT-LCD, an organic light emitting diode (OLED) display. In various further embodiments, on OLED display is a passive-matrix OLED (PMOLED) or active-matrix OLED (AMOLED) display. In some embodiments, the display can be a plasma display, a video projector or a combination of devices such as those disclosed herein.

**[0132]** The digital processing device would normally include an input device to receive information from a user. The input device can be, for example, a keyboard, a pointing device including, by way of non-limiting examples, a mouse, trackball, track pad, joystick, game controller, or stylus; a touch screen, or a multi-touch screen, a microphone to capture voice or other sound input, a video camera to capture motion or visual input or a combination of devices such as those disclosed herein.

*Non-transitory computer readable storage medium*

**[0133]** The methods, kits, and systems disclosed herein can include one or more non-transitory computer readable storage media encoded with a program including instructions executable by the operating system to perform and analyze the test described herein; preferably connected to a networked digital processing device. The computer readable storage medium is a tangible component of a digital device that is optionally removable from the digital processing device. The computer readable storage medium includes, by way of non-limiting examples, CD-ROMs, DVDs, flash memory devices, solid state memory, magnetic disk drives, magnetic tape drives, optical disk drives, cloud computing systems and services, and the like. In some instances, the program and instructions are permanently, substantially permanently, semi-permanently, or non-transitorily encoded on the media.

**[0134]** A non-transitory computer-readable storage media can be encoded with a computer program including instructions executable by a processor to create or use a classification system. The storage media can comprise (a) a database, in a computer memory, of one or more clinical features of two or more control samples, wherein (i) the two or more control samples can be from two or more subjects; and (ii) the two or more control samples can be differentially classified based on a classification system comprising two or more classes; (b) a first software module configured to compare the one or more clinical features of the two or more control samples; and (c) a second software module configured to produce a classifier set based on the comparison of the one or more clinical features. At least two of the classes can be selected from preeclampsia, non-preeclampsia, normal pregnancy, complicated pregnancy, and gestational hypertension.

*Antigen Detection (E.g., Antibodies)*

**[0135]** In some embodiments, at least one antigen binding reagent is used to detect any of the biomarkers identified herein. In some embodiments, the antigen binding reagent can be an antibody (monoclonal or polyclonal), antigen-binding fragment (e.g. Fab, Fab', F(ab)2, F(abc)2, or Fv fragment) of an antibody, or an antibody derivative (e.g. diabody, linear antibody, or scFv). In some embodiments, the at least one antigen detection moiety is an antibody from **Figure 18**. In some embodiments, the antigen binding reagent is an antigen-binding fragment (e.g. Fab, Fab', F(ab)2, F(abc)2, or Fv fragment) or antibody derivative (e.g. diabody, linear antibody, or scFv) of any of the antibodies provided in **Figure 18**.

*Kits*

**[0136]** In some embodiments, the disclosure provides assay kits for analysis of any of the sets of biomarkers included herein for the detection of preeclampsia. In some cases, the

assay kits comprise one or more antigen-binding reagents (e.g. monoclonal or polyclonal antibodies provided in FIG. 18, or antigen-binding fragments or antibody derivatives of antibodies provided in FIG. 18). In some embodiments, the one or more antigen-binding reagents comprise combinations of antigen-binding reagents with specificities for the antigens/biomarkers presented below.

**[0137]** In some embodiments, the assay kit provided comprises at least one antibody, antibody fragment, or antibody derivative specific for each biomarker in one of the following sets: sFlt.1, PlGF, KIM1, and CLEC4A; sFlt.1, PlGF, KIM1, CLEC4A, and FGF21; sFlt.1, PlGF, KIM1, CLEC4A, and CD274; sFlt.1, PlGF, KIM1, CLEC4A, and ENDOGLIN; sFlt.1, PlGF, KIM1, CLEC4A, and DECORIN; sFlt.1, PlGF, KIM1, CLEC4A, FGF21, and ENDOGLIN; sFlt.1, PlGF, KIM1, CLEC4A, FGF21, and CD274; sFlt.1, PlGF, KIM1, CLEC4A, ENDOGLIN, and DECORIN; sFlt.1, PlGF, KIM1, CLEC4A, FGF21, ENDOGLIN, and CD274; sFlt.1, PlGF, KIM1, CLEC4A, FGF21, ENDOGLIN, CD274, and DECORIN; PlGF, KIM1, CLEC4A, and ENDOGLIN; PlGF, KIM1, CLEC4A, ENDOGLIN, and DECORIN; sFlt.1, PlGF, KIM1, TFF2, FGF21, and DECORIN; sFlt.1, PlGF, KIM1, CLEC4A, CD274, and ENDOGLIN; or HGF, SYND1, CLEC4A, sFlt.1, PlGF, KIM1, CLEC4A, and FGF21.

**[0138]** In some embodiments, the assay kit provided comprises at least one antibody, antibody fragment, or antibody derivative specific for each biomarker in one of the following sets of four optionally in combination with PlGF: SFLT1, KIM1, CLEC4A, FGF21; SFLT1, KIM1, CLEC4A, endoglin; SFLT1, KIM1, CLEC4A, decorin; SFLT1, KIM1, CLEC4A, CD274; SFLT1, KIM1, CLEC4A, HGF; SFLT1, KIM1, CLEC4A, TFF2; SFLT1, KIM1, CLEC4A, PAPP.A2; SFLT1, KIM1, FGF21, endoglin; SFLT1, KIM1, FGF21, decorin; SFLT1, KIM1, FGF21, CD274; SFLT1, KIM1, FGF21, HGF; SFLT1, KIM1, FGF21, TFF2; SFLT1, KIM1, FGF21, PAPP.A2; SFLT1, KIM1, endoglin, decorin; SFLT1, KIM1, endoglin, CD274; SFLT1, KIM1, endoglin, HGF; SFLT1, KIM1, endoglin, TFF2; SFLT1, KIM1, endoglin, PAPP.A2; SFLT1, KIM1, decorin, CD274; SFLT1, KIM1, decorin, HGF; SFLT1, KIM1, decorin, TFF2; SFLT1, KIM1, decorin, PAPP.A2; SFLT1, KIM1, CD274, HGF; SFLT1, KIM1, CD274, TFF2; SFLT1, KIM1, CD274, PAPP.A2; SFLT1, KIM1, HGF, TFF2; SFLT1, KIM1, HGF, PAPP.A2; SFLT1, KIM1, TFF2, PAPP.A2; SFLT1, CLEC4A, FGF21, endoglin; SFLT1, CLEC4A, FGF21, decorin; SFLT1, CLEC4A, FGF21, CD274; SFLT1, CLEC4A, FGF21, HGF; SFLT1, CLEC4A, FGF21, TFF2; SFLT1, CLEC4A, FGF21, PAPP.A2; SFLT1, CLEC4A, endoglin, decorin; SFLT1, CLEC4A, endoglin,

CD274; SFLT1, CLEC4A, endoglin, HGF; SFLT1, CLEC4A, endoglin, TFF2; SFLT1, CLEC4A, endoglin, PAPP.A2; SFLT1, CLEC4A, decorin, CD274; SFLT1, CLEC4A, decorin, HGF; SFLT1, CLEC4A, decorin, TFF2; SFLT1, CLEC4A, decorin, PAPP.A2; SFLT1, CLEC4A, CD274, HGF; SFLT1, CLEC4A, CD274, TFF2; SFLT1, CLEC4A, CD274, PAPP.A2; SFLT1, CLEC4A, HGF, TFF2; SFLT1, CLEC4A, HGF, PAPP.A2; SFLT1, CLEC4A, TFF2, PAPP.A2; SFLT1, FGF21, endoglin, decorin; SFLT1, FGF21, endoglin, CD274; SFLT1, FGF21, endoglin, HGF; SFLT1, FGF21, endoglin, TFF2; SFLT1, FGF21, endoglin, PAPP.A2; SFLT1, FGF21, decorin, CD274; SFLT1, FGF21, decorin, HGF; SFLT1, FGF21, decorin, TFF2; SFLT1, FGF21, decorin, PAPP.A2; SFLT1, FGF21, CD274, TFF2; SFLT1, FGF21, CD274, PAPP.A2; SFLT1, FGF21, HGF, TFF2; SFLT1, FGF21, HGF, PAPP.A2; SFLT1, FGF21, TFF2, PAPP.A2; SFLT1, endoglin, decorin, CD274; SFLT1, endoglin, decorin, HGF; SFLT1, endoglin, decorin, TFF2; SFLT1, endoglin, decorin, PAPP.A2; SFLT1, endoglin, CD274, HGF; SFLT1, endoglin, CD274, TFF2; SFLT1, endoglin, CD274, PAPP.A2; SFLT1, endoglin, HGF, PAPP.A2; SFLT1, endoglin, TFF2, PAPP.A2; SFLT1, endoglin, CD274, HGF; SFLT1, decorin, CD274, TFF2; SFLT1, decorin, CD274, PAPP.A2; SFLT1, decorin, HGF, TFF2; SFLT1, decorin, HGF, PAPP.A2; SFLT1, decorin, TFF2, PAPP.A2; SFLT1, CD274, HGF, TFF2; SFLT1, CD274, HGF, PAPP.A2; SFLT1, CD274, TFF2, PAPP.A2; SFLT1, HGF, TFF2, PAPP.A2; KIM1, CLEC4A, FGF21, endoglin; KIM1, CLEC4A, FGF21, decorin; KIM1, CLEC4A, FGF21, CD274; KIM1, CLEC4A, FGF21, HGF; KIM1, CLEC4A, FGF21, TFF2; KIM1, CLEC4A, FGF21, PAPP.A2; KIM1, CLEC4A, endoglin, decorin; KIM1, CLEC4A, endoglin, CD274; KIM1, CLEC4A, endoglin, HGF; KIM1, CLEC4A, endoglin, TFF2; KIM1, CLEC4A, endoglin, PAPP.A2; KIM1, CLEC4A, decorin, CD274; KIM1, CLEC4A, decorin, HGF; KIM1, CLEC4A, decorin, TFF2; KIM1, CLEC4A, decorin, PAPP.A2; KIM1, CLEC4A, CD274, HGF; KIM1, CLEC4A, CD274, TFF2; KIM1, CLEC4A, HGF, TFF2; KIM1, CLEC4A, HGF, PAPP.A2; KIM1, CLEC4A, TFF2, PAPP.A2; KIM1, CLEC4A, endoglin, PAPP.A2; KIM1, FGF21, decorin, CD274; KIM1, FGF21, endoglin, HGF; KIM1, FGF21, endoglin, TFF2; KIM1, FGF21, endoglin, PAPP.A2; KIM1, FGF21, decorin, HGF; KIM1, FGF21, decorin, TFF2; KIM1, FGF21, decorin, PAPP.A2; KIM1, FGF21, CD274, HGF; KIM1, FGF21, CD274, TFF2; KIM1, FGF21, CD274, PAPP.A2; KIM1, FGF21, HGF, TFF2; KIM1, FGF21, HGF, PAPP.A2; KIM1, FGF21, TFF2, PAPP.A2; KIM1, endoglin, decorin, CD274; KIM1, endoglin, decorin,

HGF; KIM1, endoglin, decorin, TFF2; KIM1, endoglin, decorin, PAPP.A2; KIM1, endoglin, CD274, HGF; KIM1, endoglin, CD274, TFF2; KIM1, endoglin, CD274, PAPP.A2; KIM1, endoglin, HGF, TFF2; KIM1, endoglin, HGF, PAPP.A2; KIM1, endoglin, TFF2, PAPP.A2; KIM1, decorin, CD274, HGF; KIM1, decorin, CD274, TFF2; KIM1, decorin, CD274, PAPP.A2; KIM1, decorin, HGF, TFF2; KIM1, decorin, HGF, PAPP.A2; KIM1, decorin, TFF2, PAPP.A2; KIM1, CD274, HGF, TFF2; KIM1, CD274, HGF, PAPP.A2; KIM1, CD274, TFF2, PAPP.A2; KIM1, HGF, TFF2, PAPP.A2; CLEC4A, FGF21, endoglin, decorin; CLEC4A, FGF21, endoglin, CD274; CLEC4A, FGF21, endoglin, HGF; CLEC4A, FGF21, endoglin, TFF2; CLEC4A, FGF21, endoglin, PAPP.A2; CLEC4A, FGF21, decorin, CD274; CLEC4A, FGF21, decorin, HGF; CLEC4A, FGF21, decorin, TFF2; CLEC4A, FGF21, decorin, PAPP.A2; CLEC4A, FGF21, CD274, HGF; CLEC4A, FGF21, CD274, TFF2; CLEC4A, FGF21, CD274, PAPP.A2; CLEC4A, FGF21, HGF, TFF2; CLEC4A, FGF21, HGF, PAPP.A2; CLEC4A, FGF21, TFF2, PAPP.A2; CLEC4A, endoglin, decorin, CD274; CLEC4A, endoglin, decorin, HGF; CLEC4A, endoglin, decorin, TFF2; CLEC4A, endoglin, decorin, PAPP.A2; CLEC4A, endoglin, CD274, HGF; CLEC4A, endoglin, CD274, TFF2; CLEC4A, endoglin, CD274, PAPP.A2; CLEC4A, endoglin, HGF, TFF2; CLEC4A, endoglin, HGF, PAPP.A2; CLEC4A, endoglin, TFF2, PAPP.A2; CLEC4A, decorin, CD274, HGF; CLEC4A, decorin, CD274, TFF2; CLEC4A, decorin, CD274, PAPP.A2; CLEC4A, decorin, CD274, HGF, PAPP.A2; CLEC4A, decorin, TFF2, PAPP.A2; CLEC4A, CD274, HGF, TFF2; CLEC4A, CD274, HGF, PAPP.A2; CLEC4A, CD274, TFF2, PAPP.A2; CLEC4A, HGF, TFF2, PAPP.A2; FGF21, endoglin, decorin, CD274; FGF21, endoglin, decorin, HGF; FGF21, endoglin, decorin, TFF2; FGF21, endoglin, decorin, PAPP.A2; FGF21, endoglin, CD274, HGF; FGF21, endoglin, CD274, TFF2; FGF21, endoglin, CD274, PAPP.A2; FGF21, endoglin, HGF, TFF2; FGF21, endoglin, HGF, PAPP.A2; FGF21, endoglin, TFF2, PAPP.A2; FGF21, decorin, CD274, HGF; FGF21, decorin, CD274, TFF2; FGF21, decorin, HGF, PAPP.A2; FGF21, decorin, TFF2, PAPP.A2; FGF21, CD274, HGF, TFF2; FGF21, CD274, HGF, PAPP.A2; FGF21, CD274, TFF2, PAPP.A2; FGF21, HGF, TFF2, PAPP.A2; endoglin, decorin, CD274, HGF; endoglin, decorin, CD274, TFF2; endoglin, decorin, CD274, PAPP.A2; endoglin, decorin, HGF, TFF2; endoglin, decorin, HGF, PAPP.A2; endoglin, decorin, TFF2, PAPP.A2; endoglin, CD274, HGF, TFF2; endoglin, CD274, HGF, PAPP.A2; endoglin, CD274, TFF2, PAPP.A2; endoglin, HGF,

TFF2, PAPP.A2; decorin, CD274, HGF, TFF2; decorin, CD274, HGF, PAPP.A2; decorin, CD274, TFF2, PAPP.A2; or decorin, HGF, TFF2, PAPP.A2; CD274, HGF, TFF2, PAPP.A2.

**[0139]** In some embodiments, the assay kit provided comprises at least one antibody, antibody fragment, or antibody derivative specific for each biomarker in one of the following sets of three optionally in combination with PIGF: SFLT1, KIM1, CLEC4A; SFLT1, KIM1, FGF21; SFLT1, KIM1, endoglin; SFLT1, KIM1, decorin; SFLT1, KIM1, CD274; SFLT1, KIM1, HGF; SFLT1, KIM1, TFF2; SFLT1, KIM1, PAPP.A2; SFLT1, CLEC4A, FGF21; SFLT1, CLEC4A, endoglin; SFLT1, CLEC4A, decorin; SFLT1, CLEC4A, CD274; SFLT1, CLEC4A, HGF; SFLT1, CLEC4A, TFF2; SFLT1, CLEC4A, PAPP.A2; SFLT1, FGF21, endoglin; SFLT1, FGF21, decorin; SFLT1, FGF21, CD274; SFLT1, FGF21, HGF; SFLT1, FGF21, TFF2; SFLT1, FGF21, PAPP.A2; SFLT1, endoglin, decorin; SFLT1, endoglin, CD274; SFLT1, endoglin, HGF; SFLT1, endoglin, TFF2; SFLT1, endoglin, PAPP.A2; SFLT1, decorin, CD274; SFLT1, decorin, HGF; SFLT1, decorin, TFF2; SFLT1, decorin, PAPP.A2; SFLT1, CD274, HGF; SFLT1, CD274, TFF2; SFLT1, CD274, PAPP.A2; SFLT1, HGF, TFF2; SFLT1, HGF, PAPP.A2; SFLT1, TFF2, PAPP.A2; KIM1, CLEC4A, FGF21; KIM1, CLEC4A, endoglin; KIM1, CLEC4A, decorin; KIM1, CLEC4A, CD274; KIM1, CLEC4A, HGF; KIM1, CLEC4A, TFF2; KIM1, CLEC4A, PAPP.A2; KIM1, FGF21, endoglin; KIM1, FGF21, decorin; KIM1, FGF21, CD274; KIM1, FGF21, HGF; KIM1, FGF21, TFF2; KIM1, FGF21, PAPP.A2; KIM1, endoglin, decorin; KIM1, endoglin, CD274; KIM1, endoglin, HGF; KIM1, endoglin, TFF2; KIM1, endoglin, PAPP.A2; KIM1, decorin, CD274; KIM1, decorin, HGF; KIM1, decorin, TFF2; KIM1, decorin, PAPP.A2; KIM1, CD274, HGF; KIM1, CD274, TFF2; KIM1, CD274, PAPP.A2; KIM1, HGF, TFF2; KIM1, HGF, PAPP.A2; KIM1, TFF2, PAPP.A2; CLEC4A, FGF21, endoglin; CLEC4A, FGF21, decorin; CLEC4A, FGF21, CD274; CLEC4A, FGF21, HGF; CLEC4A, FGF21, TFF2; CLEC4A, FGF21, PAPP.A2; CLEC4A, endoglin, decorin; CLEC4A, endoglin, CD274; CLEC4A, endoglin, HGF; CLEC4A, endoglin, TFF2; CLEC4A, endoglin, PAPP.A2; CLEC4A, decorin, CD274; CLEC4A, decorin, HGF; CLEC4A, decorin, TFF2; CLEC4A, decorin, PAPP.A2; CLEC4A, CD274, HGF; CLEC4A, CD274, TFF2; CLEC4A, CD274, PAPP.A2; CLEC4A, HGF, TFF2; CLEC4A, HGF, PAPP.A2; CLEC4A, TFF2, PAPP.A2; FGF21, endoglin, decorin; FGF21, endoglin, CD274; FGF21, endoglin, HGF; FGF21, endoglin, TFF2; FGF21, endoglin, PAPP.A2; FGF21, decorin, CD274; FGF21, decorin, HGF; FGF21, decorin, TFF2; FGF21, decorin, PAPP.A2; FGF21, CD274, HGF; FGF21, CD274, TFF2; FGF21, HGF, TFF2; FGF21, HGF, PAPP.A2;

FGF21, TFF2, PAPP.A2; endoglin, decorin, CD274; endoglin, decorin, HGF; endoglin, decorin, TFF2; endoglin, decorin, PAPP.A2; endoglin, CD274, HGF; endoglin, CD274, TFF2; endoglin, CD274, PAPP.A2; endoglin, HGF, TFF2; endoglin, HGF, PAPP.A2; endoglin, TFF2, PAPP.A2; decorin, CD274, HGF; decorin, CD274, TFF2; decorin, CD274, PAPP.A2; decorin, HGF, TFF2; decorin, HGF, PAPP.A2; decorin, TFF2, PAPP.A2; CD274, HGF, TFF2; CD274, HGF, PAPP.A2; CD274, TFF2, PAPP.A2; or HGF, TFF2, PAPP.A2.

**[0140]** In some embodiments, the assay kit provided comprises at least one antibody, antibody fragment, or antibody derivative specific for each biomarker in one of the following sets of two optionally in combination with PIgf: SFLT1, KIM1; SFLT1, CLEC4A; SFLT1, FGF21; SFLT1, endoglin; SFLT1, decorin; SFLT1, CD274; SFLT1, HGF; SFLT1, TFF2; SFLT1, PAPP.A2; KIM1, CLEC4A; KIM1, FGF21; KIM1, endoglin; KIM1, decorin; KIM1, CD274; KIM1, HGF; KIM1, TFF2; KIM1, PAPP.A2; CLEC4A, FGF21; CLEC4A, endoglin; CLEC4A, decorin; CLEC4A, CD274; CLEC4A, HGF; CLEC4A, TFF2; CLEC4A, PAPP.A2; FGF21, endoglin; FGF21, decorin; FGF21, CD274; FGF21, HGF; FGF21, TFF2; FGF21, PAPP.A2; endoglin, decorin; endoglin, CD274; endoglin, HGF; endoglin, TFF2; endoglin, PAPP.A2; decorin, CD274; decorin, HGF; decorin, TFF2; decorin, PAPP.A2; CD274, HGF; CD274, TFF2; CD274, PAPP.A2; HGF, TFF2; HGF, PAPP.A2; TFF2, PAPP.A2.

**[0141]** In some embodiments, the assay kit provided comprises at least one antibody, antibody fragment, or antibody derivative specific for each biomarker in one of the following sets: PIgf, sFLT1, KIM1; PIgf, sFLT1, CLEC4A; PIgf, sFLT1, FGF21; PIgf, sFLT1, Decorin; PIgf, sFLT1, CD274; PIgf, sFLT1, HGF; PIgf, sFLT1, TFF2; PIgf, sFLT1, PAPP-A2; PIgf, Endoglin, KIM1; PIgf, Endoglin, CLEC4A; PIgf, Endoglin, FGF21; PIgf, Endoglin, Decorin; PIgf, Endoglin, CD274; PIgf, Endoglin, HGF; PIgf, Endoglin, TFF2; PIgf, Endoglin, PAPP-A2; PIgf, KIM1, CLEC4A; PIgf, KIM1, FGF21; PIgf, KIM1, Decorin; PIgf, KIM1, CD274; PIgf, KIM1, HGF; PIgf, KIM1, TFF2; PIgf, KIM1, PAPP-A2; PIgf, CLEC4A, FGF21; PIgf, CLEC4A, Decorin; PIgf, CLEC4A, CD274; PIgf, CLEC4A, HGF; PIgf, CLEC4A, TFF2; PIgf, CLEC4A, PAPP-A2; PIgf, CD274, CLEC4A; PIgf, CD274, FGF21; PIgf, CD274, HGF; PIgf, CD274, TFF2; PIgf, CD274, PAPP-A2; PIgf, Decorin, CLEC4A; PIgf, Decorin, FGF21; PIgf, Decorin, HGF; PIgf, Decorin, TFF2; PIgf, Decorin, PAPP-A2; PIgf, FGF21, TFF2, Decorin; PIgf, FGF21, TFF2, CD274; PIgf, FGF21, TFF2, HGF; PIgf, FGF21, TFF2; PIgf, FGF21, TFF2, PAPP-A2; PIgf, Endoglin, PAPP-A2, DECORIN, KIM1; PIgf, Endoglin, PAPP-A2, DECORIN,

CLEC4A; PIgf, Endoglin, PAPP-A2, DECORIN, FGF21; PIgf, Endoglin, PAPP-A2, DECORIN, CD274; PIgf, Endoglin, PAPP-A2, DECORIN, HGF; PIgf, Endoglin, PAPP-A2, DECORIN, TFF2.

**[0142]** In some embodiments, the assay kit provided is suitable for a multiplex homogenous biomarker assay, suitable for detection of all the analytes in a single reaction (e.g. in the same solution compartment). In such assays, multiple antibodies or antigen detection reagents that bind to separate epitopes are provided against the same analyte/biomarker, and detection of coincident binding/interaction of both antibodies to the same molecule of analyte/biomarker serves to detect the analyte/biomarker in the sample. Thus, such kits provide two antibodies or antigen-binding reagents against each analyte.

**[0143]** In the case of a multiplex homogenous biomarker assay detectable by TR-FRET, such kits provide a pair of antibodies or antigen-binding reagents for each analyte conjugated to a complementary pair of FRET dyes, wherein one antibody or antigen-binding reagent of the pair is conjugated to a FRET donor and the other is conjugated to a FRET acceptor. In the case of a multiplex homogenous biomarker assay detectable by LOCI, such kits provide a pair of antibodies or antigen-binding reagents wherein one antibody or antigen-binding reagent of the pair is conjugated to a photosensitizer and the other antibody or antigen-binding reagent of the pair is conjugated to an oxygen sensitive dye.

**[0144]** In some embodiments, the assay kit provided is suitable for a multiplex non-homogenous biomarker assay suitable for detection of all the analytes in separate reactions (e.g. in separate solution compartments). In some embodiments of such assays (e.g. sandwich ELISA), antibodies or antigen binding reagents against the relevant set of biomarkers are provided attached to a substrate (e.g. in a well of a multiwell plate, or in a lateral flow assay lane). A second free antibody against each of the biomarkers provided attached to the substrate is also provided; this antibody can be labeled (e.g. with a fluorescent dye, with a chemiluminescent enzyme, or a luminescent enzyme) or unlabeled. In the case where an unlabeled antibody is provided, a secondary labeled (e.g. with a fluorescent dye, with a chemiluminescent enzyme, or a luminescent enzyme) antibody or antigen-binding reagent is provided which has binding specificity against the second free antibody.

**[0145]** In some embodiments, the kit is for use as an in vitro diagnostic kit that includes one or more cartridges with reagents for testing on third-party platforms. Data collected from third-parties could be uploaded to a server (the cloud), put through a model/algorithm, and

results can be shared with a doctor or other medical practitioner. Kits may also include instructions for use.

*Exemplary Embodiments*

**[0146]** In some aspects, the present disclosure provides for a method for avoiding unnecessary treatment of preeclampsia, the method comprising: (a) contacting a biological sample that has been collected from a pregnant human female with a plurality of different probes, wherein the plurality of different probes comprises probes with specific affinity for four or more proteins selected from proteins listed in Table A or Table B; (b) determining, based on binding of the plurality of different probes to corresponding proteins, an amount or concentration for each of the four or more proteins; and (c) proceeding with treatment of said pregnant human in a manner that avoids unnecessary treatment of preeclampsia based at least in part on the amounts or concentrations of the four or more proteins determined in step (b). In some embodiments, the four or more proteins comprise: (a) placental growth factor (PIGF); (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. In some embodiments, the four or more proteins further comprise 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). In some embodiments, the four or more proteins comprise PIGF, sFlt1, KIM1, and CLEC4A. In some embodiments, the plurality of different probes comprises probes with specific affinity to fibroblast growth factor 21 (FGF21), and the four or more proteins comprise FGF21. In some embodiments, the plurality of different probes comprises probes with specific affinity for endoglin, and the four or more proteins comprise endoglin. In some embodiments, the plurality of different probes comprises probes with specific affinity for decorin, and the four or more proteins comprise decorin. In some embodiments, the plurality of different probes comprises probes with specific affinity for cluster of differentiation 274 (CD274), and the four or more proteins comprise CD274. In some embodiments, the plurality of different probes comprises probes with specific affinity for hepatocyte growth factor (HGF), and the four or more proteins comprise HGF. In some embodiments, the plurality of different probes comprises probes with specific affinity for trefoil factor 2 (TFF2), and the four or more proteins comprises TFF2. In some

embodiments, the plurality of different probes comprises probes with specific affinity for pappalysin-2 (PAPP-A2), and the four or more proteins comprise PAPP-A2. In some embodiments, the biological sample is obtained from the pregnant female after gestational week 20. In some embodiments, the biological sample has been collected from the pregnant female prior to gestational week 30. In some embodiments, the method further comprises: 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. In some embodiments, the classifier algorithm further comprises a correction for gestational age. In some embodiments, the correction for gestational age comprises a LOESS correction. In some embodiments, the classifier algorithm comprises a logistic regression. In some embodiments, the classifier algorithm comprises a logistic regression with elastic-net regularization. In some embodiments, the classifier algorithm comprises a Random Forest. In some embodiments, the biological sample is a urine, blood, amniotic fluid, exosome, plasma, or serum sample. In some embodiments, the biological sample is from blood of the pregnant human female. In some embodiments, the amount or concentration of no more than 20, no more than 15, nor more than 10, nor more than 9, no more than 8, no more than 7, no more than 6, nor more than 5, or no more than 4 proteins is determined. In some embodiments, one or more of the plurality of different probes are antibodies, antibody fragments, or antibody derivatives. In some embodiments, each of the plurality of different probes are antibodies, antibody fragments, or antibody derivatives. In some embodiments, the amount or concentration of at least one of (or all of (e.g., SYND1 and/or CLEC4A)) the four or more proteins is determined using a luminescent oxygen channeling immunoassay. In some embodiments, the amount or concentration of at least one of (or all of) the four or more proteins is determined using a time-resolved fluorescence resonance energy transfer (TR-FRET) assay. In some embodiments, the amount or concentration of at least one of (or all of) the four or more proteins is determined using a proximity extension assay. In some embodiments, the amount or concentration of at least one of (or all of) the four or more proteins is determined using an enzyme-linked immunosorbent assay (ELISA). In some embodiments, the amount or concentration of at least one of (or all of) the four or more proteins is determined using an amplified luminescent proximity homogenous assay. In some embodiments, the amount or concentration of at least one of (or all of) the four or more proteins is determined using a lateral flow assay. In some embodiments, the biological

sample is obtained from the pregnant human while in a perinatologist's office, a labor and delivery room, or triage (ER). In some embodiments, the method further comprises separating the biological sample into a plurality of different reaction vessels, the plurality of reaction vessels comprising a first reaction vessel, a second reaction vessel, a third reaction vessel, and a fourth reaction vessel, wherein contacting the biological sample with the plurality of different probes comprises delivering probes with specific affinity for PIGF in a first reaction vessel, delivering probes with specific affinity to sFlt1 to a second reaction vessel, delivering probes with specific affinity to KIM1 to a third reaction vessel, and delivering probes with specific affinity to CLEC4A to a fourth reaction vessel. In some embodiments, the step of contacting the biological sample with the plurality of different probes occurs in a single reaction vessel. In some embodiments, the biological sample was obtained from the pregnant female after the pregnant female has shown one or more symptoms of preeclampsia, wherein the symptoms of preeclampsia are selected from (1) high blood pressure and (2) proteinuria. In some embodiments, the sample was obtained from the pregnant female after the pregnant female has shown both (1) high blood pressure and (2) proteinuria. In some embodiments, the plurality of different probes comprises two sets of probes with specific affinity for each of the four or more proteins, wherein each set of the two sets of probes binds to different epitopes.

**[0147]** In some aspects, the present disclosure provides for 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 selected from the proteins listed in Table A or Table B and detecting the presence and/or quantity of the four or more proteins based on binding of the plurality of different probes to corresponding proteins. In some embodiments, 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. In some embodiments, the four or more proteins further comprise 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). In some

embodiments, the four or more proteins comprise PlGF, sFlt1, KIM1, and CLEC4A. In some embodiments, the plurality of different probes comprises probes with specific affinity to fibroblast growth factor 21 (FGF21), and the four or more proteins comprise FGF21. In some embodiments, the plurality of different probes comprises probes with specific affinity for endoglin, and the four or more proteins comprise endoglin. In some embodiments, the plurality of different probes comprises probes with specific affinity for decorin, and the four or more proteins comprise decorin. In some embodiments, the plurality of different probes comprises probes with specific affinity for cluster of differentiation 274 (CD274), and the four or more proteins comprise CD274. In some embodiments, the plurality of different probes comprises probes with specific affinity for hepatocyte growth factor (HGF), and the four or more proteins comprise HGF. In some embodiments, the plurality of different probes comprises probes with specific affinity for trefoil factor 2 (TFF2), and the four or more proteins comprises TFF2. In some embodiments, the plurality of different probes comprises probes with specific affinity for pappalysin-2 (PAPP-A2), and the four or more proteins comprise PAPP-A2. In some embodiments, the biological sample has been collected from the pregnant human female after gestational week 20. In some embodiments, the biological sample has been collected from the pregnant female prior to gestational week 30. In some embodiments, the biological sample is a urine, blood, amniotic fluid, exosome, plasma, or serum sample. In some embodiments, the biological sample is from blood of the pregnant human female. In some embodiments, the amount or concentration of no more than 20, no more than 15, nor more than 10, nor more than 9, no more than 8, no more than 7, no more than 6, nor more than 5, or no more than 4 proteins is determined. In some embodiments, one or more of the plurality of different probes are antibodies, antibody fragments, or antibody derivatives. In some embodiments, each of the plurality of different probes are antibodies, antibody fragments, or antibody derivatives. In some embodiments, the plurality of probes contact the biological sample or a fraction thereof in a single reaction vessel. In some embodiments, 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. In some embodiments, the method further comprises a second plurality of probes, wherein the second plurality of probes comprises a probe set that is specific for binding to PlGF, a probe set that is specific for binding to sFlt1, a probe set that is specific for binding to KIM1, and a probe set that is specific for binding to CLEC4A, 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. In some embodiments, 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.

**[0148]** In some aspects, the present disclosure provides for a method for managing a pregnant human subject and identifying the pregnant human subject as not at risk for preeclampsia for a specified period of time, the method comprising: (a) identifying, via a test having (1) a specificity of greater than 80% and (2) a sensitivity of greater than 85%, the pregnant subject as not at risk for developing preeclampsia within the specified period of time, wherein the specified period of time is between one week and six weeks; and (b) managing the pregnant human subject identified as not at risk for developing preeclampsia within the specified period of time by proceeding with ambulant monitoring treatment of said pregnant patient without treating the patient for preeclampsia. In some embodiments, the test has a specificity of at least 82.0%, at least 84.0%, at least 85.0%, at least 87.0%, at least 88.0%, at least 89.0%, at least 90.0%, at least 90.5%, at least 91.0%, or at least 91.5%. In some embodiments, the test has a sensitivity of at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, or at least 95%. In some embodiments, the test has a negative predictive value of at least about 95.0%, 96.0%, 97.0%, 98.0%, 98.2%, 98.4%, 98.5%, 98.7%, 99%, 99.2%, or 99.5% when applied to a random population of ethnically diverse pregnant women after gestational week 20 that exhibit one or more of (1) high blood pressure and (2) proteinuria. In some embodiments, the test has a positive predictive value of at least about 30%, at least about 32%, at least about 35%, at least about 37%; at least about 40%, at least about 42%, at least about 45%, at least about 50%, at least about 55%, or at least about 57% when applied to a random population of ethnically diverse pregnant women after gestational week 20 that exhibit one or more of (1) high blood pressure and (2) proteinuria. In some embodiments, the negative predictive value of the test is higher than the positive predictive value of the test. In some embodiments, the specified period of time is between one week and four weeks, one week and three weeks, or one week and two weeks. In some embodiments, the test comprises determining an amount or concentration of each of four or more proteins selected from proteins listed in Table A or

Table B. In some embodiments, the four or more proteins comprise PI GF, sFlt-1, KIM1, and CLEC4A. In some embodiments, the four or more proteins further comprise FGF21.

**[0149]** In some aspects, the present disclosure provides for a method of treating a pregnant human subject, the method comprising: obtaining an indicium generated, at least in part, from a determination of levels for four or more proteins listed in Table A or Table B; and changing a clinical regimen for the pregnant human subject based, at least in part, on the obtained indicium. In some embodiments, obtaining the indicium comprises: determining the levels for PI GF, sFlt1, KIM1, and CLEC4A, wherein the levels are determined from binding of each of PI GF, sFlt1, KIM1, and CLEC4A to corresponding probes. In some embodiments, the obtaining the indicium further comprises determining the level for FGF21, wherein the level of FGF21 is determined from binding of FGF21 to corresponding probes. In some embodiments, the method further comprises classifying (or ruling out a classification) the pregnant subject as having a low risk of having preeclampsia or developing preeclampsia within a specified period of time. In some embodiments, the pregnant subject is classified by any method described herein. In some embodiments, the method further comprises administering an antihypertensive drug to the patient. In some embodiments, the antihypertensive drug is a central alpha agonist, a vasodilator, a calcium-channel blocker, an alpha-blocker or a beta-blocker. In some embodiments, the antihypertensive drug is methyldopa, labetalol, nifedipine, verapamil, clonidine, hydralazine, diazoxide, prazosin, or oxprenolol.

**[0150]** In some aspects, the present disclosure provides for a mixture comprising: a fluid sample from a pregnant female subject; a first plurality of different probes, wherein the first plurality of different probes comprises different probes, each with specific affinity for four or more proteins selected from proteins listed in Table A or Table B. In some embodiments, the four or more proteins comprise: (a) placental growth factor (PI GF) (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. In some embodiments, the four or more proteins further comprise 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). In some embodiments, the four or more proteins comprise PI GF, sFlt1, KIM1, and CLEC4A. In

some embodiments, the four or more proteins comprise FGF 21. In some embodiments, the four or more proteins comprise endoglin. In some embodiments, the four or more proteins comprise decorin. In some embodiments, the four or more proteins comprise CD274. In some embodiments, the four or more proteins comprise HGF. In some embodiments, the four or more proteins comprise TFF2. In some embodiments, the four or more proteins comprise PAPP-A2. In some embodiments, the fluid sample has been collected after gestational week 20. In some embodiments, the fluid sample has been collected from the pregnant female prior to gestational week 30. In some embodiments, the mixture includes no more than 20, no more than 16, no more than 14, no more than 12, no more than 10, no more than eight, no more than seven, no more than 6, no more than 5, or nor more than 4 sets of probes that are designed to bind to different proteins in the fluid sample. In some embodiments, the fluid sample is from a blood, plasma, serum, or exosome sample. In some embodiments, the fluid sample was obtained from the subject after the subject has shown one or more symptoms of preeclampsia, wherein the symptoms of preeclampsia are selected from (1) high blood pressure and (2) proteinuria. In some embodiments, the fluid sample was obtained from the subject after the subject has shown both (1) high blood pressure and (2) proteinuria. In some embodiments, the first plurality of different probes comprises a first set of probes with specific affinity for each of the four or more proteins and a second set of probes with specific affinity for each of the four or more proteins, wherein each set of the two sets of probes binds to different epitopes. In some embodiments, the first set of probes and the second set of probes are conjugated to pairs of oligonucleotides containing complementary hybridization regions for each protein-specific probe pair. In some embodiments, the first set of probes and the second set of probes are conjugated to unique FRET pairs of fluorophores for each protein-specific probe pair. In some embodiments, for each protein-specific probe pair, one probe is conjugated to biotin or a streptavidin-binding analog thereof. In some embodiments, the mixture further comprises (a) a photosensitizer; and (b) an oxygen-sensitive dye, wherein one of (a) and (b) is capable of binding the first set of probes, and the other is capable of binding the second set of probes. In some embodiments, one or more of the first plurality of different probes are antibodies, antibody fragments, or antibody derivatives. In some embodiments, each of the first plurality of different probes are antibodies, antibody fragments, or antibody derivatives.

**[0151]** In some aspects, the present disclosure provides for a reaction plate comprising a plurality of reaction wells, wherein the plurality of reaction wells comprises: a first well

comprising (1) a first portion of a biological sample from a pregnant human subject, wherein the biological sample was obtained from a pregnant human subject after 20 weeks of gestation, and (2) a first set of probes for binding to PIgf; a second well comprising (1) a second portion of the biological sample from the pregnant human subject, and (2) a second set of probes for binding to sFlt1, endoglin, pappalysin 2 (PAPP-A2), or decorin; a third well comprising (1) a third portion of the biological sample from the pregnant human subject, and (2) a third set of probes for binding to KIM1, (2) programmed cell death 1 ligand 1 (CD274), or decorin; and a fourth well comprising (1) a fourth portion of the biological sample from the pregnant human subject, and (2) a fourth set of probes for binding to CLEC4A, FGF21, TFF2, or HGF. In some embodiments, the second set of probes in the second well are configured to bind to sFlt1. In some embodiments, the third set of probes in the third well are configured to bind to KIM1. In some embodiments, the fourth set of probes in the fourth well are configured to bind to CLEC4A. In some embodiments, the plurality of wells comprises a fifth well, the fifth well comprising (1) a fifth portion of the biological sample from the pregnant human subject and (2) a fifth set of probes for binding to FGF21. In some embodiments, the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to endoglin. In some embodiments, the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to decorin. In some embodiments, the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to CD274. In some embodiments, the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to HGF. In some embodiments, the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to TFF2. In some embodiments, the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to PAPP-A2. In some embodiments, the biological sample has been collected from the pregnant female prior to gestational week 30. In some embodiments, the biological sample is from blood of the pregnant human female. In some embodiments, the plurality of wells of the reaction include probes for specific binding to no more than 20, no more than 15, no more than 12, no more than 10, no more than 8, no more than 7, no more than 6, no more than 5, or no more than 4 proteins. In some embodiments, the probes comprise antibodies, antibody fragments, or antibody derivatives. In some embodiments, the biological sample is from the

subject after the subject has shown one or more symptoms of preeclampsia, wherein the symptoms of preeclampsia are selected from (1) high blood pressure and (2) proteinuria. In some embodiments, the sample is from the subject after the subject has shown both (1) high blood pressure and (2) proteinuria. In some embodiments, each set of probes comprises probes that specifically bind to different epitopes.

**[0152]** In some aspects, the present disclosure provides for a kit for ruling out preeclampsia in a pregnant female subject, the kit comprising: (a) probes for determining the levels of four or more proteins selected from the proteins listed in Tables A and B; (b) wherein the kit is designed to measure the levels of no more than 20, no more than 15, no more than 10, nor more than 8, no more than 7, no more than 6, nor more than 5, or no more than 4 proteins. In some embodiments, the four or more proteins comprises: (a) placental growth factor (PIGF); (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. In some embodiments, the four or more proteins comprise 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). In some embodiments, the four or more proteins comprise PIGF, sFlt1, KIM1, and CLEC4A. In some embodiments, four or more proteins comprise FGF21. In some embodiments, the four or more proteins comprise endoglin. In some embodiments, the four or more proteins comprise decorin. In some embodiments, the four or more proteins comprise CD274. In some embodiments, the four or more proteins comprise HGF. In some embodiments, the four or more proteins comprise TFF2. In some embodiments, the four or more proteins comprise PAPP-A2. In some embodiments, the kit further comprises instructions for carrying out an immunoassay. In some embodiments, the kit is an enzyme-linked immunosorbent assay kit. In some embodiments, one or more of the probes are attached to substrate. In some embodiments, kit is for a lateral flow immunoassay.

**[0153]** In some aspects, the present disclosure provides for a system for ruling out preeclampsia in a pregnant female subject for a specified period of time, the system comprising: a processor; an input module for inputting levels of at least four proteins in a biological sample, wherein the at least four proteins are selected from Tables A and B; a computer readable medium containing instructions that, when executed by the processor,

perform a first algorithm on the input levels of the at least four proteins; and an output module providing one or more indicia based on the input levels of the at least four proteins, wherein the one or more indicia are indicative of the subject not having preeclampsia for at least a specified period of time. In some embodiments, the system further comprises probes to each the at least four proteins. In some embodiments, the system is designed to output the one or more indicia based on input levels for no more than 15, no more than 10, no more than 8, no more than 7, nor more than 6, no more than 5, or no more than 4 proteins. In some embodiments, the at least four proteins comprise: (a) placental growth factor (PIGF); (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. In some embodiments, the at least four proteins comprise 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). In some embodiments, the at least four proteins comprise PIGF, sFlt1, KIM1, and CLEC4A. In some embodiments, the at least four proteins comprise FGF21. In some embodiments, the at least four proteins comprise decorin. In some embodiments, the at least four proteins comprise CD274. In some embodiments, the at least four proteins comprise HGF. In some embodiments, the at least four proteins comprise TFF2. In some embodiments, the at least four proteins comprise PAPP-A2. In some embodiments, the algorithm comprises a correction based on gestational age. In some embodiments, the algorithm comprises a logistic regression.

**[0154]** In one aspect, the disclosure provides for a method for assessing a risk of a female subject having or developing preeclampsia within a specified time period, the method comprising: (a) obtaining a sample from a pregnant female subject; (b) measuring the levels of a plurality of proteins from the sample derived from a pregnant female subject, wherein at least two of the plurality of proteins is selected from the group (“Group 2”) consisting of Tables 2, 3, 4, and 5; (c) calculating an index based, at least in part, on the levels of the plurality of proteins; and (d) determining a risk of having or developing preeclampsia in the female subject based on the index; wherein the specified period of time is at least one week. In some embodiments, the sample is a urine, blood, amniotic fluid, cervical-vaginal, exosome, plasma, or serum sample. In some embodiments, the sample is a blood sample. In

some embodiments, the sample is a serum sample. In some embodiments, the sample is a plasma sample. In some embodiments, measuring the levels of a plurality of proteins from the sample comprises contacting the proteins with a plurality of probes specific for each protein. In some embodiments, the probes may comprise antibodies. In some embodiments, at least two of the plurality of proteins are selected from Group 2. In some embodiments, at least three of the plurality of proteins are selected from Group 2. In some embodiments, at least four of the plurality of proteins are selected from Group 2. In some embodiments, at least five of the plurality of proteins are selected from Group 2. In some embodiments, at least six of the plurality of proteins are selected from Group 2. In some embodiments, at least seven of the plurality of proteins are selected from Group 2. In some embodiments, levels are measured for no more than ten proteins. In some embodiments, levels are measured for no more than nine proteins. In some embodiments, levels are measured for no more than eight proteins. In some embodiments, levels are measured for no more than seven proteins. In some embodiments, levels are measured for no more than six proteins. In some embodiments, levels are measured for no more than five proteins. In some embodiments, levels are measured for no more than four proteins. In some embodiments, levels are measured for no more than three proteins. In some embodiments, the sample was obtained from the subject after the subject has shown one or more symptoms of preeclampsia, wherein the symptoms of preeclampsia are selected from (1) high blood pressure and (2) proteinuria. In some embodiments, the sample was obtained from the subject after the subject has shown both (1) high blood pressure and (2) proteinuria. In some embodiments, the sample is obtained from the subject after week 20 of the pregnancy. In some embodiments, determining the risk of preeclampsia in the female subject comprises comparing the index to a threshold value. In some embodiments, a predefined relationship between the index and the threshold value is indicative, with a negative predictive value of at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 97.5%, at least 98%, at least 98.5%, or at least 99%, of the subject not having or developing preeclampsia when used on an unbiased population of pregnant women that have both high blood pressure and proteinuria. In some embodiments, a predefined relationship between the index and the threshold value is indicative, with a negative predictive value of at least 90%, of the subject not having or developing preeclampsia. In some embodiments, the negative predictive value is higher than any negative predictive value of any test that measures only one or more of sFLT-1, PIgf, endoglin, and PAPP-A. In some

embodiments, the plurality of proteins comprises soluble fms-like tyrosine kinase-1 (“sFLT-1”), and the index is calculated, in part, based on the level of sFLT-1 in the sample. In some embodiments, the plurality of proteins comprises placental growth factor (“PIGF”), and the index is calculated, in part, based on the level of PIGF in the sample. In some embodiments, the index is calculated, at least in part, based on the levels of both sFLT-1 and PIGF. In some embodiments, the plurality of proteins comprises pregnancy-associated plasma protein A (PAPP-A), and the index is calculated, in part, based on the levels of PAPP-A in the sample. In some embodiments, the index is calculated based on the levels of no protein other than the proteins of Group 1, sFLT-1, PIGF, endoglin, and PAPP-A. In some embodiments, the levels of the plurality of proteins are determined via an immunoassay. In some embodiments, the levels of the at least two proteins are determined by one or more enzyme-linked immunosorbent assays. In some embodiments, the levels of the at least two proteins are determined by one or more luminescent oxygen channeling immunoassays (LOCI). In some embodiments, the levels of the at least two proteins are determined by one or more of mass spectrometry, ELISPOT, nanoparticles, or radioimmunoassays. In some embodiments, the sample is obtained from the subject in a perinatologist’s office, a labor and delivery room, or triage (ER).

**[0155]** In a further aspect, the disclosure provides for a method for assessing whether or not a pregnant female subject currently has or will develop (or will not develop) preeclampsia within a specified period of time, the method comprising: performing a binary classification test on a first sample derived from a pregnant female subject who has both high blood pressure and proteinuria, wherein the test comprises measuring the levels of one or more proteins in the first sample, wherein the one or more proteins are selected from the group consisting of Tables 2, 3, 4, and 5; wherein the specified time period is between one week and six weeks; and wherein the test has a negative predictive value of greater than 90% when used on an unbiased population of pregnant women that have both high blood pressure and proteinuria. In some embodiments, the binary classification test is a computer implemented two-way classification algorithm. In some embodiments, the binary classification test is a decision tree, random forest, Bayesian network, support vector machine, neural network, linear discriminant analysis (LDA), gradient boosting method (GBM), elastic-net logistic regression, or logistic regression test. In some embodiments, the method further comprises obtaining a sample from the subject. In some embodiments, the sample is a urine, blood, amniotic fluid, exosome, plasma, or serum sample. In some embodiments, the sample is a

serum sample. In some embodiments, the sample is a plasma sample. In some embodiments, the binary classification test has a positive predictive power of at least 85% when used on an unbiased population of pregnant women that have both high blood pressure and proteinuria. In some embodiments, the binary classification test has a negative predictive value that is greater than its positive predictive value. In some embodiments, the binary classification test has a specificity of at least 85%. In some embodiments, the binary classification test has a sensitivity of at least 85%. In some embodiments, the specified time period is between 10 days and three weeks.

**[0156]** In another aspect, the disclosure provides for a method of classifying a pregnant human subject as having a low risk of having or developing preeclampsia within a specified time period, the method comprising: (a) obtaining a sample from a pregnant human subject who has been identified as having high blood pressure or proteinuria; (b) running a test to obtain a protein expression profile, wherein the protein expression profile includes levels of two or more proteins from Tables 2, 3, 4, and 5; (c) applying a classifier algorithm to the expression profile, wherein the classifier algorithm calculates an index; and comparing the index to a reference value to determine whether the pregnant human subject has a low risk of having or developing preeclampsia.

**[0157]** In another aspect, the disclosure provides for a method of treatment comprising: (a) classifying a pregnant subject as having a low risk of having or developing preeclampsia according to any method described herein; and (b) changing a therapeutic regimen for the subject based on the classification. In some embodiments, the method further comprises administering an antihypertensive drug to the patient if the test indicates that the pregnant female subject will not develop preeclampsia within the specified time period. In some embodiments, the antihypertensive drug is a central alpha agonist, a vasodilator, a calcium-channel blocker, an alpha-blocker or a beta-blocker. In some embodiments, the antihypertensive drug is methyldopa, labetalol, nifedipine, verapamil, clonidine, hydralazine, diazoxide, prazosin, or oxprenolol.

**[0158]** In yet another aspect, the disclosure provides for a kit for confirming the presence or absence of preeclampsia in a female subject, the kit comprising: (a) reagents for detecting one or more protein selected from the group consisting of Tables 2, 3, 4, and 5; and optionally (b) reagents for detecting sPIGF and/or sFLT-1, wherein the kit is designed to measure the levels of not more than 10 proteins. In some embodiments, the kit further comprises reagents for

measuring the levels of PAPP-A. In some embodiments, the kit is an enzyme-linked immunosorbent assay kit.

**[0159]** In another aspect, the disclosure provides for a system for assessing the likelihood that a pregnant subject has or will develop preeclampsia within a specified period of time, the system comprising: (a) a first agent that selectively binds to the one or more proteins in a sample from a pregnant subject, wherein the one or more proteins are selected from the group consisting of Group 2; (b) optionally a second agent that selectively binds to placental growth factor (PIGF); (c) optionally a third agent that selectively bind to soluble fms-like tyrosine kinase 1 (sFlt-1); (d) an input module for inputting levels of optionally PIGF, optionally sFlt-1, and the one or more proteins from the group consisting of Tables 2, 3, 4, and 5; (d) a processor; (e) a computer readable medium containing instructions which, when executed by the processor, performs a first algorithm on the input levels of optionally PIGF, optionally sFlt-1 and the one or more protein from Group 2; (f) an output module providing one or more indicia based on the input levels of optionally PIGF, optionally sFlt-1 and the one or more proteins from Group 2, wherein the one or more indicia represent the presence or absence of preeclampsia in the pregnant subject. In one embodiment, the first and second agents do not bind to the same protein. In another embodiment, the system is designed to output the one or more indicia based on input levels for no more than ten proteins.

**[0160]** In another aspect, the disclosure provides for a computer-implemented method of assessing the likelihood a pregnant subject has or will develop preeclampsia within a specified period of time, comprising: (a) receiving, at a computer, expression level data derived from a plasma or serum sample from the pregnant subject; (b) applying, by the computer, a classifier algorithm to the expression level data derived from the plasma or serum sample from the pregnant subject using a classification rule or a class probability equation; and (c) 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 a having a probability of having preeclampsia with a negative predictive value of greater than 80 percent, wherein the pregnant subject has hypertension or proteinuria. In some embodiments, the expression level data comprises levels of proteins selected from the group consisting of Tables 2, 3, 4, and 5. In some embodiments, the classifier algorithm is logistic regression. In some embodiments, the classifier algorithm is a decision tree, random forest, Bayesian network, support vector machine, neural network, or logistic regression algorithm.

## EXAMPLES

**[0161]** Examples 1–7 describe an initial, smaller study design to identify markers that can be used to rule out the need for treatment of preeclampsia. Examples 8–16 describe follow-on, larger studies that provided additional information regarding the discriminatory of biomarkers and combinations of biomarkers in the context of assessing risks associated with, for example, women with one or more symptoms of preeclampsia.

**Example 1—Initial Preliminary Study Design**

**[0162]** Samples of serum and urine for biomarker analysis were obtained from a Progenity Multicenter specimen procurement study, which was designed to, *inter alia*, identify biomarkers that improve the detection or ruling out of preeclampsia with improved performance relative to the sFlt/PIGF ratio method described by Zeisler et al. (NEJM 274(2017):13-22). More particularly, pregnant women who were 18 years or older (20 weeks to 39 weeks of gestation at first visit) with suspected preeclampsia (based on new onset symptoms, elevated blood pressure, proteinuria, edema or others) were selected for participation. Baseline procedures were performed, including collection of demographic, medical and obstetric histories, list of concomitant medications, weight, height, blood pressure, and other clinical information, as well as obtaining blood and urine samples for use in biomarker assays. After discharge, all patients in the study were followed by interim research visits every 14 days (+/- 3 days). For patients who developed PreE, the time (in days) from baseline sampling, the gestational age at diagnosis, and the severity of the disease was recorded. Patients who did not develop preeclampsia before or at delivery were included in the NEGATIVE-PRE-E CONTROL (NonPreE) group. For these NEGATIVE PRE-E CONTROLS, the time from baseline sampling (in days) to either delivery or loss to follow-up was recorded.

**[0163]** The interim study visits occurred every 14 days [+/- 3 days] and continued until the subject either: 1) reached 37 weeks' gestation, 2) developed PreE, 3) delivered, or 4) was lost to follow-up.

**[0164]** Delivery outcomes (maternal and neonatal clinical information) were collected on all subjects enrolled in the study. Additionally, if possible during admission for delivery, blood and urine samples were collected for analysis at delivery.

**[0165]** The discovery set of samples for further analysis consisted of a total of 70 samples that were separated into non-preeclampsia or preeclampsia based on whether they delivered pre-37 weeks gestation: 40 non-preeclampsia (NonPreE) and 30 with preeclampsia (PreE). The 70 samples were grouped into four further subcohorts based on preeclampsia status and

whether or not sFlt/PIGF ratio was predictive: (A) control patients who delivered at term and were not diagnosed with preeclampsia. (true negatives and false positives, n=20); (B) patients clinically diagnosed with preeclampsia with sFlt/PIGF ratio of 38 or higher (true positives, n=20); (C) patients clinically diagnosed with preeclampsia with sFlt/PIGF ratio of less than 38 (false negatives, n=10); and (D) patients who delivered at term and were not diagnosed with preeclampsia with sFlt/PIGF ratio of 38 or higher (false positives, n=20).

**[0166]** A comparison of the subcohort statistics for the current study is provided in Table 1. As in the Zeisler study, a high degree of false classification based on the sFlt1/PIGF ratio criterion was observed: a significant proportion of the patients identified by the ratio as having preeclampsia are false positives, and a significant proportion of the patients who actually developed preeclampsia were not detected by the ratio (false negatives).

**Table 1: Sub-cohort statistics for this study and comparison to Zeisler et al.**

<i>Cohort</i>	<i>Description</i>	<i>N</i> ( <i>Zeisler</i> <i>study</i> )	<i>N</i> ( <i>current</i> <i>study</i> )	<i>sFlt1/PIGF</i> <i>predictive</i> <i>status</i>	<i>Prevalence</i> ( <i>current</i> <i>study</i> )	<i>Prevalence</i> ( <i>Zeisler</i> <i>study</i> )	<i>Avg sFlt/PIGF</i> ( <i>current</i> <i>study</i> )
<b>A</b>	Control - Complicated Pregnancy diagnosis, No PREECLAMPSI A Delivered 37 weeks or later	253	20	True Negatives or False Positives	28.50%	77%	33 (0.5-150)
<b>B</b>	True Positives - PREECLAMPSI A Delivered before 37 weeks (sFlt/PIGF >= 38)	21	20	True Positives	28.50%	6.40%	337 (66-1123)
<b>C</b>	False Negatives - PREECLAMPSI A Delivered before 37 weeks (sFlt/PIGF <38)	10	10	False Negatives	14.30%	3%	15 (3-33)
<b>D</b>	False Positives - Complicated Pregnancy, No PREECLAMPSI A Delivered 37 weeks or later, (sFlt/PIGF >= 38)	43	20	False Positives	28.50%	13.10%	112 (66-1123)

#### *Diagnostic Criteria*

**[0167]** Patients were diagnosed with suspected preeclampsia based on new onset of hypertension (sSBP>140 mmHg or sDBP>90 mmHg or both) with accompanying proteinuria (defined with the cutoffs of 2+ protein by dipstick,  $\geq 300$  mg of protein per 24-hour urine

collection,  $\geq 30$  mg of protein per deciliter in a spot urine sample, or a ratio of protein to creatinine of  $\geq 30$  mg per millimole). sFlt/PIGF criteria for suspected preeclampsia were an sFlt/PIGF ratio greater than or equal to 38. For the purposes of analysis, patients diagnosed with suspected preeclampsia who delivered preterm were classified as actual preeclampsia (true positive). For the purposes of analysis, patients diagnosed with suspected preeclampsia who did not deliver preterm were classified as complicated pregnancy (false positive).

**[0168]** Exclusion criteria for patients from the study included male, not pregnant, age less than 18 or greater than 45 years, pregnancy with multiple gestation, pregnancy with gestational age less than 20 or greater than 39 weeks, or pregnancy with known fetal abnormalities.

#### **Example 2—Quantification of Protein Biomarkers**

**[0169]** Serum samples collected according to a standard procedure from 68 patients (one non-preeclampsia and one preeclampsia sample failed quality control checks) were analyzed retrospectively. Briefly, filled red top blood collection tubes were allowed to clot at room temperature for 30–60 minutes, were centrifuged 20 minutes at 1300g to remove the clot, and were then aliquoted for long term storage below  $-80^{\circ}\text{C}$ . Hemolysis, date and time of blood collection, and date and time of freezing were recorded. Both single analyte analysis of suspected biomarkers (of Fibronectin, PI GF, sFlt1, and PAPP-A) and unbiased panel analyses of proteins associated with inflammation, immune response, oncology, organ damage, immunooncology, and metabolism (containing 92 biomarkers in each panel) were performed. PI GF was represented in both single analyte analysis and the unbiased panel analysis, whereas sFlt1, PAPP-A, and Fibronectin were not.

##### *Single Candidate Analyte Analysis*

**[0170]** sFlt1, PAPP-A, PI GF, and Fibronectin single analytes were measured by a biotin/fluorescein-based AlphaScreen™ assay. Antibodies labeled with biotin and fluorescein was prepared fresh each time by combining 2.5 Antibody mix with 125  $\mu\text{l}$  dilution buffer and placing the mixture on ice. This proximity mix was placed in a single well of a standard white 96 well plate (Biorad, Hemel Hempstead, UK) followed by 2  $\mu\text{l}$  of target antigen or sample, which was appropriately diluted with 1 $\times$  serum dilution buffer (SDB II, 4483013, Life Technologies) if needed. No protein controls (NPC) consisted of 2  $\mu\text{l}$  of proximity mix and 2  $\mu\text{l}$  of 1 $\times$  SDB II. The plate was sealed using an optically clear heat seal with a PX1 PCR plate sealer (Biorad, Hemel Hempstead, UK), centrifuged at 780 g for 2 min (Rotina 380R Hettich Zentrifuge, Germany) and incubated for 1 h at  $20^{\circ}\text{C}$ . Following

removal of the seal, 16  $\mu$ l of anti-fluorescein acceptor beads (10  $\mu$ gs) and St./AV sensitizer beads (2  $\mu$ gs) (Perkin Elmer) was added to each well, the plate was sealed again, spun as before and the incubation was performed at 37 °C for 60 min. The assay was read on a standard ALPHA screen reader.

*Unbiased Multiplex Analyte Analysis*

[0171] For unbiased discovery of biomarkers, proximity extension assays were used. A pair of oligonucleotide-conjugated antibodies specific to each panel protein was added to 1  $\mu$ L of serum. Antibody-protein antibody sandwiches were detected by the hybridization of the nucleotide pairs in close proximity, followed by an extension reaction to generate a unique sequence product. These sequences were then quantitated by microfluidic qPCR. A total of 552 distinct marker levels including markers implicated in inflammation, immune response, oncology, organ damage, immuno-oncology, and metabolism were measured in this assay.

**Example 3—Single Protein Screening for Distinguishing Nonpreeclampsia from Preeclampsia**

[0172] A response screening of non-preeclampsia vs preeclampsia using ANOVA for each of the 552 markers was performed, defining a FDR LogWorth >2 as significance. A plot of FDR LogWorth vs Effect Size (**Figure 1A**) was generated to analyze the value of single biomarkers for distinguishing Nonpreeclampsia vs PreE. Three biomarkers (CLEC4A, SYND1, and PIGF) meet the FDR LogWorth criteria for significance (>2), while 6 additional biomarkers (PGF, FES, TGF-alpha 2, APLP1, KIM1, and NOS32) show an FDR LogWorth more significant than most of the biomarkers. A summary of these top distinguishing markers is provided in **Table 2**; while visual representations of the data spread for each of the top 3 biomarkers for non-preeclampsia vs preeclampsia is shown in **Figure 1B**.

**Table 2: Top Nine Biomarkers from Nonpreeclampsia vs Preeclampsia Response Screening**

Marker	PValue	FDR PValue	FDR LogWorth
<b>CLEC4A</b>	<.0001	0.0040	2.40
<b>SYND1</b>	<.0001	0.0040	2.40
<b>PIGF</b>	<.0001	0.0040	2.40
<b>PGF</b>	<.0001	0.0123	1.91
<b>APLP1</b>	0.0028	0.1948	0.71
<b>TGF-alpha 2</b>	0.0025	0.1948	0.71
<b>FES</b>	0.0018	0.1948	0.71
<b>KIM1</b>	0.0028	0.1948	0.71
<b>NOS3 2</b>	0.0034	0.2084	0.68

**Example 4—Subcohort Analysis of Nine Biomarkers From Example 3**

**[0173]** The expression levels of each of the top nine biomarkers identified in **Example 3** were further analyzed with respect to their expression levels in each subcohort identified in **Example 1** (A=nonPreE/true negatives, B=PreE/true positive, C=PreE/false negative, D=nonPreE/false positive). The results are graphically presented in **Figure 2**. Consistent with the high false positive/negative rate of the sFlt1/PlGF ratio assay, PlGF (**Figure 2, top right panel**) shows poor discrimination power for the C and D groups, even though it distinguishes A from B. However, other biomarkers (**CLEC4A, Figure 2, top left** and **SYND1, Figure 2, middle**), show the capability to distinguish between A and B cohorts as well as C and D cohorts.

**Example 5—Random Bootstrap Forest Identification of Predictive Biomarkers**

**[0174]** As an alternative to the method of **Example 3** random bootstrap forest predictor screening was run on the expression level data from the 552 unbiased biomarkers assessed in multiplex screening. The top 20 predictors discovered by this method ranked by contribution are shown in **Table 3**.

**Table 3: Top 20 Nonpreeclampsia vs Preeclampsia Predictors Resulting from Random Bootstrap Forest Analysis**

<i>Predictor</i>	<i>Contribution</i>	<i>Portion</i>	<i>Rank</i>
<b>SYND1</b>	4.03	0.1013	1
<b>UPA</b>	1.63	0.0410	2
<b>AMN</b>	1.24	0.0313	3
<b>ZBTB16</b>	1.24	0.0312	4
<b>PGF</b>	1.15	0.0290	5
<b>TGFalpha2</b>	1.10	0.0278	6
<b>PIGF</b>	1.09	0.0275	7
<b>NOS3_2</b>	1.08	0.0271	8
<b>ERBB4</b>	1.01	0.0254	9
<b>HGF2</b>	0.71	0.0179	10
<b>CXCL6</b>	0.66	0.0167	11
<b>ALDH3A1</b>	0.65	0.0165	12
<b>GDNF</b>	0.64	0.0163	13
<b>GLB1</b>	0.63	0.0159	14
<b>CALCA</b>	0.57	0.0145	15
<b>CCL20</b>	0.56	0.0141	16
<b>CD70</b>	0.55	0.0140	17
<b>CLEC4A</b>	0.52	0.0132	18
<b>CAPG</b>	0.52	0.0131	19
<b>APLP1</b>	0.51	0.0129	20

**Example 6—Four-Cohort Analysis of Single Candidate Analytes**

**[0175]** Candidate analytes identified in previous work: sFlt1, PlGF (e.g., Zeisler et al. NEJM 274(2017):13-22), PAPP-A (see, e.g., Spencer et al. Prenat Diagn. 28(2008):7-10.), and Fibronectin (see, e.g., Taylor et al. Am J Obstet Gynecol. 165(1991):895-901) were measured

and analyzed by the four-cohort analysis as above. Scatter plots of the analysis are shown in **Figure 3**. While all show ability to discriminate non-preeclampsia vs preeclampsia (A vs B), all show cohort confusion as the pairs of A and C, B and D are more similar (when the ideal relationship should be A~B, C~D).

#### **Example 7—Development of Multi-predictor Models for preeclampsia**

**[0176]** Random bootstrap forest predictor screening (10 rounds) was applied to the 552 biomarkers expression levels analyzed in the multiplex analysis combined with the four candidate biomarker expression levels into a single comprehensive data set (556 markers). The top 50 markers resulting from this analysis are displayed in **Table 3** by median rank, where the top row represents the top 10 markers; the second row represents the second 10 markers, and so on.

**Table 4: Top 50 Markers from Random Bootstrap Predictor Screening of 556 Markers by Median Rank**

111_SY ND1	117_CL EC4A	155_ER BB4	112_uP A	111_A MN	112_Pl GF	112_PG F	128_NO S3 2	105_ZBT B16	144_FGF -21
195_NT- proBNP	135_TG F-alpha 2	170_DC N	159_SO ST	148_EN TPD2	125_CA PG	134_AP LP1	148_SE Z6L	115_CLE C4C	Log[Fibr onectin, ng/ml]
102_GL B1	156_HG F 2	192_WI F-1	128_S1 00A4	Log[PlG F, ng/ml]	189_CE ACAM5	168_CX CL6	130_Gal -9	182_SIT 1	156_HG F
162_IL- 10	117_CX CL11	102_VE GF-A	105_M CP-3	190_CC L20	106_GD NF	Log[PA PP-A, ng/ml]	101_IL- 8	Log[sFlt- 1, ng/ml]	108_CD2 44
107_CD CP1	103_BD NF	115_M CP-1	122_CX CL9	113_IL- 6	116_IL- 17A	114_IL- 17C	109_IL- 7	111_LAP TGF- beta-1	110_OP G

**[0177]** To identify likely components of a logistic model in an unbiased fashion, the top 19 of these markers were then fit to a graded response (GR) model, followed by 250 bootstrap fits. This resulted in nine markers (CAPG, ZBTB16, SYND1, CLEC4C, TGF alpha 2, uPA, CLEC4A, PGF, and AMN) that had a p-value <1 (meaning they had non-zero coefficients in >50% of the 250 models built from bootstrapped samples). These markers are presented in Table 5.

**Table 5: Top 9 Markers Resulting from Multivariate Analysis Using Graded Response Model**

125_CAPG	105_ZBTB16	111_SYND1
115_CLEC4C	135_TGF-alpha 2	112_uPA
117_CLEC4A	112_PGF	111_AMN

**[0178]** Summary statistics and a ROC curve for a logistic regression model built for distinguishing non-preeclampsia from preeclampsia using the nine predictors of **Table 5** are presented in **Figure 4**. When applied to the data generated in this study, the model had an AUC of 0.992. A preliminary estimate from the ROC curve of this data gives a specificity of approximately 90% for a specificity value of 95%.

**[0179]** For comparison, an additional logistic regression model was run using the two candidate markers (sFlt1, PIGF) from Zeisler et al., along with the addition of CLEC4A and SYND1 (the top 2 single markers identified in **Example 3**). Summary statistics and a ROC curve for a logistic regression model built for distinguishing non-preeclampsia from preeclampsia using these four markers are presented in **Figure 5**. When applied to the data generated in this study, the model had an AUC of 0.908.

#### **Example 8—Additional Biomarker Analysis**

**[0180]** Additional single-plex analysis of additional candidate biomarkers CCL2, CD134, DCN, HGF, NOS3, PI GF, CD274, CDCP1, FGF-21, TGF $\alpha$ , UPA, CLEC4A, CLEC4C, ZBTB16, APLP1, DPP7, GRAP2, ITGB7, PAG1, TFF2, AMN, CAPG, CLEC1A5, FES, KIM1, PGF, ERBB4, GPNMB, PPY, and SYND1 was performed on the serum samples using an AlphaScreen<sup>TM</sup> assay as in **Example 2**, and the expression levels presented by sub-cohort as in **Example 4**. Scatter plots of the biomarker expression levels are presented in **Figures 7-12**.

#### **Example 9—Expanded Study Design**

**[0181]** An expanded study using the same inclusion/exclusion criteria as **Example 1** was conducted to further identify and validate biomarkers for preeclampsia. An overview of the process used is set forth in the flow diagram of FIG. 17, which shows a method 100, in which the levels of biomarkers are determined 101, the resulting data undergoes a log transformation 102 and a Loess correction for gestational age 103. Then machine learning 104 is used to determine an algorithm suitable for identifying a subject who does not need to be treated for preeclampsia. A breakdown of the samples collected from patients is detailed in **Table 6**. After filtering (samples with duplication were removed) bona fide (-) and bona fide (+) samples collected from the study were further separated into training and test sets according to a 75/25 ratio, while preserving the ratio of (-) to (+) samples. Bona fide PreE positive (+) samples were from patients diagnosed clinically using 2013 ACOG criteria who delivered preterm (i.e. in less than 37 weeks gestational age), where the sample was collected after clinical diagnosis and before labor, and where the sample was collected within 2 weeks

of preeclampsia diagnosis. Bona fide PreE negative (-) samples were from patients having at least one of the preeclampsia symptoms as defined by the ACOG 2013 guidelines who gave birth at full-term (i.e. delivery at 37 weeks gestational age or later), who had no clinical diagnostics of preeclampsia in the current pregnancy, and wherein the sample was collected before week 38 of gestational age.

**Table 6: Breakdown of Patient Samples for Expanded Preeclampsia Study**

	<i>Bonafide (+) for PreE</i>	<i>Bonafide (-) for PreE</i>	<i>PreE (delivered term)</i>	<i>PreE negative (delivered preterm)</i>	<i>Other</i>	<i>Excluded</i>	<i>Total</i>
<b>Study</b>	56	534	44	64	167	45	921
<b>Training</b>	41	400	--	--	--	--	441
<b>Test</b>	13	133	--	--	--	--	146

**[0182]** Bona fide PreE positive (+) samples were from patients diagnosed clinically using 2013 ACOG criteria who delivered preterm. Bona fide PreE negative (-) samples displayed at least 1 symptom according to the 2013 ACOG criteria but who delivered at term. Samples that did not fit into (+) or (-) categories were excluded from algorithm development and testing. Ethnicity/race information for this cohort is provided in Table 6A.

**Table 6A: Breakdown of Ethnicity/Race for Expanded Preeclampsia Study**

<i>Race</i>	<i>Non-preeclampsia</i>	<i>Preeclampsia</i>	<i>Total</i>
<b>AMERICAN INDIAN/ALASKA NATIVE</b>	1	1	2
<b>ASIAN</b>	3	0	3
<b>BLACK/AFRICAN AMERICAN</b>	242	21	263
<b>NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER</b>	1	0	1
<b>WHITE</b>	276	24	300
<b>UNKNOWN</b>	17	0	17
<b>Total</b>	540	46	586

<i>Ethnicity</i>	<i>Non-preeclampsia</i>	<i>Preeclampsia</i>	<i>Total</i>
<b>HISPANIC OR LATINO</b>	12	2	14
<b>NOT HISPANIC OR LATINO</b>	295	39	334
<b>Unknown</b>	233	5	238
<b>Total</b>	540	46	586

#### **Example 10: Development of Naïve Multivariate Models for Preeclampsia**

**[0183]** A series of 16 markers (CLEC4A, HGF, PIgf, KIM1, FGF-21, FN, DCN, SYND1, CD-274, TFF-2, PAPP-A, ADAM-12, sFLT1, PAPP-A2, ENG, and UPA) was selected by hierarchical clustering of high-throughput protein expression on the bona fide (+) and (-) samples of **Example 9** (wherein the bona fide criteria are the same as in Example 9). Following selection, assays for protein level of each analyte were developed and log (protein level) or ratios of log(protein level) with and without their bivariate interaction terms were used for these markers as features to build naïve multivariate models predicting preeclampsia.

Starting from the set of log-transformed expression data in the “training” set described in **Example 9**, the models were built Random Forest using (RF), GBM (gradient boosting machine), and Electric Net Logistic Regression (“Enet LR”) algorithms. The following procedure was used in connection with the full set of 16 expression markers:

- 1) Samples were randomly segregated into further “training” and “test” subsets at a 10:1 ratio;
- 2) Training sets were downsampled to balance classes;
- 3) 10-fold cross validation to optimize for sensitivity was performed;
- 4) Steps 2-3 were repeated 25x;
- 5) Steps 1-4 were repeated 40x; and
- 6) NPV, PPV, sensitivity, specificity, AUC, and AUP (area under the precision-recall curve) was reported for each algorithmic approach compared to a “baseline” model that just uses an sFlt1/PIGF expression ratio of 58 to detect preeclampsia. The features for each naïve algorithm and their contribution that resulted from this procedure are shown in **Table 7**, and the performance characteristics are presented in **Table 8**.

**Table 7: Features of Naïve RF/GBM/EnetLR models**

<i>RF log Baseline</i>		<i>GBM log Baseline</i>		<i>Enet_LR log Baseline</i>	
<b>f</b>	score	<b>f</b>	score	<b>f</b>	score
<b>PIGF</b>	296.7181	<b>PIGF</b>	738.0964	<b>(Intercept)</b>	69.7385
<b>SFLT.1</b>	129.3988	<b>SFLT.1</b>	226.7236	<b>FGF21</b>	45.17518
<b>PIGF:SFLT.1</b>	100.9284	<b>FGF21</b>	202.6028	<b>CLEC4A</b>	36.41802
<b>FGF21</b>	53.55566	<b>PAPP.A2</b>	116.983	<b>SFLT.1</b>	22.44577
<b>ENDOGLIN:PIGF</b>	53.2343	<b>PIGF:SFLT.1</b>	94.02904	<b>KIM1:TFF2</b>	21.95812
<b>PAPP.A2</b>	40.6594	<b>KIM1</b>	75.38029	<b>KIM1</b>	20.85404
<b>PAPP.A2:PIGF</b>	39.38708	<b>ENDOGLIN:PIGF</b>	71.08517	<b>UPA:CLEC4A</b>	14.30922
<b>ENDOGLIN</b>	30.33046	<b>ENDOGLIN:PAP.P.A</b>	66.06796	<b>TFF2:CLEC4A</b>	14.13368
<b>ENDOGLIN:SFLT.1</b>	28.51433	<b>DECORIN</b>	61.41614	<b>PIGF</b>	13.17691
<b>KIM1</b>	25.61497	<b>ENDOGLIN</b>	61.34832	<b>CD274:PAPP.A</b>	12.55998
<b>DECORIN</b>	23.96056	<b>UPA:CLEC4A</b>	61.05637	<b>PAPP.A2</b>	12.20951
<b>ENDOGLIN:PAP.P.A</b>	19.88032	<b>PAPP.A2:PIGF</b>	60.14436	<b>KIM1:SYND1</b>	10.9187
<b>PAPP.A2:UPA</b>	14.54226	<b>CD274:SFLT.1</b>	55.89387	<b>DECORIN</b>	10.79185
<b>KIM1:SYND1</b>	14.35827	<b>HGF:PIGF</b>	55.10297	<b>CD274</b>	10.5466
<b>CLEC4A</b>	14.07216	<b>FIBRONECTIN</b>	50.98952	<b>FGF21:TFF2</b>	9.898555
<b>PAPP.A:PAPP.A2</b>	13.34582	<b>ENDOGLIN:UPA</b>	34.46373	<b>SYND1</b>	9.032184
<b>HGF:PIGF</b>	12.48165	<b>CD274:PIGF</b>	33.72928	<b>PIGF:SYND1</b>	8.146656
<b>UPA:CLEC4A</b>	12.32938	<b>CD274</b>	29.81524	<b>UPA:SYND1</b>	8.03418
<b>CD274:SFLT.1</b>	11.19453	<b>PAPP.A:PAPP.A2</b>	29.62774	<b>ADAM.12:FGF21</b>	7.866035
<b>PAPP.A:SFLT.1</b>	9.771549	<b>CD274:PAPP.A2</b>	28.26661	<b>ADAM.12:CD274</b>	7.849305

**Table 8: Performance of Naïve RF/GBM/EnetLR Models Against Baseline sFLT1/PIGF Model and Improved Embodiments**

	<i>NPV</i>	<i>PPV</i>	<i>Specificity</i>	<i>Sensitivity</i>	<i>AUP</i>	<i>AUC</i>
<b>RF (naïve)</b>	96.62%	32.1%	84.83%	69.42%	0.6001	0.8527
<b>GBM (naïve)</b>	96.89%	28.4%	81.79%	72.88%	0.5756	0.8555
<b>Enet LR (naïve)</b>	96.89%	27.26%	80.26%	73.46%	0.5167	0.8429
<b>sFlt1/PIGF</b>	97.32%	17.7%	64.80	81.52%	0.6462	0.8553
<b>Stacked (Enet LR/RF)</b>	97.77%	25.29%	75.41%	81.92%	0.4993	0.8627
<b>Enet LR (KIM1/FGF21/CL EC4A features)</b>	95.88%	17.46%	67.33%	70.19%	28.02%	76.58%
<b>Stacked (Enet LR/RF) (KIM1/FGF21/CL EC4A features)</b>	98.28%	17.70%	64.80%	88.65%	39.22%	84.23%

**[0184]** The new models all showed improvements in specificity and PPV.

**[0185]** To improve false negative detection (NPV/sensitivity), algorithm optimization was first performed. The performance of each algorithm was examined in individual samples from the “false negative” category. 10/20 samples were classified as negative by RF/GBM/LR; 7/20 samples were classified as negative by GBM/LR; and only 2/20 samples were classified as negative by LR.

**[0186]** Accordingly, a “stacked” structure involving a combination of Elastic net logistic regression and Random forest was investigated as a method to reduce false negatives. The performance of the stacked model is shown in **Table 8**. An exemplary description of a stacked model for use in diagnosing or ruling out preeclampsia is shown in **Figure 19**. As hypothesized, the stacked model structure improved sensitivity, NPV, and AUC versus the individual models and the sFlt1/PIGF model.

**[0187]** To further improve optimization of the model performance characteristics, feature optimization was next performed.

*I. Feature selection using rational selection and clustering*

**[0188]** The first applied approach sought to more rationally choose genes as features to improve detection. The fold upregulation/downregulation of each biomarker feature was analyzed graphically in the “false negative samples”. This analysis is illustrated in **Figure 20**. For these samples, PI GF, END, PAPP-A2, and sFlt1 all had low signal (in terms of changes of fold expression), suggesting that they are insufficient for the detection of a subset of preeclampsia samples. However, KIM-1, FGF-21, and CLEC4A had signal in both false negative and true negative samples, suggesting they may broadly improve detection of all

subsets of preeclampsia samples. Accordingly, both a regular Enet and “stacked” RF/Enet model was constructed using just KIM-1, FGF-21, and CLEC4A as features (see **Table 8**). This model had marked improvements in NPV and some improvement in sensitivity versus the sFlt1/PIGF baseline model, confirming that models using KIM-1, FGF-21, and CLEC4A improve sensitivity of detection of preeclampsia.

### *II. Feature selection using principal component analysis*

**[0189]** The second applied approach examined principal components (from a PCA performed on the expression data) as features, and examined the signal of each principal component in the bona fide positive samples (wherein the bona fide criteria are the same as in Example 9). This analysis showed that the first 4 principal components (PC1, PC2, PC4, and PC9) explain 61.5% of the variance; and that PC4 in particular showed signal in the false negative samples PC1 and PC2 did not. Most of this signal appeared to originate from CLEC4A, HGF, FGF21, KIM1, and TFF2, which are contributors to PC4. Based on the assumption the four principal components form a minimal set for classification, models was generated using the top four principal components using the same algorithms used above. The performance of models built using these algorithms is presented in **Table 9**. The stacked model using the top four principal components as features showed improved characteristics versus the sFlt1/PIGF model in NPV, PPV, specificity, sensitivity, and AUC.

**Table 9: Performance of models using principal components as features**

	<i>NPV</i>	<i>PPV</i>	<i>Specificity</i>	<i>Sensitivity</i>	<i>AUP</i>	<i>AUC</i>
<b>RF (top 4 PC)</b>	97.81%	29.57%	80.66%	81.15%	0.6022	0.8865
<b>Enet LR (top 4 PC)</b>	97.63%	32.99%	83.50%	79.04%	0.6155	0.8838
<b>Stacked Enet LR/RF (top 4 PC)</b>	97.94%	27.18%	77.24%	83.08%	0.6137	0.8882
<b>Stacked Enet LR/RF (naïve)</b>	97.77%	25.29%	75.41%	81.92%	0.4993	0.8627
<b>sFlt1/PIGF</b>	97.32%	17.7%	64.80%	81.52%	0.6462	0.8553

### *III. Feature selection Using Lasso-LR*

**[0190]** The third approach utilized Lasso-LR on the full set of sample expression data after removal of universal false negatives and false positives to identify a set of biomarker features that optimizes performance (a sample is designated as Universal False Negative if the frequency of sample is reported as False Negative by a minimum of two prediction methods is  $\geq 0.9$ , and Universal False Positive if the frequency of the sample is reported as False Positive by a minimum of 3 prediction methods is  $\geq 0.8$ ). Lasso-LR was run (using alpha=1, lambda=0.01) with 10-fold cross validation repeated 500 times for 10 different

seeds to generate the feature ranking presented in **Figure 21**. Graphs of expression level in preeclampsia versus non-preeclampsia samples for the top 11 of these markers is presented in **Figure 13**. The top 2-10 features from this ranking were used to generate LR models, the performance of which are presented in **Table 10**.

**Table 10: Performance of models using 2-10 biomarkers as features identified by Lasso-LR**

	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>Lasso 2 Features LR</b>	98.62%	40.30%	89.04%	84.55%	79.24%	92.89%
<b>Lasso 3 Features LR</b>	98.91%	41.67%	89.52%	87.73%	80.52%	93.64%
<b>Lasso 4 Features LR</b>	99.10%	40.43%	88.70%	90.00%	81.41%	94.21%
<b>Lasso 5 Features LR</b>	99.09%	39.60%	88.30%	90.00%	81.14%	94.04%
<b>Lasso 6 Features LR</b>	99.01%	37.94%	87.61%	89.09%	78.30%	94.00%
<b>Lasso 7 Features LR</b>	98.99%	37.52%	87.44%	88.86%	78.31%	93.95%
<b>Lasso 8 Features LR</b>	99.03%	37.67%	87.56%	89.32%	78.08%	93.70%
<b>Lasso 9 Features LR</b>	98.97%	37.73%	87.65%	88.64%	77.42%	93.46%
<b>Lasso 10 Features LR</b>	98.95%	37.41%	87.41%	88.41%	76.63%	93.93%

**[0191]** Sensitivity was maximized using 4-5 features (PIGF/sFLT1/KIM1/CLEC4A or PIGF/sFLT1/KIM1/CLEC4A/CD274), after which additional protein marker features caused decreases in sensitivity. To estimate which, of any, of the 5<sup>th</sup> markers contribute most to sensitivity and other parameters in a model, models using the 4-marker combination (PIGF/sFLT1/KIM1/CLEC4A) plus all combinations of 5<sup>th</sup> markers (CD274 or TFF2 or ADAM12 or DCN or END or HGF or FGF21 or PAPP-A1 or FN or SYND1 or UPA or PAPP-A) were generated and their performance characteristics were compared (**Table 11**).

**Table 11: Performance of models with top 4 markers + one additional marker**

	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>4 Feature_SPKC (“sFLT1/PIGF/KIM1/CLEC4A”)</b>	99.10%	40.43%	88.70%	90.00%	81.41%	94.21%
<b>5 Feature_SPKC+FGF21</b>	99.10%	40.97%	88.65%	90.00%	79.95%	94.58%
<b>5 Feature_SPKC+PAPPA</b>	99.05%	39.97%	88.56%	89.55%	81.27%	94.14%
<b>5 Feature_SPKC+CD274</b>	99.09%	39.60%	88.30%	90.00%	81.14%	94.04%
<b>5 Feature_SPKC+TFF2</b>	98.99%	38.20%	87.83%	88.86%	78.89%	94.11%
<b>5 Feature_SPKC+DECORIN</b>	99.11%	40.24%	88.57%	90.23%	81.05%	94.08%
<b>5 Feature_SPKC+ENDOGLIN</b>	99.10%	40.86%	88.91%	90.00%	81.11%	94.04%
<b>5 Feature_SPKC+ADAM12</b>	99.09%	40.24%	88.43%	90.00%	80.84%	93.92%
<b>5 Feature_SPKC+HGF</b>	99.04%	40.08%	88.61%	89.32%	80.25%	94.02%
<b>5 Feature_SPKC+UPA</b>	99.09%	39.59%	88.39%	90.00%	80.18%	94.03%
<b>5 Feature_SPKC+FIBRONECTIN</b>	99.01%	39.52%	88.24%	89.09%	80.61%	93.88%
<b>5 Feature_SPKC+SYND1</b>	99.09%	39.87%	88.44%	90.00%	80.38%	93.69%
<b>5 Feature_SPKC+PAPPA2</b>	99.07%	39.92%	88.39%	89.77%	80.33%	94.07%

**Example 11: Correction of Optimized Multivariate Model for Gestational Age-Dependent Expression**

**[0192]** The models developed and evaluated in **Example 10** were next tested to see if the inclusion of gestational age, via the addition of a Loess model adjustment of biomarker expression levels prior to application of the logistic regression, would improve the performance parameters of the models. **Figure 14** depicts an exemplary procedure wherein a Loess model is used to perform gestational-age correction of biomarker (PIGF) expression levels, and **Figure 17** illustrates a procedure where this can be incorporated into the model-building workflow. **Table 12** depicts performance parameters of the models with and without the Loess gestational age (GA) correction, wherein “Loess GA Removal” corresponds to models that account for a gestational age and “No GA Removal” corresponds to models that do not account for gestational age. **Table 12** demonstrates that for the 5- and 4-biomarker models, gestational age correction improves the performance parameters of the models.

**Table 12: Performance of Models With Top 5 or 4 Markers With and Without Gestational Age Correction**

	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>5_Features_SFLT, PIGF, KIM1, FGF21, CLEC4A LR Loess GA Removal</b>	99.14%	48.79%	91.91%	90.23%	82.77%	94.95%
<b>5_Features_SFLT, PIGF, KIM1, FGF21, CLEC4A LR No GA Removal</b>	98.78%	31.92%	84.26%	87.05%	69.49%	93.20%
<b>4_Features_SFLT, PIGF, KIM1, CLEC4A LR Loess GA Removal</b>	99.20%	48.85%	91.78%	90.91%	83.47%	94.70%
<b>4_Features_SFLT, PIGF, KIM1, CLEC4A LR No GA Removal</b>	98.88%	32.05%	84.39%	87.27%	72.35%	93.03%

**Example 12: Performance of Optimized Multivariate Models Upon Reclassification of Hard-to-Classify Samples (Adjudication)**

**[0193]** In the model building/analysis up through **Example 12**, several of the samples from the preeclampsia study were classified by the models as negative or positive for preeclampsia despite having the opposite clinical label. Thirty of these samples were reassessed for preeclampsia in a blinded manner by clinicians, and 9 of the 30 samples changed labels. A group of independent-specialist physicians were employed to adjudicate and affirm or modify the initial expanded study classification status of bona fide PreE positive and PreE negative samples (wherein the bona fide criteria are the same as in Example 9). The review was performed according to pre-set criteria based upon ACOG (American College of Obstetricians and Gynecologists) guidelines applied to the available clinical data. The performance parameters of the models trained upon this updated patient population were calculated and are shown in **Table 13**.

**Table 13: Performance of models with top 5 or 4 markers with Patient Population having Diagnostic Labels Corrected**

	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>5_Features_SFLT,PIGF,KIM1,FGF 21,CLEC4A_LR Loess</b>	99.14%	48.79%	91.91%	90.23%	82.77%	94.95%
<b>5_Features_SFLT,PIGF,KIM1,FGF 21,CLEC4A_RF Loess</b>	98.92%	42.62%	89.61%	87.95%	76.34%	94.35%
<b>5_Features_SFLT,PIGF,KIM1,FGF 21,CLEC4A_Stacked_LRRF Loess</b>	99.09%	41.20%	88.61%	90.00%	81.64%	95.11%
<b>4_Features_SFLT,PIGF,KIM1, CLEC4A_LR Loess</b>	99.20%	48.85%	91.78%	90.91%	83.47%	94.70%
<b>4_Features_SFLT,PIGF,KIM1, CLEC4A_RF Loess</b>	98.73%	43.05%	89.94%	85.68%	75.78%	94.49%
<b>4_Features_SFLT,PIGF,KIM1, CLEC4A_Stacked_LRRF Loess</b>	98.77%	43.15%	89.78%	86.14%	73.44%	93.93%
<b>SFLT/PIGF&gt;58</b>	98.49%	18.12%	65.74%	88.29%	71.58%	90.70%

**[0194]** After adjudication by clinicians, four samples nonetheless continued to be classified with high frequency as false negatives. The models were again rebuilt by training on an updated patient population lacking these four high-frequency false-negatives (a sample was designated as Universal False Negative if the frequency of sample is reported as False Negative by a minimum of two prediction methods is  $\geq 0.9$ ). The performance parameters for these updated models are presented in **Table 14**, and suggest that the exclusion of these false negative samples from the training paradigm improves model performance in terms of AUP and AUC.

**Table 14: Performance of Models With Top 5 or 4 Markers With Patient Population Having Diagnostic Labels Corrected and 4 Top False Negatives Removed**

	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>5_Features_SFLT,PIGF,KIM1,FGF 21,CLEC4A_LR Loess</b>	99.14%	48.79%	91.91%	90.23%	82.77%	94.95%
<b>5_Features_SFLT,PIGF,KIM1,FGF 21,CLEC4A_LR Loess top 4 FNs removed</b>	99.78%	48.35%	91.91%	97.36%	93.84%	98.82%
<b>4_Features_SFLT,PIGF,KIM1, CLEC4A_LR Loess</b>	99.20%	48.85%	91.78%	90.91%	83.47%	94.70%
<b>4_Features_SFLT,PIGF,KIM1, CLEC4A_LR Loess top 4 FNs removed</b>	99.84%	48.42%	91.78%	98.09%	89.19%	98.92%

**Example 13: Performance of Optimized Multivariate Models Upon Threshold Adjustment**

**[0195]** Next, the sensitivity threshold was adjusted using several values to see if the specificity threshold of the top-performing models could be optimized. The results of the model with several different threshold values are presented in Table 15. The results

demonstrate that specificity can be traded down to 81.7% to increase sensitivity up to 94.77%.

**Table 15: Sensitivity/Specificity Threshold Optimization for Top Performing Models**

	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>5 Features_SFLT,PIGF,KIM1,FGF21,CLEC4A_LR_Loess (Threshold=.5)</b>	99.14%	48.79%	91.91%	90.23%	82.77%	94.95%
<b>5 Features_SFLT,PIGF,KIM1,FGF21,CLEC4A_LR_Loess (Threshold=.45)</b>	99.20%	46.52%	91.06%	90.91%	82.77%	94.95%
<b>5 Features_SFLT,PIGF,KIM1,FGF21,CLEC4A_LR_Loess (Threshold=.3)</b>	99.33%	37.09%	86.80%	92.73%	82.77%	94.95%
<b>5 Features_SFLT,PIGF,KIM1,FGF21,CLEC4A_LR_Loess (Threshold=.2)</b>	99.48%	30.47%	81.70%	94.77%	82.77%	94.95%

**Example 14: Performance of Optimized Multivariate Models in a Time-to-Delivery Analysis**

**[0196]** Performance of the Enet-LR model using the top 5 or 4 biomarkers as features was evaluated in samples from pregnant patients that were 1, 2, 4, or 6 weeks out from delivery. The performance characteristics for the model in each scenario are presented in **Table 12**. Generally, sensitivity and PPV decreased according to increased time to delivery, whereas specificity and NPV increased with time to delivery.

**Table 16: Performance of Optimized Multivariate Models in a Time-to-Delivery Analysis**

	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>5 Features_SFLT, PIGF, KIM1, FGF21, CLEC4A_LR_Loess vs WTD</b>						
Within 1 week	97.68%	61.63%	77.43%	95.30%	91.04%	94.01%
Within 2 weeks	97.59%	59.43%	82.11%	93.05%	87.35%	93.20%
Within 4 weeks	98.55%	49.78%	83.03%	92.91%	81.41%	93.43%
Within 6 weeks	98.90%	47.29%	85.00%	93.11%	80.83%	94.09%
All Data	99.14%	48.79%	91.91%	90.23%	82.77%	94.95%
SFLT/PIGF>58	98.49%	18.12%	65.74%	88.29%	71.58%	90.70%
<b>4 Features_SFLT, PIGF, KIM1, CLEC4A_LR_Loess vs WTD</b>						
Within 1 week	97.30%	59.58%	76.19%	94.57%	93.17%	94.64%
Within 2 weeks	97.39%	59.40%	82.22%	92.41%	88.71%	93.06%
Within 4 weeks	98.38%	50.74%	84.15%	92.19%	83.87%	93.39%
Within 6 weeks	98.74%	46.84%	85.36%	92.13%	82.85%	93.81%
All Data	99.20%	48.85%	91.78%	90.91%	83.47%	94.70%
SFLT/PIGF>58	98.49%	18.12%	65.74%	88.29%	71.58%	90.70%

**Example 15: Interchangeability of High-Signal Markers in Top-performing models**

**[0197]** The top-performing markers discovered in this analysis, sFLT-1, KIM-1, and CLEC-4A were examined to see if combinations of the other lower-signal markers discovered in the study could be substituted for them.

**[0198]** For sFLT-1, it was discovered that a combination of Endoglin, PAPP-A2, and Decorin could produce models with similar performance characteristics to those involving sFLT-1, PI GF, KIM-1, and CLEC-4A. The results in Table 17 demonstrate that a model involving Endoglin, PAPP-A2, and Decorin substituted for sFLT-1 has similar performance characteristics as one involving sFLT-1, with only a minor loss in AUC/AUP.

**Table 17: Performance of Alternative Model with sFLT-1 substituted for END, PAPP-A2, and DCN**

	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>No SFLT.1</b>						
<b>Model 1_4 Features - SFLT.1, PI GF, KIM1, CLEC4A,</b>	99.10%	40.43%	88.70%	90.00%	81.41%	94.21%
<b>4features, PI GF, KIM, CLEC4A, ENDOGLIN_LR_noSFLT</b>	98.99%	43.13%	90.02%	88.64%	79.05%	93.71%
<b>5features, PI GF, KIM, CLEC4A, ENDOGLIN, PAPP.A2_LR_noSFLT</b>	99.06%	39.81%	88.52%	89.55%	76.83%	93.57%
<b>5features, PI GF, KIM, CLEC4A, ENDOGLIN, DECORIN_LR_noSFLT</b>	98.97%	41.94%	89.59%	88.41%	78.56%	93.59%

**[0199]** For KIM-1, it was discovered that a substitution with CD274 and/or Decorin had similar performance parameters, although a model involving CD274 alone without Decorin had slightly better AUP than one involving Decorin alone without CD274 (see Table 18).

**Table 18: Performance of Models with Decorin and/or CD274 Substituted for KIM-1**

	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>No KIM1</b>						
<b>Model 1_4 Features - SFLT.1, PI GF, KIM1, CLEC4A,</b>	99.10%	40.43%	88.70%	90.00%	81.41%	94.21%
<b>4_Features_SFLT,PI GF,CLEC4A,CD274_LR_noKIM</b>	98.84%	37.60%	87.61%	87.27%	80.22%	93.75%
<b>4_Features_SFLT,PI GF,CLEC4A,DECO_RIN_LR_noKIM</b>	98.86%	37.51%	87.37%	87.50%	79.81%	93.75%
<b>5_Features_SFLT,PI GF,CLEC4A,CD274,DECORIN_LR_noKIM</b>	98.86%	37.02%	87.22%	87.50%	79.69%	93.55%

**[0200]** For CLEC4A, it was discovered that models substituting CLEC4A for FGF21, TFF2 and/or HGF result in similar performance characteristics (Table 19). Table 19 also demonstrates that, of these models, those using HGF or FGF21 have slightly superior AUP/AUC to those using TFF2.

**Table 19: Performance of Models with FGF21, TFF2, and/or HGF Substituted for CLEC4A**

	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>No CLEC4A</b>						
<b>Model 1_4 Features - SFLT.1, PIGF, KIM1, CLEC4A,</b>	99.10%	40.43%	88.70%	90.00%	81.41%	94.21%
<b>4_Features_SFLT,PIGF,KIM1,FGF21_LR_noCLEC4A</b>	98.93%	39.90%	88.56%	88.18%	78.96%	94.00%
<b>4_Features_SFLT,PIGF,KIM1,HGF_LR_noCLEC4A</b>	98.84%	40.81%	89.22%	87.05%	80.54%	93.37%
<b>4_Features_SFLT,PIGF,KIM1,TFF2_LR_noCLEC4A</b>	98.90%	39.57%	88.59%	87.73%	78.39%	93.60%
<b>6_Features_SFLT,PIGF,KIM1,TFF2,HGF,TFF2_LR_noCLEC4A</b>	98.97%	39.02%	88.09%	88.64%	77.54%	93.66%

**Example 16: Independent Cohort Validation of High Performance Models**

**[0201]** An independent cohort of patient samples collected as described in Example 1 and Example 9 was used to validate the performance of the high-performance models developed in the previous examples. These originally consisted of 451 samples, which was reduced to 342 bona fide positive or negative for preeclampsia samples (308 bona fide negative and 34 bona fide positive). After adjudication procedures in which a group of independent-specialist physicians were employed to adjudicate and affirm or modify the initial expanded study classification status of bona fide PreE positive and PreE negative samples (as in Example 12) this cohort was reduced to a final set of 331 patient samples, with 221 being bona-fide negative for preeclampsia and 32 being bona-fide positive for preeclampsia. The models selected for validation on the 331 patient sample set are shown in **Table 20**. In **Table 20**, where exclusion of data from the training set is indicated, a sample is referred to as False Negative (FN) if the frequency of sample is reported as False Negative by a minimum of two prediction methods is  $\geq 0.9$ , and a sample is referred to as False Positive (FP) if the frequency of the sample is reported as False Positive by a minimum of 3 prediction methods is  $\geq 0.8$ .

**Table 20: Details for Models Selected for Validation in Independent Cohort**

<i>Model ID</i>	<i>Panel</i>	<i>Algorithm</i>	<i>Score cutoff</i>	<i>Training set data (exclusion of false neg/false pos samples?)</i>	<i>Gest-age adj?</i>
<b>M_12</b>	Top4 PC 16 Marker+Interactions	LR-Enet	0.5	U-{FN,FP}	LOESS
<b>M_2</b>	sFlt-1, PIGF, KIM1, FGF21, CLEC4A	LR-Enet	0.5	U-{FN}	LOESS
<b>M_11.1</b>	sFlt-1, PIGF, KIM1, FGF21, CLEC4A,ENDOGLIN,CD274,DECORIN	LR-Enet	0.5	U-{FN}	LOESS

Model ID	Panel	Algorithm	Score cutoff	Training set data (exclusion of false neg/false pos samples?)	Gest-age adj?
<b>M_44</b>	sFlt-1, PI GF, KIM1, FGF21, CLEC4A, ENDOGLIN	Stacked: LR- Enet->RF	(0.5,0.5)	U	LOESS
<b>M_44.1</b>	sFlt-1, PI GF, KIM1, FGF21, CLEC4A, ENDOGLIN	Stacked: LR- Enet->RF	(0.5,0.5)	U	N/A
<b>M_39</b>	sFlt-1, PI GF, KIM1, FGF21, CLEC4A, ENDOGLIN, CD274	RF	0.5	U-{FN}	LOESS
<b>M_14</b>	PI GF, KIM1, CLEC4A, ENDOGLIN	LR-Enet	0.5	U	LOESS
<b>M_29</b>	sFlt-1, PI GF, KIM1, CLEC4A	LR-Enet	0.5	U+{FN->TN, FP->TP}	LOESS
<b>M_6.1</b>	PI GF, sFlt-1, KIM1, TFF2, DECORIN, FGF21	LR-Enet	0.5	U-{FN}	LOESS
<b>M_2.1</b>	sFlt-1, PI GF, KIM1, FGF21, CLEC4A	LR-Enet	0.3	U-{FN}	LOESS
<b>M_39.1</b>	PI GF, KIM1, DECORIN, PAPA.2, TFF2, FGF21, CD274	RF	0.5	U-{FP}	LOESS
<b>M_4.1</b>	sFlt-1, PI GF, KIM1, ENDOGLIN, CLEC4A	LR-Enet	0.3	U-{FP,FN}	LOESS
<b>M_33.1</b>	sFlt-1, PI GF, KIM1, ENDOGLIN, CLEC4A	RF	0.3	U-{FP,FN}	LOESS
<b>M_1</b>	sFlt-1, PI GF, KIM1, CLEC4A	LR-Enet	0.5	U	N/A
<b>M_8</b>	HGF, SYND1, CD274 (top) sFlt-1, PI GF, KIM1, FGF21, CLEC4A (bottom)	Stacked:LR- Enet->LR-Enet	(0.7,0.5)	U	LOESS

**[0202]** The validation data for the performance parameters of the models built in Table 20 is shown in Table 21. When the models are ranked by performance, the 4.1 model (Enet logistic regression using sFLT-1, PI GF, KIM1, and END using a cutoff of 0.3, with exclusion of false positive and negative samples, and using loess correction for gestational age) has the highest performance. Notably, the AUC of the top 3 models on this independent cohort is consistent with (equivalent or better than) the performance seen in the previous examples (e.g. Example 14).

**[0203]** Table 21: Performance Parameters for Models Selected for Validation in Independent Cohort

Model	Performance				
	sen	sp	npv	ppv	AUC
<b>model4.1_preds</b>	96.9	86.6	99.6	43.7	96.3%
<b>model11_preds</b>	90.6	92.6	98.9	56.9	97.1%
<b>model12_preds</b>	81.2	96	98	68.4	96.5%
<b>model1_preds</b>	96.9	74.9	99.6	29.2	--

Model	Performance				
	sen	sp	npv	ppv	AUC
model6.1_preds	84.4	94	98.3	60	--
model2_preds	84.4	93	98.2	56.2	--
model14_preds	87.5	89.6	98.5	47.5	--
model29_preds	87.5	89.6	98.5	47.5	--
model44_preds	90.6	86	98.8	40.8	--
model44.1_preds	90.6	84.9	98.8	39.2	--
model8_preds	90.6	84.9	98.8	39.2	--
model2.1_preds	90.6	84.6	98.8	38.7	--
model39_preds	81.2	92.3	97.9	53.1	--
model39.1_preds	81.2	89	97.8	44.1	--
model33.1_preds	87.5	82.3	98.4	34.6	--

**[0204]** Based on this positive performance data, an additional 29 models were built (to create a total of 44), for which the performance characteristics on the independent cohort were calculated and are presented in Table 22. The corresponding biomarker/features used in each model, along with the model coefficients (“beta” value for each feature/biomarker in the case of logistic regression, and “feature importance” value for each feature/biomarker in the case of Random Forest or GBM) are presented in Table 23. In the case where “stacked” models are presented, the relevant coefficients for each step are separated into separate rows in Table 23.

**Table 22: Performance Parameters for Additional Models Against Validation Cohort**

Model	NPV	PPV	Spec	Sen	AUP	AUC
<b>Logistic Regression Models</b>						
Model1_LR	99.20%	48.85%	91.78%	90.91%	83.47%	94.70%
Model2_LR	99.14%	48.79%	91.91%	90.23%	82.77%	94.95%
Model3_LR	99.22%	48.56%	91.78%	91.14%	83.87%	94.69%
Model4_LR	99.18%	47.54%	91.39%	90.68%	83.08%	94.49%
Model5_LR	99.10%	47.57%	91.59%	89.77%	81.92%	94.45%
Model6_LR	99.21%	49.67%	92.17%	90.91%	81.66%	95.23%
Model7_LR	99.12%	47.91%	91.65%	90.00%	82.41%	94.92%
Model8_LR	99.20%	46.22%	90.96%	90.91%	83.11%	94.42%
Model9_LR	99.08%	45.85%	91.07%	89.55%	81.77%	94.31%
Model10_LR	99.20%	48.54%	91.81%	90.91%	82.05%	95.12%
Model11_LR	99.05%	45.36%	90.98%	89.32%	81.10%	94.83%
Model13_LR	99.04%	48.43%	91.80%	89.09%	80.80%	93.96%
Model14_LR	98.94%	46.64%	91.35%	87.95%	80.64%	93.90%
<b>Random Forest Models</b>						
Model30_RF	98.73%	43.05%	89.94%	85.68%	75.78%	94.49%
Model31_RF	98.75%	44.07%	90.39%	85.91%	74.38%	94.88%
Model32_RF	98.77%	42.95%	89.78%	86.14%	78.40%	94.42%
Model33_RF	98.62%	42.95%	90.19%	84.32%	71.18%	93.94%
Model34_RF	98.77%	43.67%	90.06%	86.14%	73.30%	93.70%
Model35_RF	98.71%	43.33%	89.98%	85.45%	72.09%	94.12%
Model36_RF	98.78%	44.56%	90.54%	86.14%	76.23%	94.73%
Model37_RF	98.77%	45.93%	91.04%	85.91%	77.42%	94.07%
Model38_RF	98.68%	43.67%	90.11%	85.00%	73.78%	93.58%
Model39_RF	98.77%	43.15%	89.78%	86.14%	73.44%	93.93%
Model40_RF	98.72%	40.77%	88.89%	85.68%	73.43%	93.24%

<i>Model</i>	<i>NPV</i>	<i>PPV</i>	<i>Spec</i>	<i>Sen</i>	<i>AUP</i>	<i>AUC</i>
<b>Stacked Models</b>						
<b>Model41_LRRF</b>	99.17%	40.64%	88.30%	90.91%	82.57%	95.39%
<b>Model42_LRRF</b>	99.09%	41.20%	88.61%	90.00%	81.64%	95.11%
<b>Model43_LRRF</b>	99.17%	41.17%	88.50%	90.91%	82.07%	95.28%
<b>Model44_LRRF</b>	99.16%	41.20%	88.65%	90.68%	80.81%	95.20%
<b>Model45_LRRF</b>	99.07%	39.67%	88.13%	89.77%	80.23%	94.32%
<b>GBM Models</b>						
<b>Model46_GBM</b>	98.89%	41.81%	89.57%	87.50%	69.03%	94.43%
<b>Model47_GBM</b>	98.81%	43.51%	90.17%	86.59%	69.18%	94.90%
<b>Model48_GBM</b>	98.83%	42.98%	90.02%	86.82%	69.11%	94.43%
<b>Model49_GBM</b>	98.82%	44.16%	90.39%	86.59%	70.62%	94.68%
<b>Model50_GBM</b>	98.85%	44.02%	90.30%	87.05%	70.12%	93.82%
<b>Model51_GBM</b>	98.82%	44.68%	90.65%	86.59%	70.40%	95.00%
<b>Model52_GBM</b>	98.81%	43.36%	90.13%	86.59%	69.09%	94.79%
<b>Model53_GBM</b>	98.88%	44.19%	90.26%	87.27%	70.72%	94.55%
<b>Model54_GBM</b>	98.82%	44.81%	90.52%	86.59%	70.41%	94.03%
<b>Model55_GBM</b>	98.83%	44.52%	90.46%	86.82%	71.10%	94.89%
<b>Model56_GBM</b>	98.81%	44.14%	90.31%	86.59%	70.82%	94.43%
<b>Optimization Extra Models</b>						
<b>Model6.1_LR</b>	99.04%	45.06%	90.76%	89.09%	79.26%	94.41%
<b>Model44.1_LRRF</b>	98.96%	31.84%	83.69%	89.09%	72.51%	94.01%
<b>Model39_1_RF</b>	98.80%	41.85%	89.46%	86.59%	70.79%	92.33%
<b>Model8.1_LRRF</b>	98.88%	17.69%	65.06%	90.91%	51.95%	87.48%

**Table 23: Model Coefficients for Models Shown in Table 22**

<i>Mode l</i>	(Intercept)	<i>PLGF</i>	<i>SFLT.1</i>	<i>CLEC4A</i>	<i>CD274</i>	<i>ENDOGLIN</i>	<i>DECORIN</i>	<i>FGF21</i>	<i>KIM1</i>	<i>PAPP A.2</i>	<i>TFF2</i>	<i>HGF</i>	<i>SYND1</i>
<b>Model1_L_R</b>	4.07	2.53	-1.65	-0.60	NA	NA	NA	NA	-1.24	NA	NA	NA	NA
<b>Model2_L_R</b>	3.64	2.22	-1.41	-0.52	NA	NA	NA	-0.47	-1.04	NA	NA	NA	NA
<b>Model3_L_R</b>	3.11	1.78	-1.31	-0.44	0.37	NA	NA	NA	-1.01	NA	NA	NA	NA
<b>Model4_L_R</b>	4.41	2.82	-1.42	-0.64	NA	-0.62	NA	NA	-1.24	NA	NA	NA	NA
<b>Model5_L_R</b>	4.09	2.36	-1.45	-0.52	NA	NA	-0.90	NA	-1.12	NA	NA	NA	NA
<b>Model6_L_R</b>	3.92	2.08	-1.11	-0.67	NA	-0.77	NA	-0.80	-1.10	NA	NA	NA	NA
<b>Model7_L_R</b>	3.75	2.20	-1.44	-0.49	0.36	NA	NA	-0.47	-1.14	NA	NA	NA	NA
<b>Model8_L_R</b>	4.81	2.67	-1.67	-0.77	0.69	-0.74	NA	NA	-1.58	NA	NA	NA	NA
<b>Model9_L_R</b>	5.06	2.85	-1.53	-0.75	NA	-0.59	-1.14	NA	-1.33	NA	NA	NA	NA
<b>Model10_LR</b>	4.06	1.95	-1.18	-0.67	0.50	-0.82	NA	-0.77	-1.26	NA	NA	NA	NA
<b>Model11_LR</b>	4.42	2.09	-1.19	-0.63	0.47	-0.71	-0.97	-0.88	-1.26	NA	NA	NA	NA
<b>Model13_LR</b>	3.26	2.34	NA	-0.51	NA	-1.06	NA	NA	-0.78	NA	NA	NA	NA
<b>Model14_LR</b>	3.14	1.94	NA	-0.43	NA	-0.90	-0.72	NA	-0.76	NA	NA	NA	NA
<b>Model30_RF</b>	NA	19.6 <sub>3</sub>	8.25	1.21	NA	NA	NA	NA	2.51	NA	NA	NA	NA
<b>Model31_RF</b>	NA	14.1 <sub>6</sub>	9.36	1.56	NA	NA	NA	3.29	3.00	NA	NA	NA	NA
<b>Model32_RF</b>	NA	17.3 <sub>2</sub>	8.94	1.13	1.09	NA	NA	NA	2.75	NA	NA	NA	NA
<b>Model33_RF</b>	NA	20.6 <sub>1</sub>	3.46	0.80	NA	3.11	NA	NA	1.99	NA	NA	NA	NA
<b>Model34_RF</b>	NA	13.8 <sub>9</sub>	8.98	1.42	NA	NA	4.25	NA	2.62	NA	NA	NA	NA
<b>Model35_RF</b>	NA	18.3 <sub>1</sub>	4.00	0.80	NA	4.68	NA	0.91	1.74	NA	NA	NA	NA
<b>Model36_RF</b>	NA	12.7 <sub>0</sub>	8.92	1.49	1.84	NA	NA	3.30	2.86	NA	NA	NA	NA

<i>Mode l</i>	<i>(Intercept)</i>	<i>PLG F</i>	<i>SFL T.1</i>	<i>CLE C4A</i>	<i>CD2 74</i>	<i>ENDO GLIN</i>	<i>DECO RIN</i>	<i>FGF 21</i>	<i>KIM I</i>	<i>PAPP A.2</i>	<i>TFF 2</i>	<i>HG F</i>	<i>SYN DI</i>
Mod el37_RF	NA	11.35	7.12	1.38	1.63	7.32	NA	NA	2.43	NA	NA	NA	NA
Mod el38_RF	NA	13.65	6.30	0.95	NA	6.73	2.04	NA	1.59	NA	NA	NA	NA
Mod el39_RF	NA	16.20	4.60	0.77	0.49	5.57	NA	0.97	1.57	NA	NA	NA	NA
Mod el40_RF	NA	16.73	4.17	0.60	0.39	5.11	1.31	0.66	1.29	NA	NA	NA	NA
Mod el46_GBM	NA	66.01	21.22	3.33	NA	NA	NA	NA	7.21	NA	NA	NA	NA
Mod el47_GBM	NA	65.67	20.11	2.72	NA	NA	NA	2.31	6.27	NA	NA	NA	NA
Mod el48_GBM	NA	66.14	21.00	2.64	1.52	NA	NA	NA	6.48	NA	NA	NA	NA
Mod el49_GBM	NA	58.34	13.48	2.82	NA	14.19	NA	NA	5.82	NA	NA	NA	NA
Mod el50_GBM	NA	65.30	20.18	2.27	NA	NA	5.64	NA	5.53	NA	NA	NA	NA
Mod el51_GBM	NA	57.23	13.62	2.40	NA	13.37	NA	2.38	5.08	NA	NA	NA	NA
Mod el52_GBM	NA	65.23	19.58	2.22	1.43	NA	NA	2.13	6.10	NA	NA	NA	NA
Mod el53_GBM	NA	58.14	13.37	2.66	1.45	14.05	NA	NA	5.52	NA	NA	NA	NA
Mod el54_GBM	NA	57.57	11.59	2.12	NA	13.36	4.59	NA	4.94	NA	NA	NA	NA
Mod el55_GBM	NA	56.94	12.93	2.22	1.07	13.25	NA	2.28	5.00	NA	NA	NA	NA
Mod el56_GBM	NA	56.94	11.28	1.66	0.78	12.42	3.96	2.02	4.31	NA	NA	NA	NA
Mod el_39_1_RF	NA	19.15	NA	NA	0.69	NA	2.05	0.88	1.53	5.69	1.30	NA	NA
Mod el40_RF2	NA	16.73	4.17	0.60	0.39	5.11	1.31	0.66	1.29	NA	NA	NA	NA
Mod el41_LR_First_Level	4.07	2.53	-1.65	-0.60	NA	NA	NA	NA	-1.24	NA	NA	NA	NA
Mod el41_RF_S_econ	NA	19.63	8.25	1.21	NA	NA	NA	NA	2.51	NA	NA	NA	NA

<i>Mode l</i>	<i>(Intercept)</i>	<i>PLG F</i>	<i>SFL T.I</i>	<i>CLE C4A</i>	<i>CD2 74</i>	<i>ENDO GLIN</i>	<i>DECO RIN</i>	<i>FGF 21</i>	<i>KIM I</i>	<i>PAPP A.2</i>	<i>TFF 2</i>	<i>HG F</i>	<i>SYN DI</i>
<b>d_Le vel</b>													
<b>Mod el42_LR_First_Le vel</b>	3.64	2.22	-1.41	-0.52	NA	NA	NA	-0.47	-1.04	NA	NA	NA	NA
<b>Mod el42_RF_S econ_d_Le vel</b>	NA	14.1 <sub>6</sub>	9.36	1.56	NA	NA	NA	3.29	3.00	NA	NA	NA	NA
<b>Mod el43_LR_First_Le vel</b>	4.41	2.82	-1.42	-0.64	NA	-0.62	NA	NA	-1.24	NA	NA	NA	NA
<b>Mod el43_RF_S econ_d_Le vel</b>	NA	20.6 <sub>1</sub>	3.46	0.80	NA	3.11	NA	NA	1.99	NA	NA	NA	NA
<b>Mod el44_LR_First_Le vel</b>	3.92	2.08	-1.11	-0.67	NA	-0.77	NA	-0.80	-1.10	NA	NA	NA	NA
<b>Mod el44_RF_S econ_d_Le vel</b>	NA	18.3 <sub>1</sub>	4.00	0.80	NA	4.68	NA	0.91	1.74	NA	NA	NA	NA
<b>Mod el45_LR_First_Le vel</b>	4.42	2.09	-1.19	-0.63	0.47	-0.71	-0.97	-0.88	-1.26	NA	NA	NA	NA
<b>Mod el45_RF_S econ_d_Le vel</b>	NA	16.7 <sub>3</sub>	4.17	0.60	0.39	5.11	1.31	0.66	1.29	NA	NA	NA	NA
<b>Mod el_44 .1_R_F</b>		13.9 <sub>4</sub>	5.65	1.36	NA	5.79	NA	1.50	2.32	NA	NA	NA	NA
<b>Mod el8.1_LR_Second_le vel</b>	3.64	2.22	-1.41	-0.52	NA	NA	NA	-0.47	-1.04	NA	NA	NA	NA
<b>Mod el8.1</b>	0.71	NA	NA	NA	0.68	NA	NA	NA	NA	NA	NA	-1.0	0.51

<i>Mode l</i>	<i>(Intercept)</i>	<i>PLG F</i>	<i>SFL T.1</i>	<i>CLE C4A</i>	<i>CD2 74</i>	<i>ENDO GLIN</i>	<i>DECO RIN</i>	<i>FGF 21</i>	<i>KIM 1</i>	<i>PAPP A.2</i>	<i>TFF 2</i>	<i>HG F</i>	<i>SYN D1</i>
<u>LR-First Level s</u>													7
<u>Model 6. 1 LR</u>	4.06	2.29	-1.44	NA	NA	NA	-0.93	-0.67	-1.14	NA	-0.44	NA	NA

**[0205]** Ethnicity information for the 331 patient sample set used for validation in this example is provided in Table 24.

**Table 24: Ethnicity/Race Breakdown for Patients in the 331 Independent Sample Validation Cohort**

<i>Race</i>	<i>Non-preeclampsia</i>	<i>Preeclampsia</i>	<i>Total</i>
<b>AMERICAN INDIAN/ALASKA NATIVE</b>	0	0	0
<b>ASIAN</b>	7	0	7
<b>BLACK/AFRICAN AMERICAN</b>	36	6	42
<b>NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER</b>	3	0	3
<b>WHITE</b>	253	26	279
<b>Total</b>	299	32	331

<i>Ethnicity</i>	<i>Non-preeclampsia</i>	<i>Preeclampsia</i>	<i>Total</i>
<b>HISPANIC OR LATINO</b>	10	1	11
<b>NOT HISPANIC OR LATINO</b>	287	31	318
<b>Unknown</b>	2	0	2
<b>Total</b>	299	32	331

**[0206]** While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

## CLAIMS

## WHAT IS CLAIMED IS:

1. A method for avoiding unnecessary treatment of preeclampsia, the method comprising:
  - (a) contacting a biological sample that has been collected from a pregnant human female with a plurality of different probes, wherein the plurality of different probes comprises probes with specific affinity for four or more proteins selected from proteins listed in Table A or Table B;
  - (b) determining, based on binding of the plurality of different probes to corresponding proteins, an amount or concentration for each of the four or more proteins; and
  - (c) proceeding with treatment of said pregnant human in a manner that avoids unnecessary treatment of preeclampsia based at least in part on the amounts or concentrations of the four or more proteins determined in step (b).
2. The method of claim 1, wherein the four or more proteins comprise:
  - (a) placental growth factor (PIGF);
  - (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 (3) decorin.
3. The method of claim 2, wherein the four or more proteins further comprise 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).
4. The method of any one of claims 1–3, wherein the four or more proteins comprise PIGF, sFlt1, KIM1, and CLEC4A.
5. The method of any one of claims 1–4, wherein the plurality of different probes comprises probes with specific affinity to fibroblast growth factor 21 (FGF21), and the four or more proteins comprise FGF21.
6. The method of any one of claims 1–5, wherein the plurality of different probes comprises probes with specific affinity for endoglin, and the four or more proteins comprise endoglin.

7. The method of any one of claims 1–6, wherein the plurality of different probes comprises probes with specific affinity for decorin, and the four or more proteins comprise decorin.

8. The method of any one of claims 1–7, wherein the plurality of different probes comprises probes with specific affinity for cluster of differentiation 274 (CD274), and the four or more proteins comprise CD274.

9. The method of any one of claims 1–8, wherein the plurality of different probes comprises probes with specific affinity for hepatocyte growth factor (HGF), and the four or more proteins comprise HGF.

10. The method of any one of claims 1–9, wherein the plurality of different probes comprises probes with specific affinity for trefoil factor 2 (TFF2), and the four or more proteins comprises TFF2.

11. The method of any one of claims 1–10, wherein the plurality of different probes comprises probes with specific affinity for pappalysin-2 (PAPP-A2), and the four or more proteins comprises PAPP-A2.

12. The method of any one of claims 1–11, wherein the biological sample is obtained from the pregnant female after gestational week 20.

13. The method of any one of claims 1–12, wherein the biological sample has been collected from the pregnant female prior to 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, wherein the classifier algorithm further comprises a correction for gestational age.

16. The method of claim 15, wherein the correction for gestational age comprises a LOESS correction.

17. The method of any one of claims 14–16, wherein the classifier algorithm comprises a logistic regression.

18. The method of any one of claims 14–17, wherein the classifier algorithm comprises a logistic regression with elastic-net regularization.

19. The method of any one of claims 14–16, wherein the classifier algorithm comprises a Random Forest.
20. The method of any one of claims 1–19, wherein the biological sample is a urine, blood, amniotic fluid, exosome, plasma, or serum sample.
21. The method of any one of claims 1–19, wherein the biological sample is from blood of the pregnant human female.
22. The method of any one of claims 1–21, wherein the amount or concentration of no more than 20, no more than 15, nor more than 10, nor more than 9, no more than 8, no more than 7, no more than 6, nor more than 5, or no more than 4 proteins is determined.
23. The method of any one of claims 1–22, wherein one or more of the plurality of different probes are antibodies or antibody fragments.
24. The method of any one of claims 1–23, wherein each of the plurality of different probes are antibodies or antibody fragments.
25. The method of any one of claims 1–24, wherein the amount or concentration of at least one of the four or more proteins is determined using a luminescent oxygen channeling immunoassay.
26. The method of any one of claims 1–25, wherein the amount or concentration of at least one of the four or more proteins is determined using a time-resolved fluorescence resonance energy transfer (TR-FRET) assay.
27. The method of any one of claims 1–26, wherein the amount or concentration of at least one of the four or more proteins is determined using a proximity extension assay.
28. The method of any one of claims 1–27, wherein the amount or concentration of at least one of the four or more proteins is determined using an enzyme-linked immunosorbent assay (ELISA).
29. The method of any one of claims 1–28, wherein the amount or concentration of at least one of the four or more proteins is determined using an amplified luminescent proximity homogenous assay.
30. The method of any one of claims 1–29, wherein the amount or concentration of at least one of the four or more proteins is determined using a lateral flow assay.
31. The method of any one of claims 1–30, wherein the biological sample is obtained from the pregnant human while in a perinatologist's office, a labor and delivery room, or triage (ER).

32. The method of any one of claims 1–31, further comprising separating the biological sample into a plurality of different reaction vessels, the plurality of reaction vessels comprising a first reaction vessel, a second reaction vessel, a third reaction vessel, and a fourth reaction vessel, wherein contacting the biological sample with the plurality of different probes comprises delivering probes with specific affinity for PI GF in a first reaction vessel, delivering probes with specific affinity to sFlt1 to a second reaction vessel, delivering probes with specific affinity to KIM1 to a third reaction vessel, and delivering probes with specific affinity to CLEC4A to a fourth reaction vessel.

33. The method of any one of claims 1–29, wherein the step of contacting the biological sample with the plurality of different probes occurs in a single reaction vessel.

34. The method of any one of claims 1–33, wherein the biological sample was obtained from the pregnant female after the pregnant female has shown one or more symptoms of preeclampsia, wherein the symptoms of preeclampsia are selected from (1) high blood pressure and (2) proteinuria.

35. The method of claim 34, wherein the sample was obtained from the pregnant female after the pregnant female has shown both (1) high blood pressure and (2) proteinuria.

36. The method of any one of claims 1–35, wherein the plurality of different probes comprises two sets of probes with specific affinity for each of the four or more proteins, wherein each set of the two sets of probes binds to different epitopes.

37. 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 selected from the proteins listed in Table A or Table B;

detecting the presence and/or quantity of the four or more proteins based on binding of the plurality of different probes to corresponding proteins.

38. The method of claim 37, 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.

39. The method of claim 38, wherein the four or more proteins further comprise 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).

40. The method of any one of claims 37–39, wherein the four or more proteins comprise PIGF, sFlt1, KIM1, and CLEC4A.

41. The method of any one of claims 37–40, wherein the plurality of different probes comprises probes with specific affinity to fibroblast growth factor 21 (FGF21), and the four or more proteins comprise FGF21.

42. The method of any one of claims 37–41, wherein the plurality of different probes comprises probes with specific affinity for endoglin, and the four or more proteins comprise endoglin.

43. The method of any one of claims 37–42, wherein the plurality of different probes comprises probes with specific affinity for decorin, and the four or more proteins comprise decorin.

44. The method of any one of claims 37–43, wherein the plurality of different probes comprises probes with specific affinity for cluster of differentiation 274 (CD274), and the four or more proteins comprise CD274.

45. The method of any one of claims 37–44, wherein the plurality of different probes comprises probes with specific affinity for hepatocyte growth factor (HGF), and the four or more proteins comprise HGF.

46. The method of any one of claims 37–45, wherein the plurality of different probes comprises probes with specific affinity for trefoil factor 2 (TFF2), and the four or more proteins comprises TFF2.

47. The method of any one of claims 37–46, wherein the plurality of different probes comprises probes with specific affinity for pappalysin-2 (PAPP-A2), and the four or more proteins comprises PAPP-A2.

48. The method of any one of claims 37–47, wherein the biological sample has been collected from the pregnant human female after gestational week 20.

49. The method of any one of claims 37–48, wherein the biological sample has been collected from the pregnant female prior to gestational week 30.

50. The method of any one of claims 37–49, wherein the biological sample is a urine, blood, amniotic fluid, exosome, plasma, or serum sample.

51. The method of any one of claims 37–49, wherein the biological sample is from blood of the pregnant human female.

52. The method of any one of claims 37–51, wherein the amount or concentration of no more than 20, no more than 15, nor more than 10, nor more than 9, no more than 8, no more than 7, no more than 6, nor more than 5, or no more than 4 proteins is determined.

53. The method of any one of claims 37–52, wherein one or more of the plurality of different probes are antibodies or antibody fragments.

54. The method of any one of claims 37–53, wherein each of the plurality of different probes are antibodies or antibody fragments.

55. The method of any one of claims 37–54, wherein the plurality of probes contact the biological sample or a fraction thereof in a single reaction vessel.

56. The method of any one of claims 37–54, 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.

57. The method of any one of claims 37–56, further comprising a second plurality of probes, wherein the second plurality of probes comprises a probe set that is specific for binding to PIGF, a probe set that is specific for binding to sFlt1, a probe set that is specific for binding to KIM1, and a probe set that is specific for binding to CLEC4A, 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.

58. The method of claim 57, 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.

59. A method for managing a pregnant human subject and identifying the pregnant human subject as not at risk for preeclampsia for a specified period of time, the method comprising:

(a) identifying, via a test having (1) a specificity of greater than 80% and (2) a sensitivity of greater than 85%, the pregnant subject as not at risk for developing preeclampsia within the specified period of time, wherein the specified period of time is between one week and six weeks; and

(b) managing the pregnant human subject identified as not at risk for developing preeclampsia within the specified period of time by proceeding with ambulant monitoring treatment of said pregnant patient without treating the patient for preeclampsia.

60. The method of claim 59, wherein the test has a specificity of at least 82.0%, at least 84.0%, at least 85.0%, at least 87.0%, at least 88.0%, at least 89.0%, at least 90.0%, at least 90.5%, at least 91.0%, or at least 91.5%.

61. The method of claim 59 or 60, wherein the test has a sensitivity of at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, or at least 95%.

62. The method of any one of claims 59–61, wherein the test has a negative predictive value of at least about 95.0%, 96.0%, 97.0%, 98.0%, 98.2%, 98.4%, 98.5%, 98.7%, 99%, 99.2%, or 99.5% when applied to a random population of ethnically diverse pregnant women after gestational week 20 that exhibit one or more of (1) high blood pressure and (2) proteinuria.

63. The method of any one of claims 59–62, wherein the test has a positive predictive value of at least about 30%, at least about 32%, at least about 35%, at least about 37%; at least about 40%, at least about 42%, at least about 45%, at least about 50%, at least about 55%, or at least about 57% when applied to a random population of ethnically diverse pregnant women after gestational week 20 that exhibit one or more of (1) high blood pressure and (2) proteinuria.

64. The method of any one of claims 59–63, wherein the negative predictive value of the test is higher than the positive predictive value of the test.

65. The method of any one of claims 59–63, wherein the specified period of time is between one week and four weeks, one week and three weeks, or one week and two weeks.

66. The method of any one of claims 59–65, wherein the test comprises determining an amount or concentration of each of four or more proteins selected from proteins listed in Table A or Table B.

67. The method of claim 66, wherein the four or more proteins comprise PIGF, sFlt-1, KIM1, and CLEC4A.

68. The method of claim 67, wherein the four or more proteins further comprise FGF21.

69. A method of treating a pregnant human subject, the method comprising: obtaining an indicium generated, at least in part, from a determination of levels for four or more proteins listed in Table A or Table B; and changing a clinical regimen for the pregnant human subject based, at least in part, on the obtained indicium.

70. The method of claim 69, wherein obtaining the indicium comprises: determining the levels for PIIGF, sFlt1, KIM1, and CLEC4A, wherein the levels are determined from binding of each of PIIGF, sFlt1, KIM1, and CLEC4A to corresponding probes.

71. The method of claim 70, wherein the obtaining the indicium further comprises determining the level for FGF21, wherein the level of FGF21 is determined from binding of FGF21 to corresponding probes.

72. The method of any one of claims 69–71, further comprising classifying the pregnant subject as having a low risk of having preeclampsia or developing preeclampsia within a specified period of time.

73. The method of claim 72, wherein the pregnant subject is classified by any method described herein.

74. The method of any one or claims 69–73, further comprising administering an antihypertensive drug to the patient.

75. The method of claim 74, wherein the antihypertensive drug is a central alpha agonist, a vasodilator, a calcium-channel blocker, an alpha-blocker or a beta-blocker.

76. The method of claim 74, wherein the antihypertensive drug is methyldopa, labetalol, nifedipine, verapamil, clonidine, hydralazine, diazoxide, prazosin, or oxprenolol.

77. A mixture comprising:  
a fluid sample from a pregnant female subject;  
a first plurality of different probes, wherein the first plurality of different probes comprises different probes, each with specific affinity for four or more proteins selected from proteins listed in Table A or Table B.

78. The mixture of claim 77, wherein the four or more proteins comprise:  
(a) placental growth factor (PIIGF);

(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.

79. The method of claim 78, wherein the four or more proteins further comprise 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).

80. The mixture of any one of claims 77–79, wherein the four or more proteins comprise PIgf, sFlt1, KIM1, and CLEC4A.

81. The mixture of any one of claims 77–80, wherein the four or more proteins comprise FGF 21.

82. The mixture of any one of claims 77–81, wherein the four or more proteins comprise endoglin.

83. The mixture of any one of claims 77–82, wherein the four or more proteins comprise decorin.

84. The mixture of any one of claims 77–83, wherein the four or more proteins comprise CD274.

85. The mixture of any one of claims 77–84, wherein the four or more proteins comprise HGF.

86. The mixture of any one of claims 77–85, wherein the four or more proteins comprise TFF2.

87. The mixture of any one of claims 77–86, wherein the four or more proteins comprise PAPP-A2.

88. The mixture of any one of claims 77–87 wherein the fluid sample has been collected after gestational week 20.

89. The mixture of any one of claims 77–88, wherein the fluid sample has been collected from the pregnant female prior to gestational week 30.

90. The mixture of any one of claims 77–89, wherein the mixture includes no more than 20, no more than 16, no more than 14, no more than 12, no more than 10, no more than

eight, no more than seven, no more than 6, no more than 5, or no more than 4 sets of probes that are designed to bind to different proteins in the fluid sample.

91. The mixture of any one of claims 77–90, wherein the fluid sample is from a blood, plasma, serum, or exosome sample.

92. The method of any one of claims 77–91, wherein the fluid sample was obtained from the subject after the subject has shown one or more symptoms of preeclampsia, wherein the symptoms of preeclampsia are selected from (1) high blood pressure and (2) proteinuria.

93. The method of claim 77–92, wherein the fluid sample was obtained from the subject after the subject has shown both (1) high blood pressure and (2) proteinuria.

94. The method of any one of claims 77–93, wherein the first plurality of different probes comprises a first set of probes with specific affinity for each of the four or more proteins and a second set of probes with specific affinity for each of the four or more proteins, wherein each set of the two sets of probes binds to different epitopes.

95. The mixture of claim 94, wherein the first set of probes and the second set of probes are conjugated to pairs of oligonucleotides containing complementary hybridization regions for each protein-specific probe pair.

96. The mixture of claim 94, wherein the first set of probes and the second set of probes are conjugated to unique FRET pairs of fluorophores for each protein-specific probe pair.

97. The mixture of claim 94, wherein, for each protein-specific probe pair, one probe is conjugated to biotin or a streptavidin-binding analog thereof.

98. The mixture of claim 94, further comprising (a) a photosensitizer; and (b) an oxygen-sensitive dye, wherein one of (a) and (b) is capable of binding the first set of probes, and the other is capable of binding the second set of probes.

99. The mixture of any one of claims 77–98, wherein one or more of the first plurality of different probes are antibodies or antibody fragments.

100. The mixture of any one of claims 77–99, wherein each of the first plurality of different probes are antibodies or antibody fragments.

101. A reaction plate comprising a plurality of reaction wells, wherein the plurality of reaction wells comprises:

a first well comprising (1) a first portion of a biological sample from a pregnant human subject, wherein the biological sample was obtained from a pregnant human subject after 20 weeks of gestation, and (2) a first set of probes for binding to PIGF;

a second well comprising (1) a second portion of the biological sample from the pregnant human subject, and (2) a second set of probes for binding to sFlt1, endoglin, pappalysin 2 (PAPP-A2), or decorin;

a third well comprising (1) a third portion of the biological sample from the pregnant human subject, and (2) a third set of probes for binding to KIM1, (2) programmed cell death 1 ligand 1 (CD274), or decorin; and

a fourth well comprising (1) a fourth portion of the biological sample from the pregnant human subject, and (2) a fourth set of probes for binding to CLEC4A, FGF21, TFF2, or HGF.

102. The reaction plate of claim 101, wherein the second set of probes in the second well are configured to bind to sFlt1.

103. The reaction plate of claim 101 or claim 102, wherein the third set of probes in the third well are configured to bind to KIM1.

104. The reaction plate of any one of claims 101–103, wherein the fourth set of probes in the fourth well are configured to bind to CLEC4A.

105. The reaction plate of any one of claims 101–104, wherein the plurality of wells comprises a fifth well, the fifth well comprising (1) a fifth portion of the biological sample from the pregnant human subject and (2) a fifth set of probes for binding to FGF21.

106. The reaction plate of any one of claims 101–105, wherein the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to endoglin.

107. The reaction plate of any one of claims 101–106, wherein the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to decorin.

108. The reaction plate of any one of claims 101–107, wherein the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to CD274.

109. The reaction plate of any one of claims 101–108, wherein the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to HGF.

110. The reaction plate of any one of claims 101–109, wherein the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to TFF2.

111. The reaction plate of any one of claims 101–110, wherein the plurality of reaction wells comprises a well, the well comprising a portion of the biological sample and a set of probes for binding to PAPP-A2.

112. The reaction plate of any one of claims 101–111, wherein the biological sample has been collected from the pregnant female prior to gestational week 30.

113. The reaction plate of any one of claims 101–112, wherein the biological sample is from blood of the pregnant human female.

114. The reaction plate of any one of claims 101–113, wherein the plurality of wells of the reaction include probes for specific binding to no more than 20, no more than 15, no more than 12, no more than 10, no more than 8, no more than 7, no more than 6, no more than 5, or no more than 4 proteins.

115. The reaction plate of any one of claims 101–114, wherein the probes comprise antibodies or antibody fragments.

116. The reaction plate of any one of claims 101–115, wherein the biological sample is from the subject after the subject has shown one or more symptoms of preeclampsia, wherein the symptoms of preeclampsia are selected from (1) high blood pressure and (2) proteinuria.

117. The reaction plate of claim 101–116, wherein the sample is from the subject after the subject has shown both (1) high blood pressure and (2) proteinuria.

118. The reaction plate of any one of claims 101–117, wherein each set of probes comprises probes that specifically bind to different epitopes.

119. A kit for ruling out preeclampsia in a pregnant female subject, the kit comprising:

(a) probes for determining the levels of four or more proteins selected from the proteins listed in Tables 6 and 7;

(b) wherein the kit is designed to measure the levels of no more than 20, no more than 15, no more than 10, nor more than 8, no more than 7, no more than 6, nor more than 5, or no more than 4 proteins.

120. The kit of claim 119, wherein the four or more proteins comprises:

(a) placental growth factor (PIGF);

(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.

121. The kit of claim 120, wherein the four or more proteins comprise 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).

122. The kit of any one of claims 119–121, wherein the four or more proteins comprise PIGF, sFlt1, KIM1, and CLEC4A.

123. The kit of any one of claims 119–122, wherein the four or more proteins comprise FGF21.

124. The kit of any one of claims 119–123, wherein the four or more proteins comprise endoglin.

125. The kit of any one of claims 119–124, wherein the four or more proteins comprise decorin.

126. The kit of any one of claims 119–125, wherein the four or more proteins comprise CD274.

127. The kit of any one of claims 119–126, wherein the four or more proteins comprise HGF.

128. The kit of any one of claims 119–127, wherein the four or more proteins comprise TFF2.

129. The kit of any one of claims 119–128, wherein the four or more proteins comprise PAPP-A2.

130. The kit of any one of claims 119–129, further comprising instructions for carrying out an immunoassay.

131. The kit of any one of claims 119–130, wherein the kit is an enzyme-linked immunosorbent assay kit.

132. The kit of any one of claims 119–131, wherein one or more of the probes are attached to substrate.

133. The kit of any one of claims 119–132, wherein the kit is for a lateral flow immunoassay.

134. A system for ruling out preeclampsia in a pregnant female subject for a specified period of time, the system comprising:

a processor;  
an input module for inputting levels of at least four proteins in a biological sample, wherein the at least four proteins are selected from Tables 6 and 7;  
a computer readable medium containing instructions that, when executed by the processor, perform a first algorithm on the input levels of the at least four proteins; and  
an output module providing one or more indicia based on the input levels of the at least four proteins, wherein the one or more indicia are indicative of the subject not having preeclampsia for at least a specified period of time.

135. The system of claim 134, further comprising probes to each the at least four proteins.

136. The system of claim 134 or claim 135, wherein the system is designed to output the one or more indicia based on input levels for no more than 15, no more than 10, no more than 8, no more than 7, nor more than 6, no more than 5, or no more than 4 proteins.

137. The system of any one of claims 134–136, wherein the at least four proteins comprise:

(a) placental growth factor (PIGF);

(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.

138. The system of any one of claims 134–137, wherein the at least four proteins comprise 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).

139. The system of any one of claims 134–138, wherein the at least four proteins comprise PIGF, sFlt1, KIM1, and CLEC4A.

140. The system of any one of claims 134–139, wherein the at least four proteins comprise FGF21.

141. The system of any one of claims 134–140, wherein the at least four proteins comprise decorin.

142. The system of any one of claims 134–141, wherein the at least four proteins comprise CD274.

143. The system of any one of claims 134–142, wherein the at least four proteins comprise HGF.

144. The system of any one of claims 134–143, wherein the at least four proteins comprise TFF2.

145. The system of any one of claims 134–144, wherein the at least four proteins comprise PAPP-A2.

146. The system of any one of claims 134–145, wherein the algorithm comprises a correction based on gestational age.

147. The system of any one of claims 134–146, wherein the algorithm comprises a logistics regression. A method for classifying a pregnant human subject as not having and/or not going to develop preeclampsia within a specified time period, the method comprising:

obtaining a sample from a pregnant human subject who has been identified as having one or more symptoms or risk factors for preeclampsia;

running a test to obtain a protein expression profile, wherein the protein expression profile includes levels of two or more proteins from Tables A and B;

applying a classifier algorithm to the expression profile, wherein the classifier algorithm calculates an index; and

comparing the index to a reference value to determine whether to classify the pregnant human subject as not having and/or not going to develop preeclampsia within the specified time period.

148. The method of claim 147, wherein the test has:

a specificity of at least 80%, at least 82%, at least 85%, at least 87%, at least 90%, at least 92%, at least 95%, at least 97%, or at least 99%; and

a sensitivity of at least 80%, at least 82%, at least 85%, at least 87%, at least 90%, at least 92%, at least 95%, at least 97%, or at least 99%.

149. The method of claim 147 or claim 148, wherein the one or more symptoms comprises one or both of high blood pressure and proteinuria.

150. The method of any one of claims 147–149, wherein the specified period of time is between one and six weeks (e.g., between one and four weeks).

151. The method of any one of claims 147–150, wherein the protein expression profile includes levels of three or more proteins from Tables A and B.

152. The method of any one of claims 147–151, wherein the protein expression profile includes levels of four or more proteins from Tables A and B.

153. The method of any one of claims 147–152, wherein the protein expression profile includes levels of five or more proteins from Tables A and B.

154. The method of any one of claims 147–153, wherein the expression profiles of no more than 15, 10, 8, or 6 proteins are determined.

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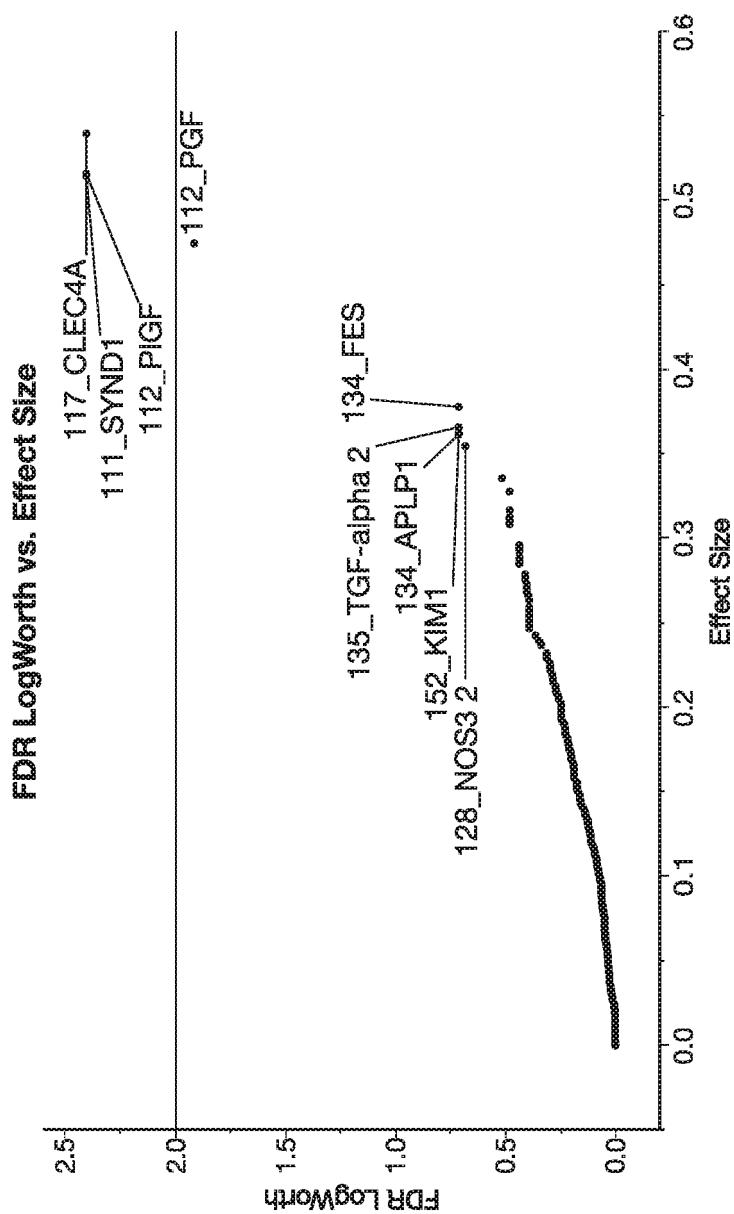


FIG. 1A

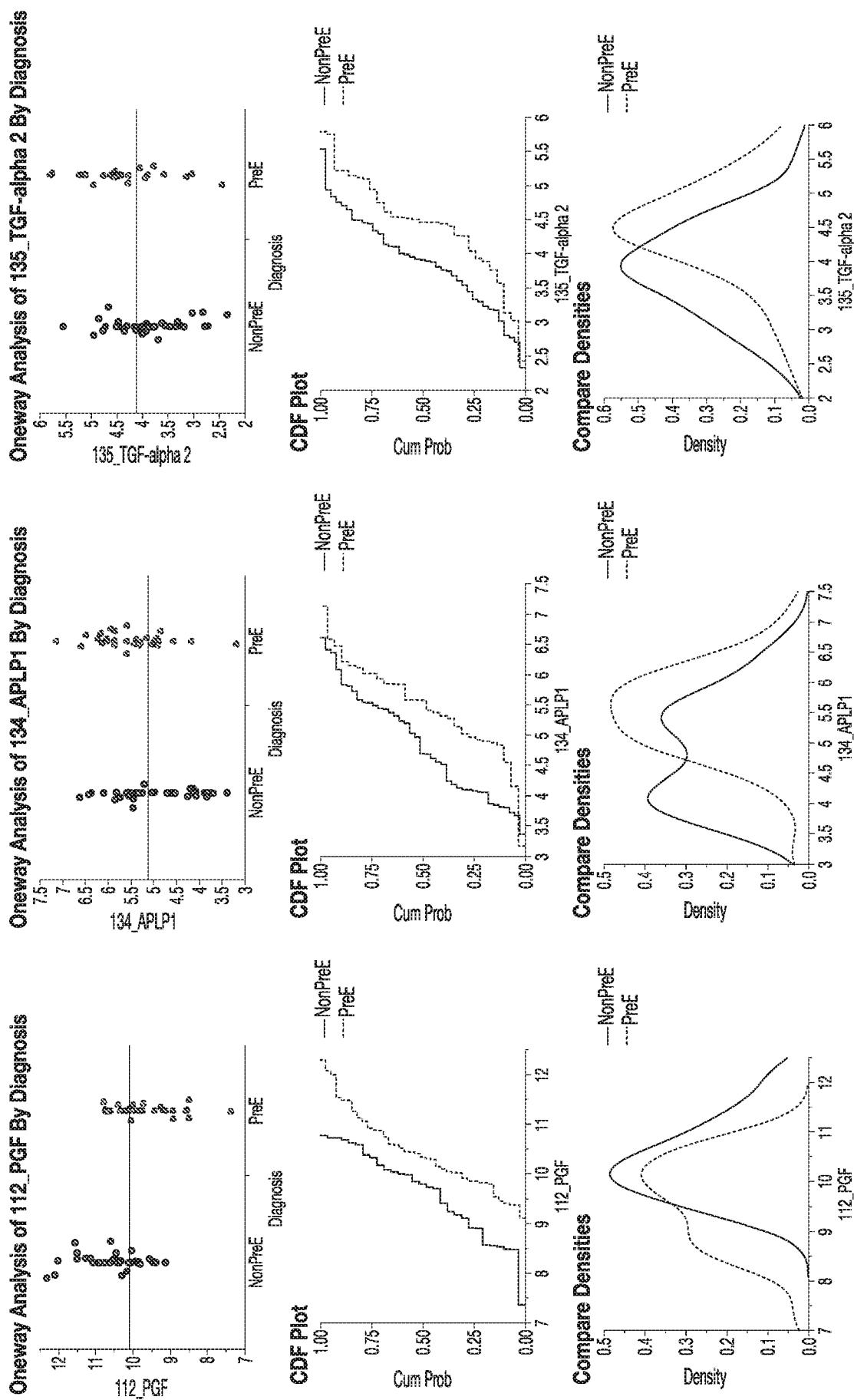


FIG. 1B

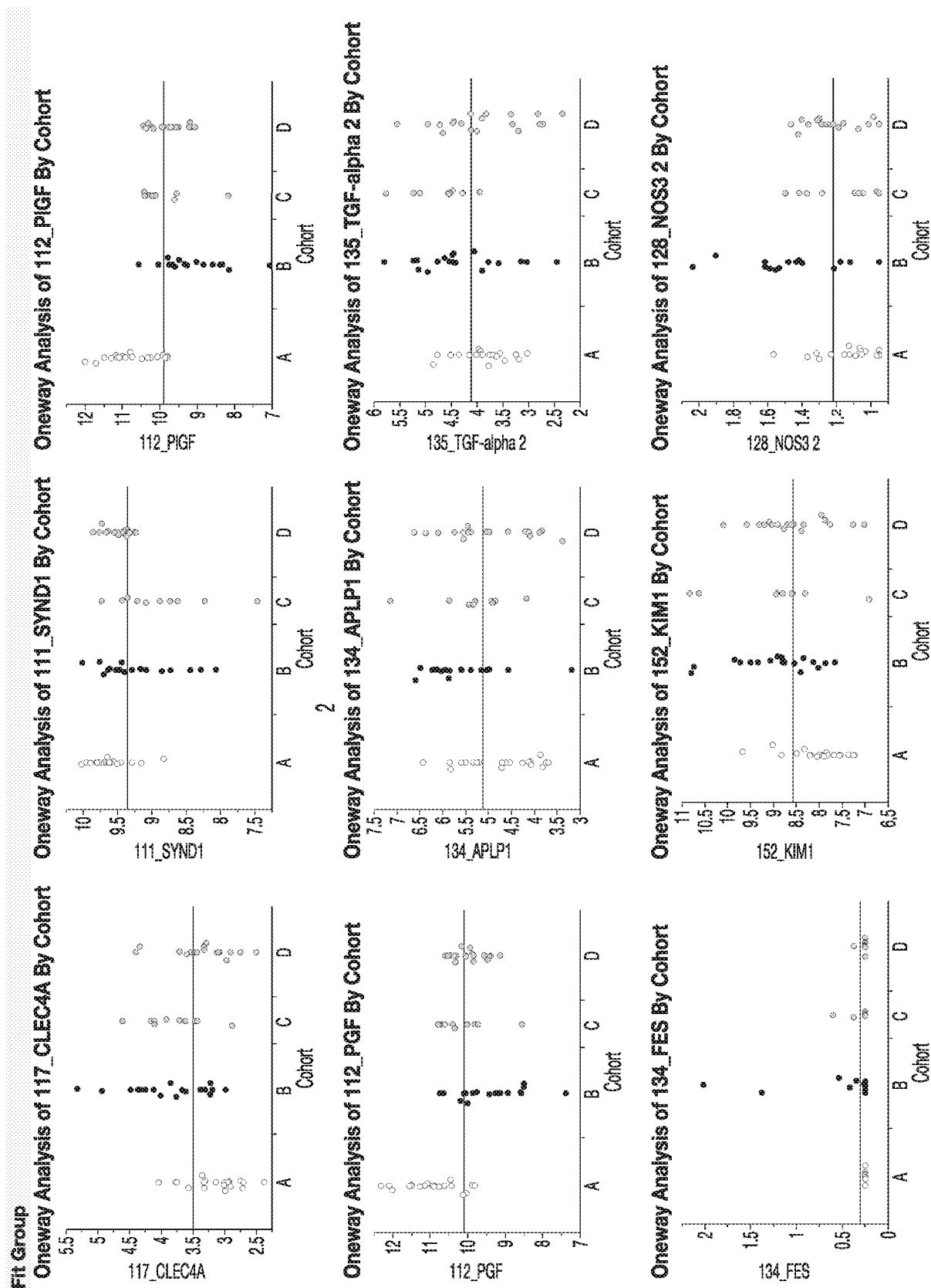


FIG. 2

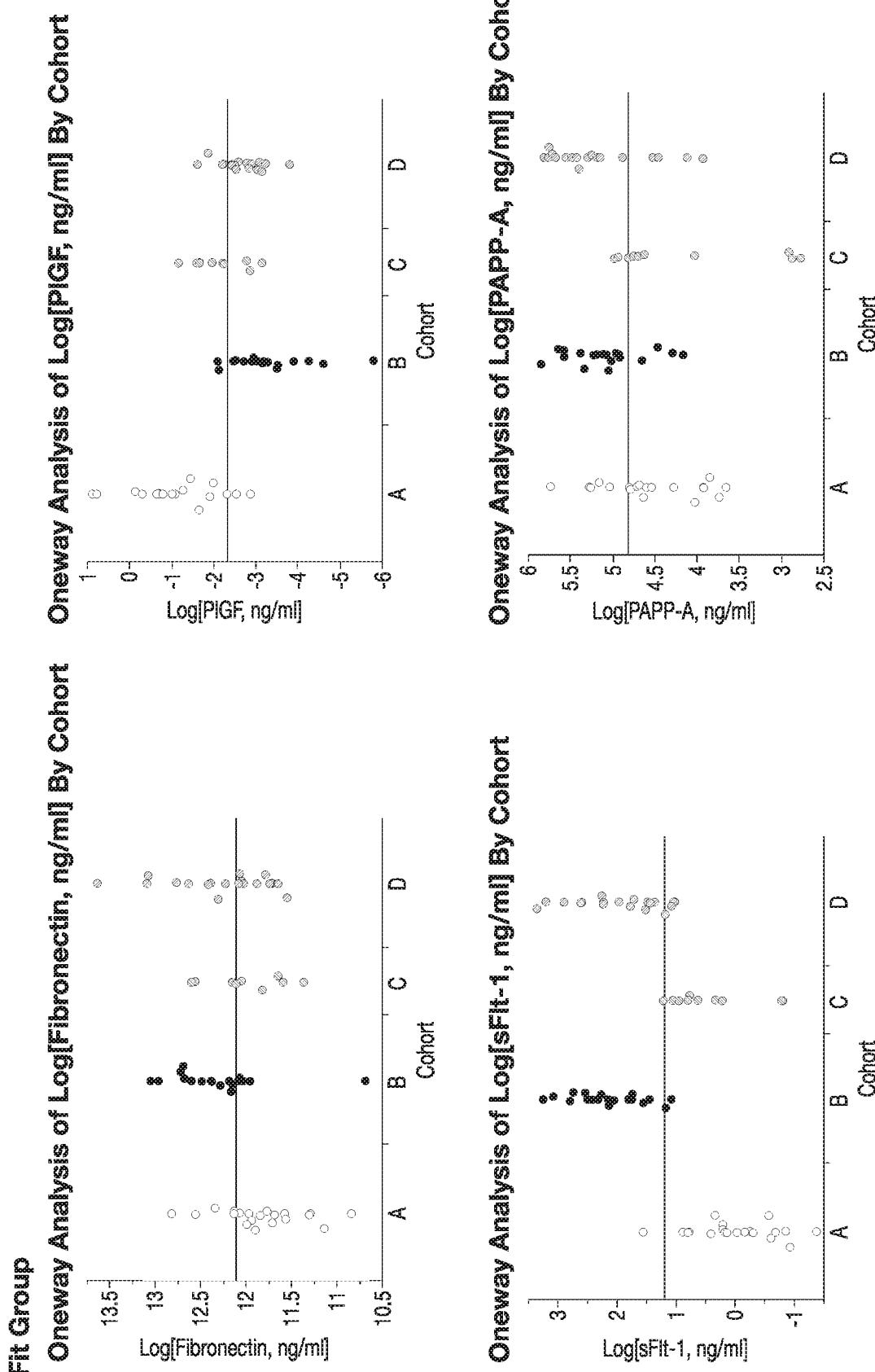
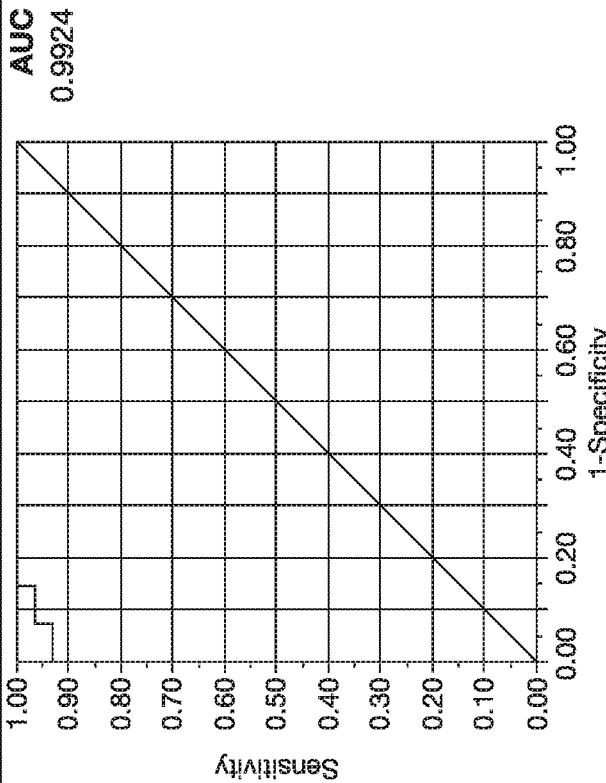


FIG. 3

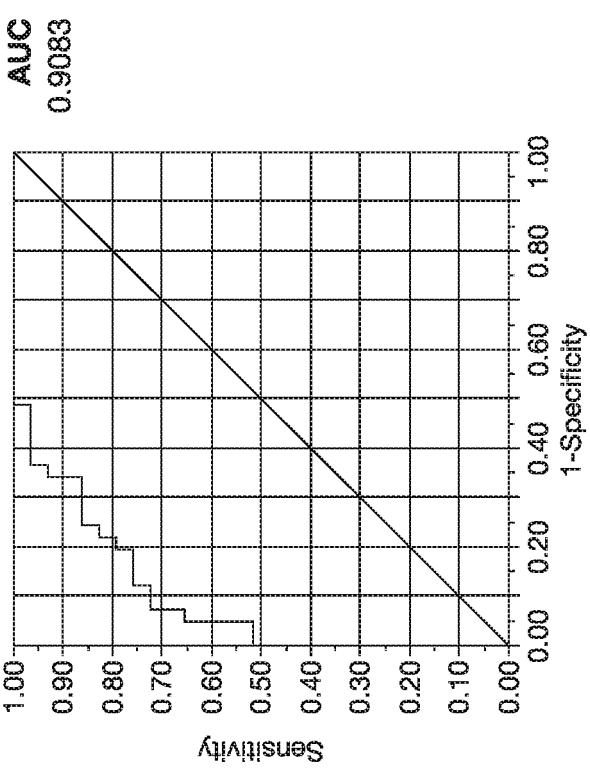
**Parameter Estimates for Original Predictors**

Term	Estimate	Std Error	Wald	ChiSquare	Prob > ChiSquare	Lower 95%	Upper 95%
125_CAPG	-6.184577	1.0392762	35.412626	<.0001*	<.0001*	-8.221521	-4.147634
135_TGF-alpha 2	3.9259522	0.7326208	28.716501	<.0001*	<.0001*	2.4900418	5.3618626
105_ZBTB16	5.7438121	1.1502479	24.93547	<.0001*	<.0001*	3.4893676	7.9982565
112_UPA	1.5803318	0.3671819	18.523964	<.0001*	<.0001*	0.8606684	2.2999951
111_SYND1	-4.852426	1.245346	15.182305	<.0001*	<.0001*	-7.293259	-2.411592
Intercept	50.572105	14.374212	12.378099	0.0004*	22.399167	78.745043	
115_CLEC4C	-2.760179	0.8209154	11.305189	0.0008*	4.369144	-1.151215	
112_PGF	-2.46649	0.7620116	10.476968	0.0012*	-3.960005	-0.972975	
111_AMN	1.5861991	0.5062273	9.8180288	0.0017*	0.5940118	2.5783863	
117_CLEC4A	1.8775839	1.0094619	3.459544	0.0629	-0.100925	3.8560929	

**ROC Curve for Diagnosis = PreE****Training****FIG. 4**

**Parameter Estimates for Original Predictors**

Term	Estimate	Std Error	ChiSquare	Wald	Prob > ChiSquare	Lower 95%	Upper 95%
Intercept	24.827765	9.5866804	6.7071616	0.0096*	6.0382171	43.617314	
Log[ <i>Flt-1</i> , ng/ml]	0.5379997	0.36249	2.2027847	0.1378	-0.172468	1.248467	
117_CLEC4A	2.7973718	0.8122199	11.86187	0.0006*	1.2054501	4.3892935	
111_SYN1	-2.707178	1.0339722	6.8551346	0.0088*	-4.733727	-0.68063	
112_PIGF	-1.059331	0.4844859	4.7808008	0.0288*	-2.008906	-0.109756	

**ROC Curve for Diagnosis = PreE****Training****FIG. 5**

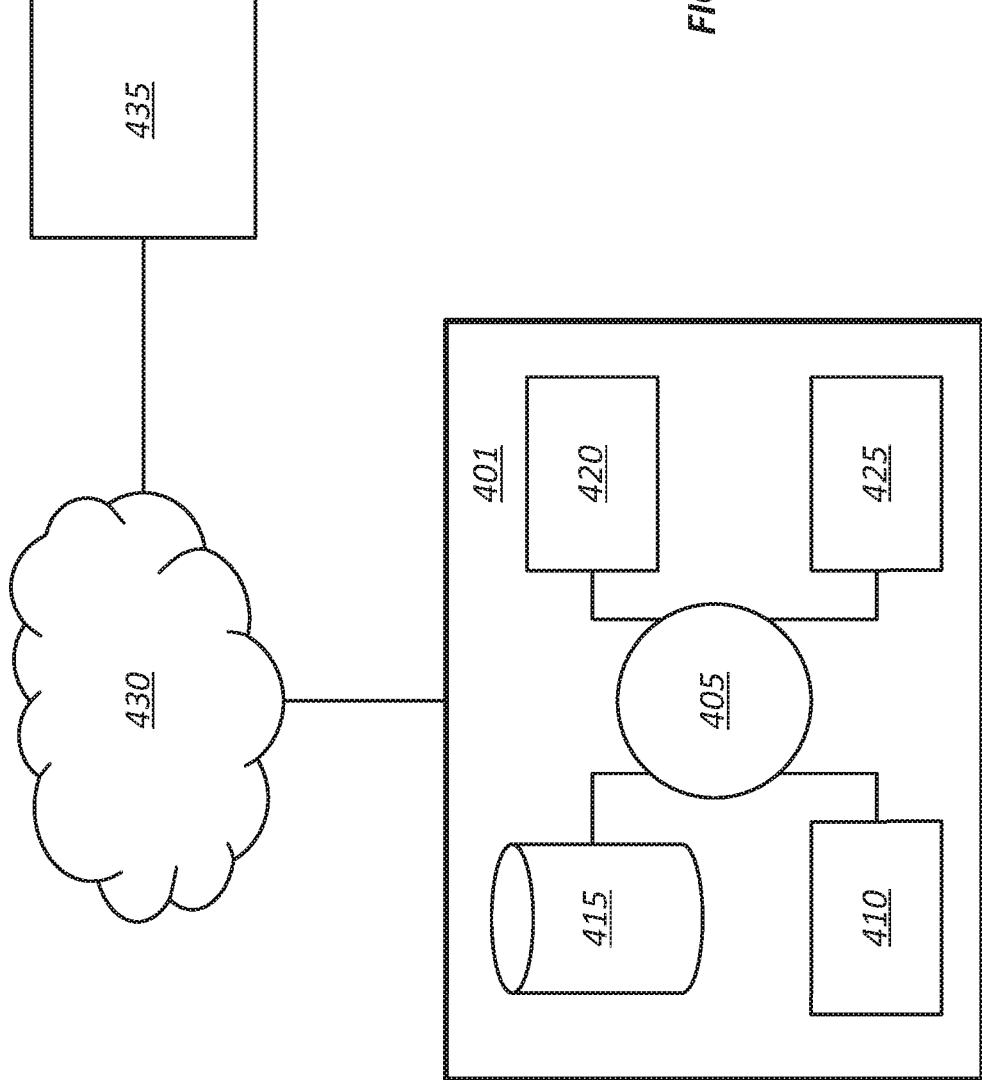
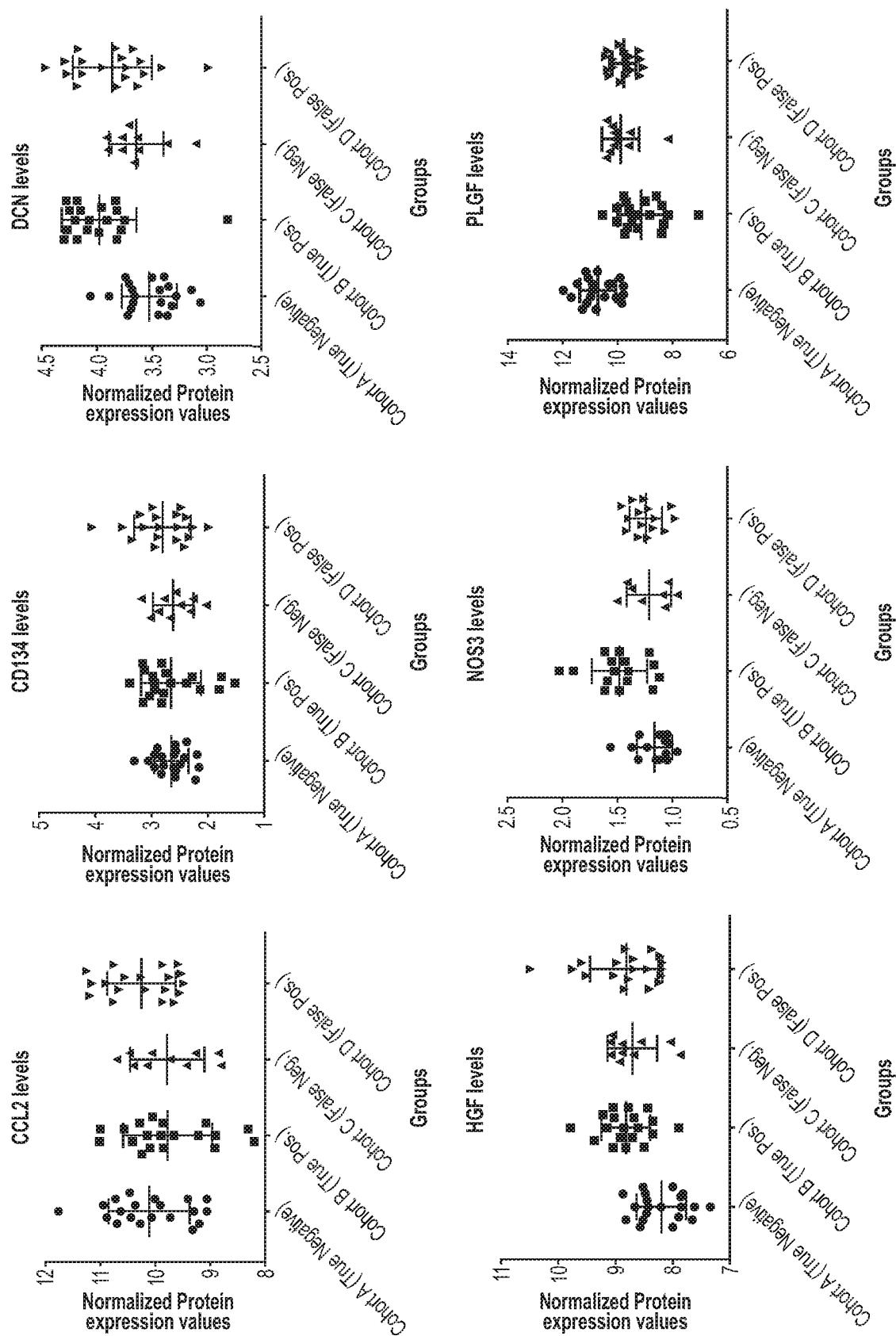


FIG. 7



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FIG. 8

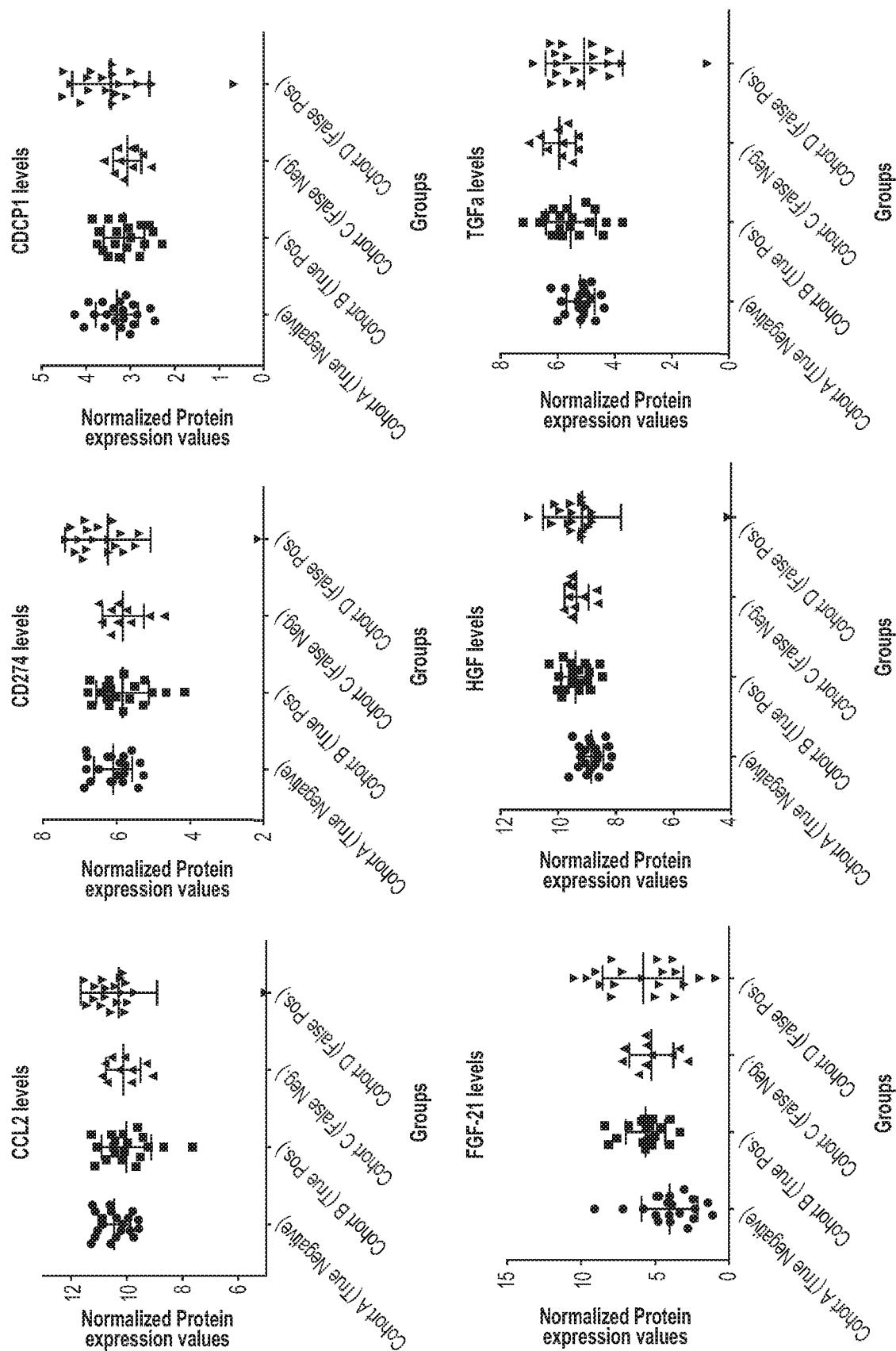
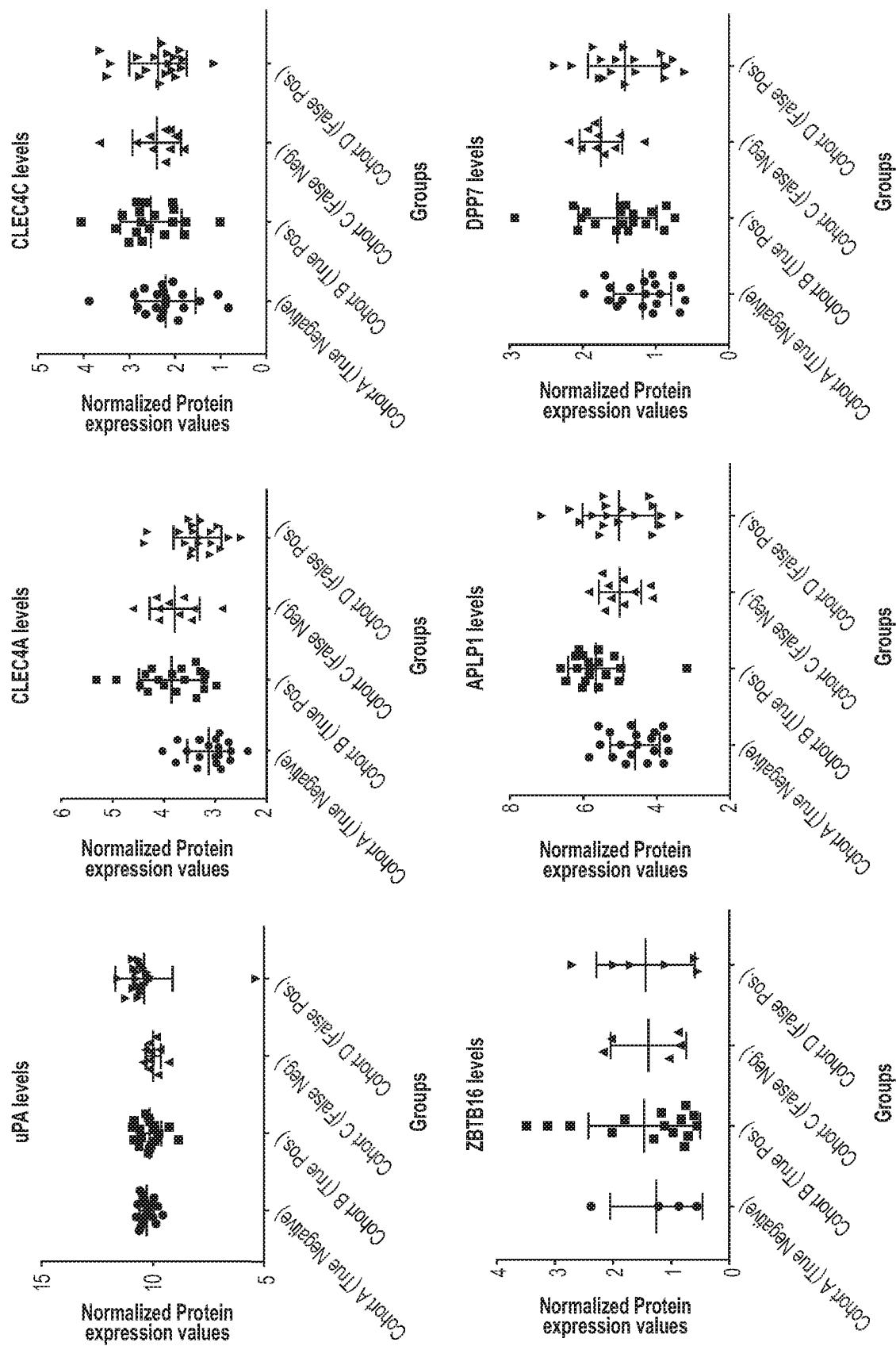


FIG. 9



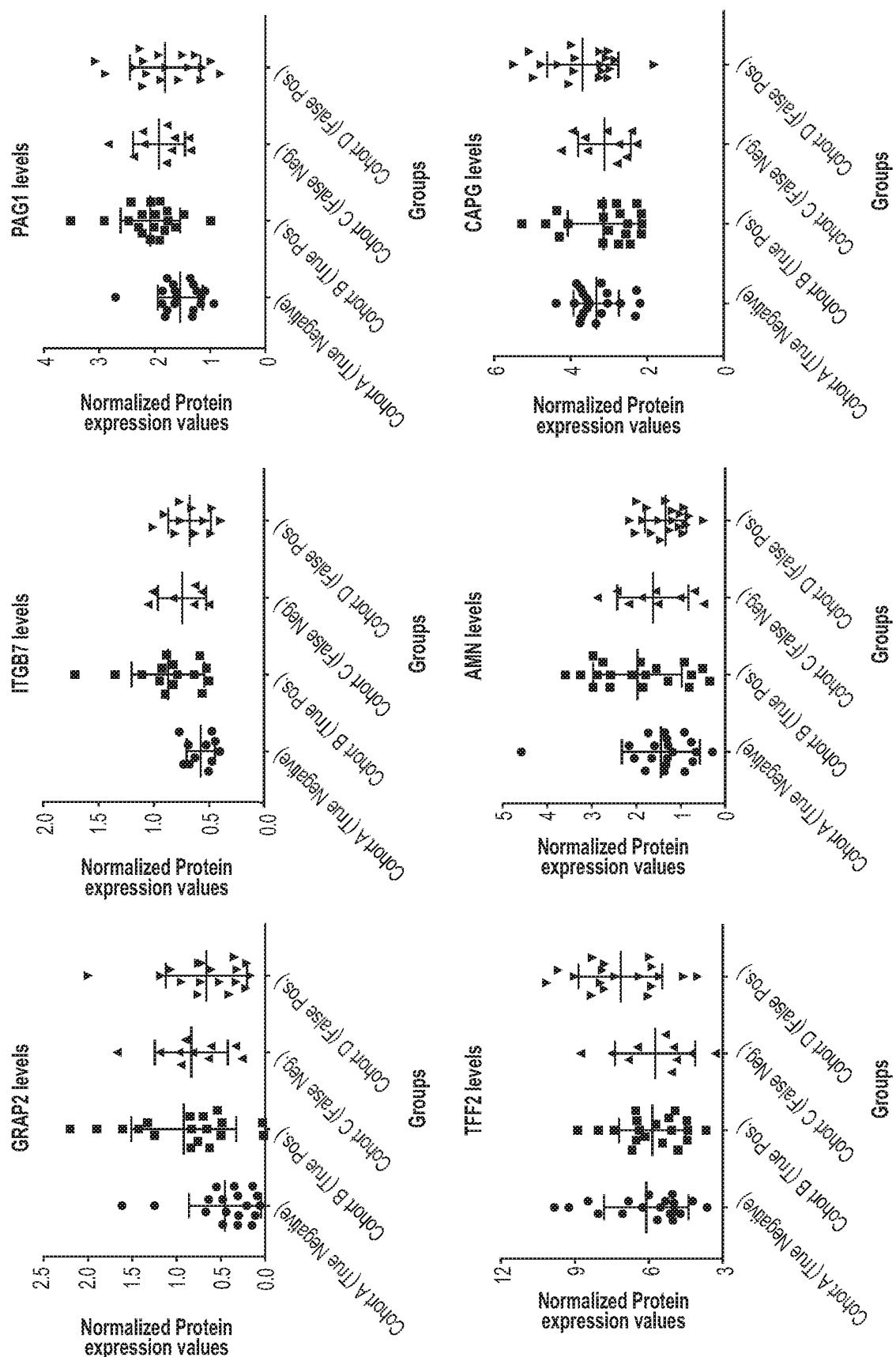


FIG. 10

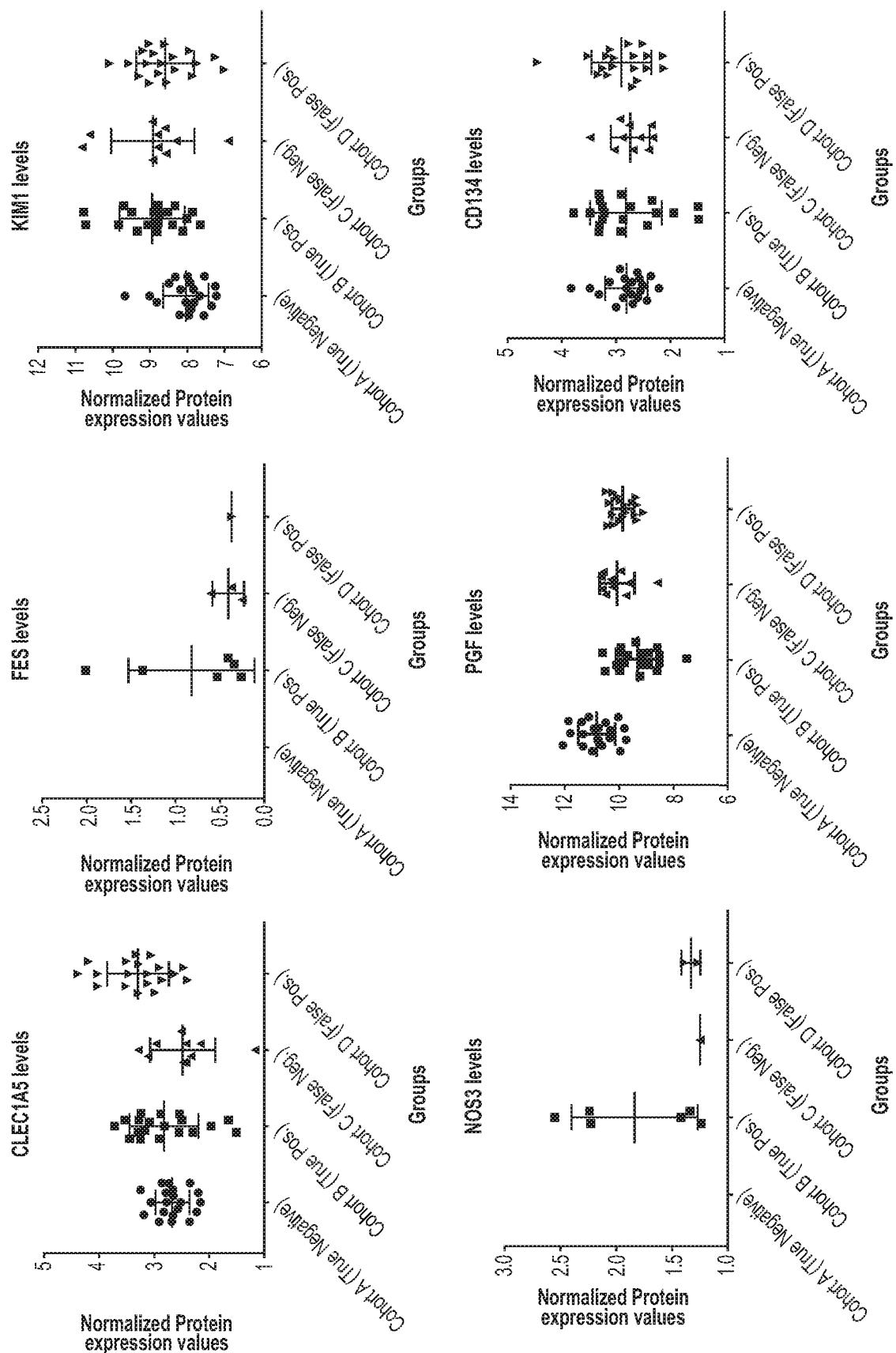


FIG. 11

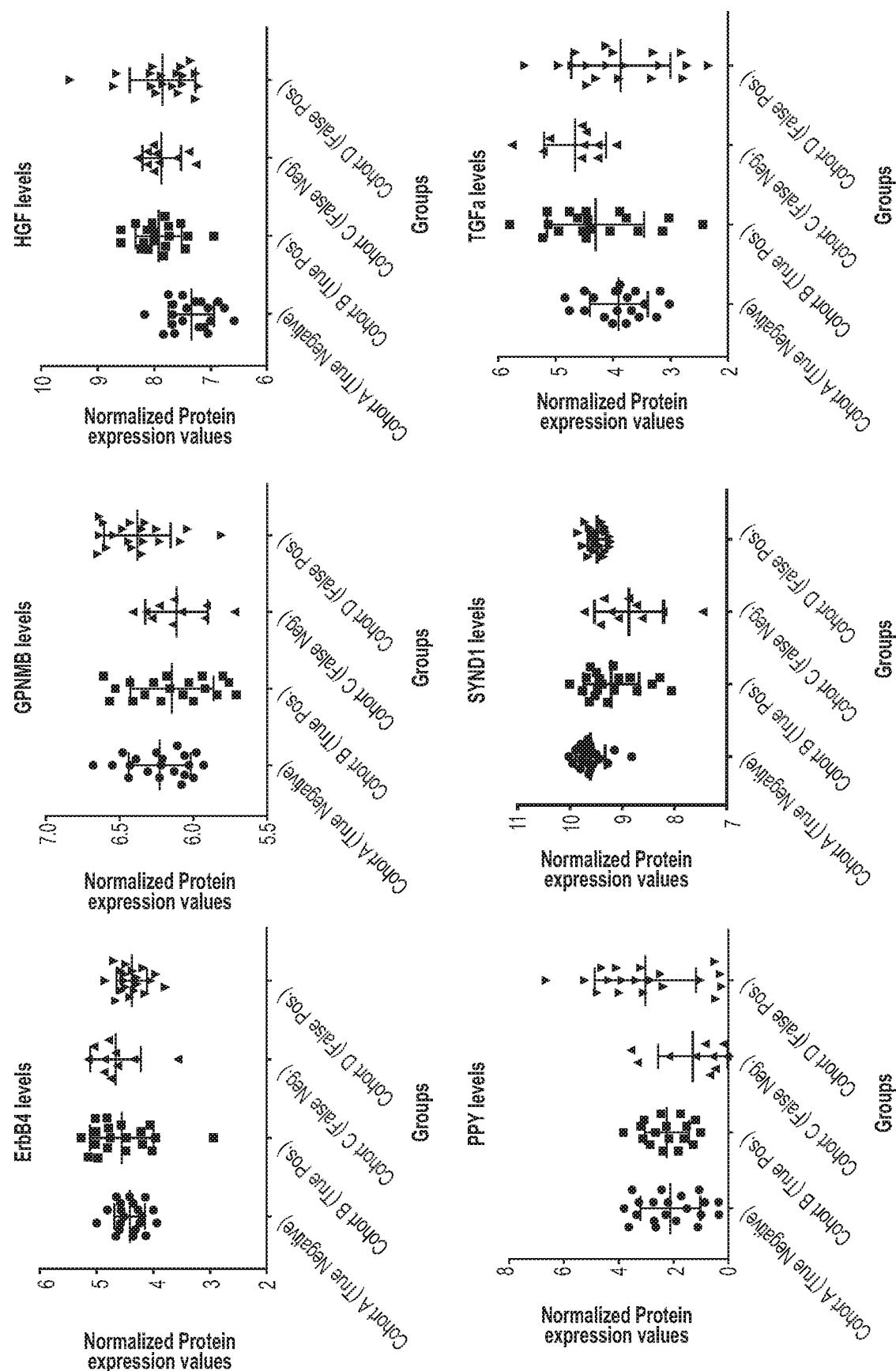


FIG. 12

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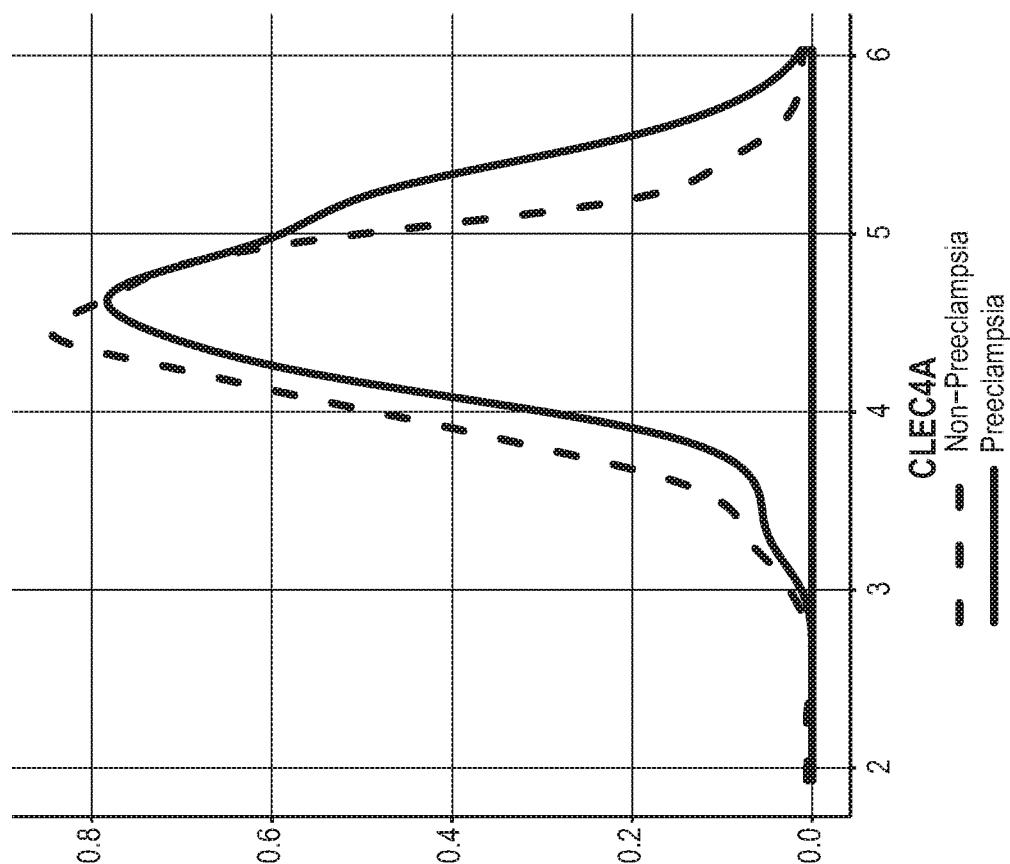


FIG. 13B

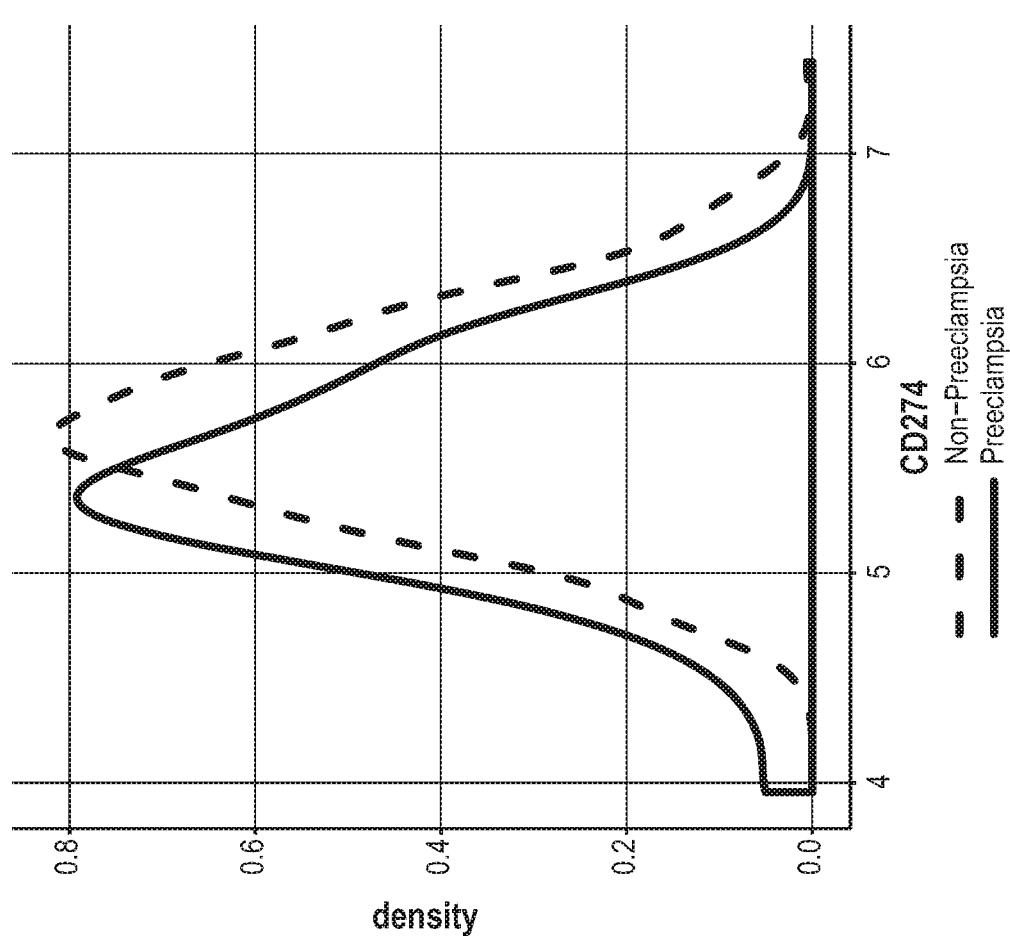


FIG. 13A

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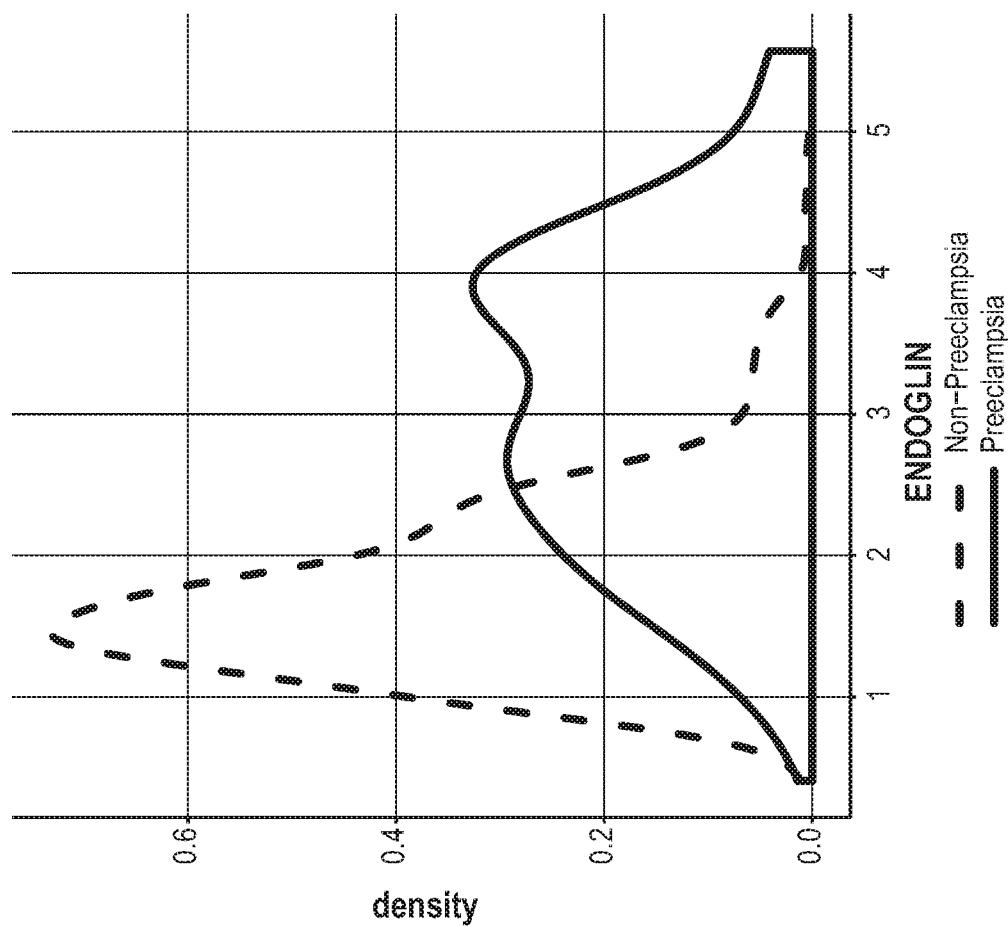


FIG. 13D

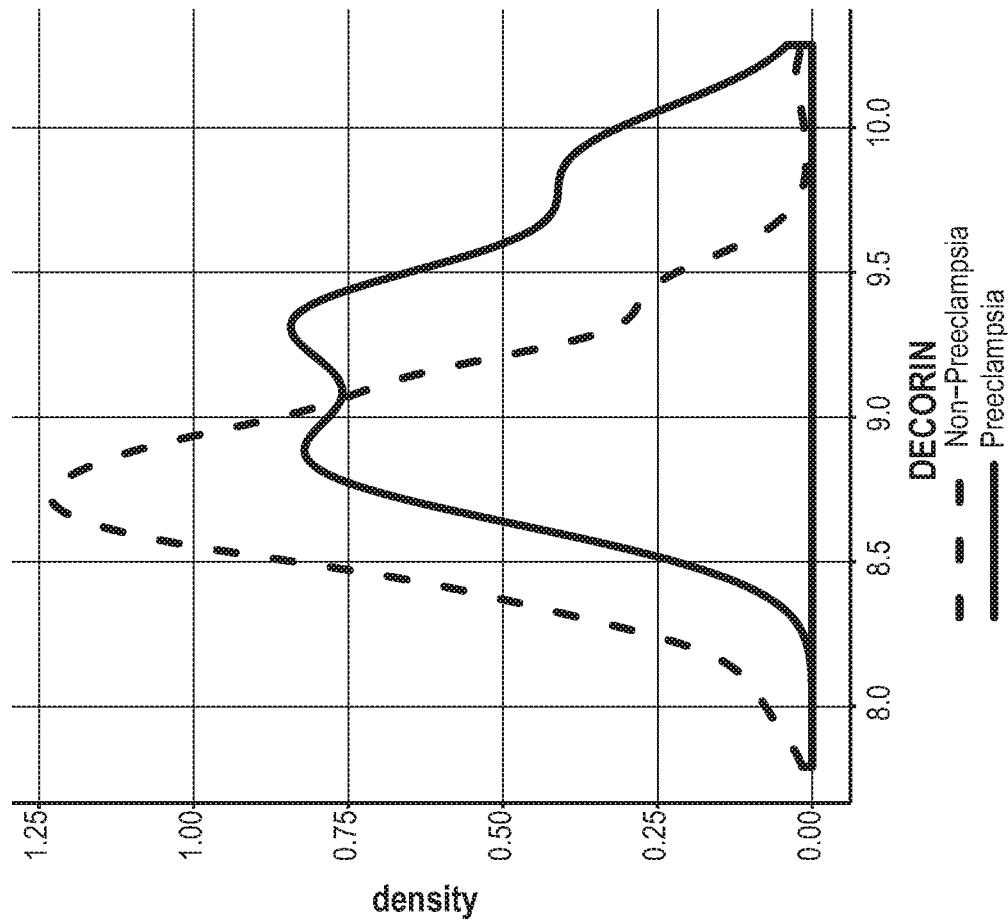


FIG. 13C

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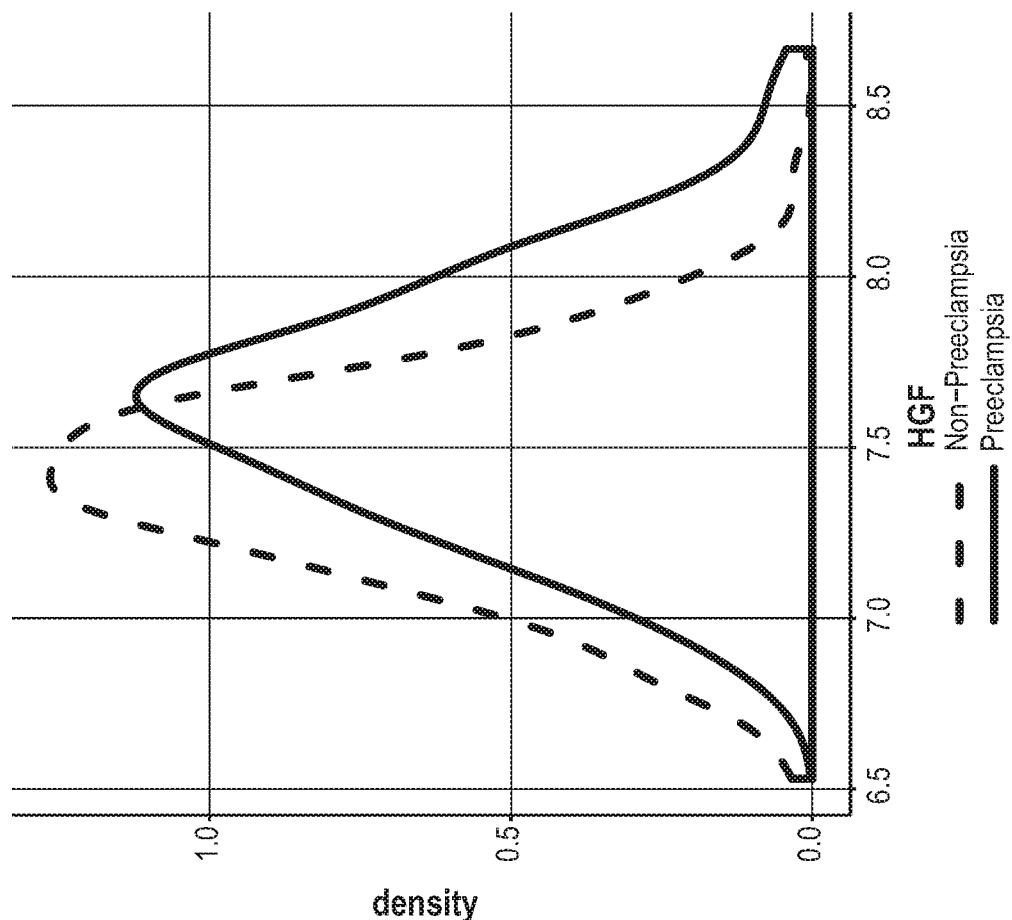


FIG. 13F

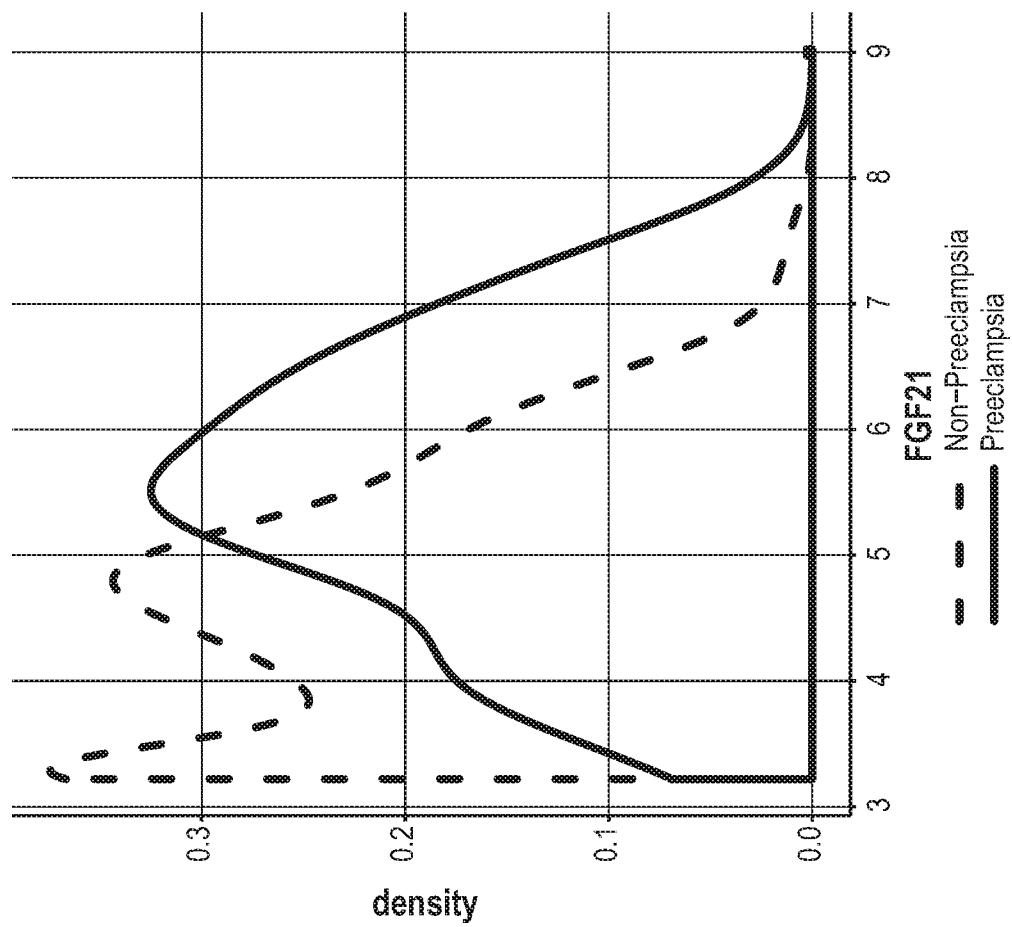


FIG. 13E

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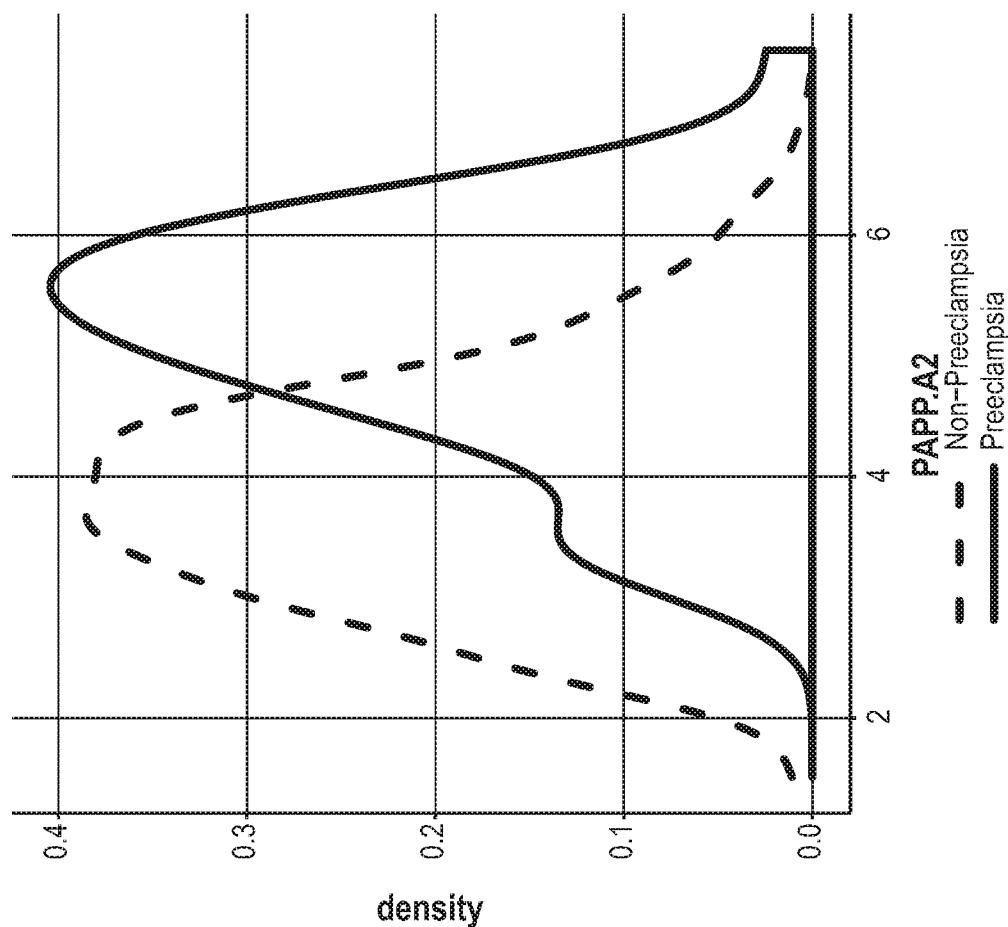


FIG. 13H

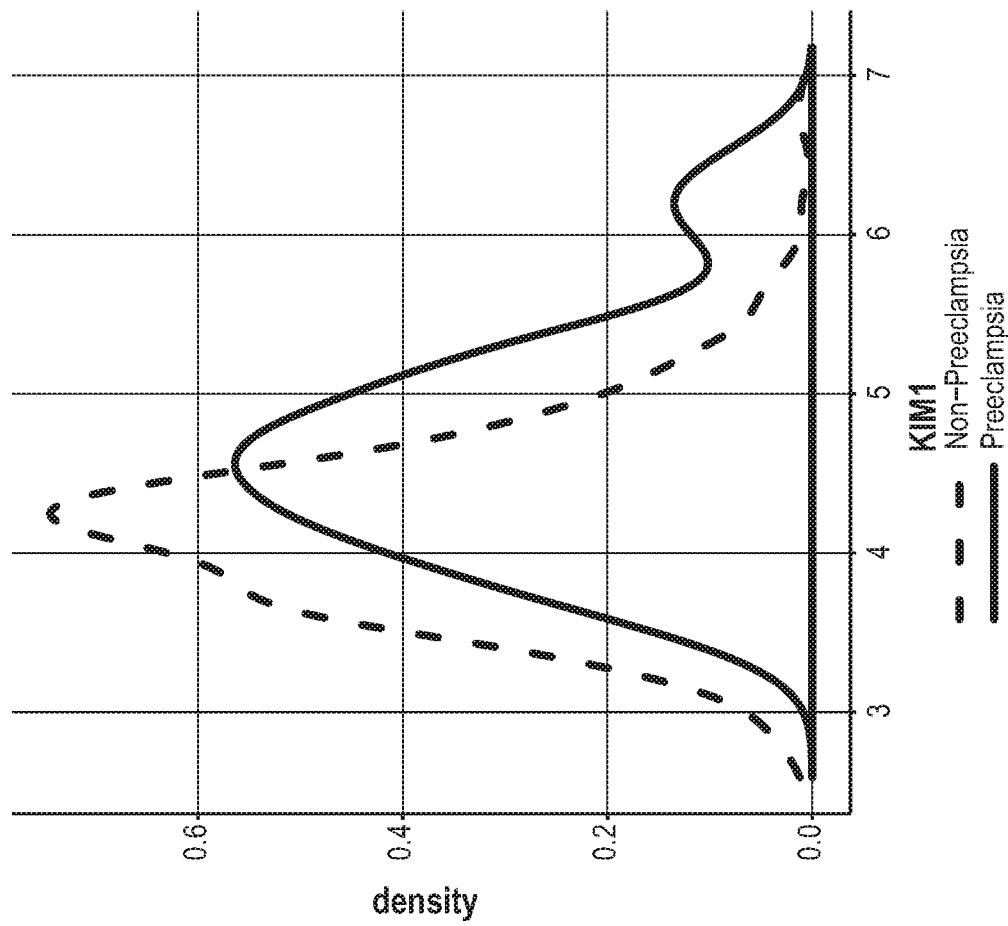


FIG. 13G

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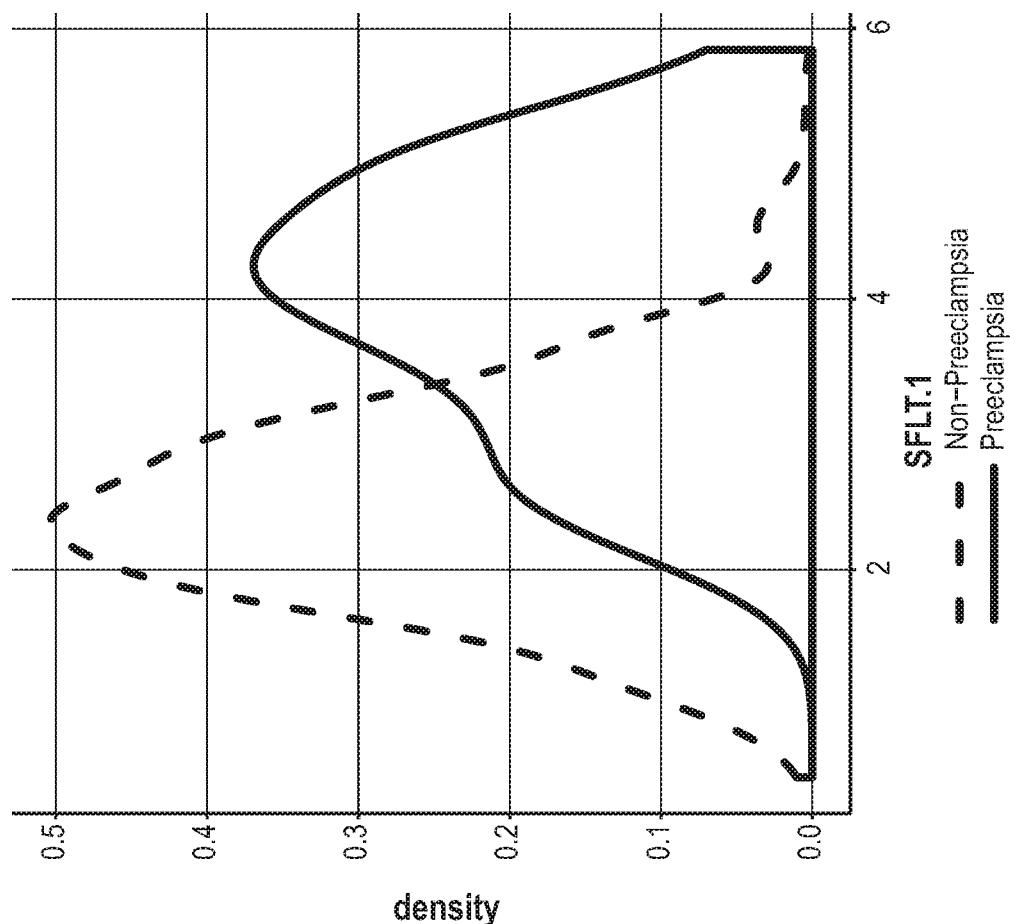


FIG. 13J

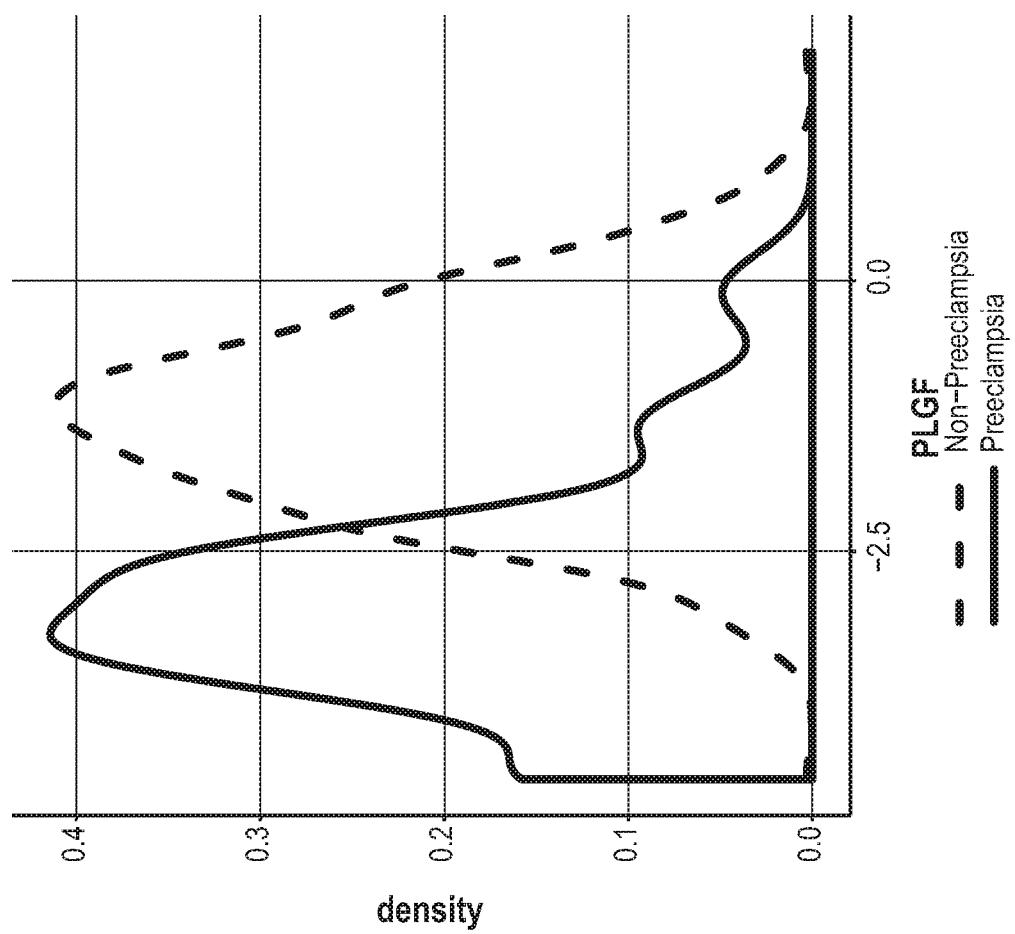


FIG. 13I

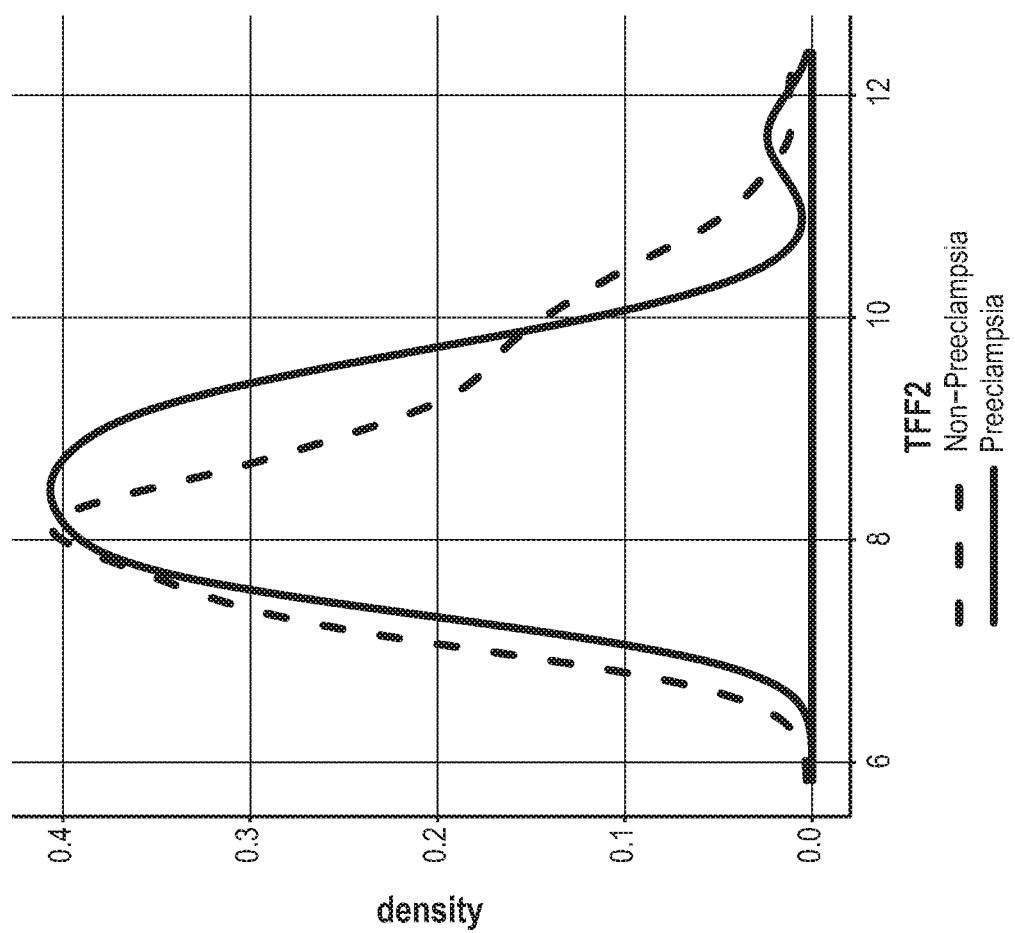


FIG. 13K

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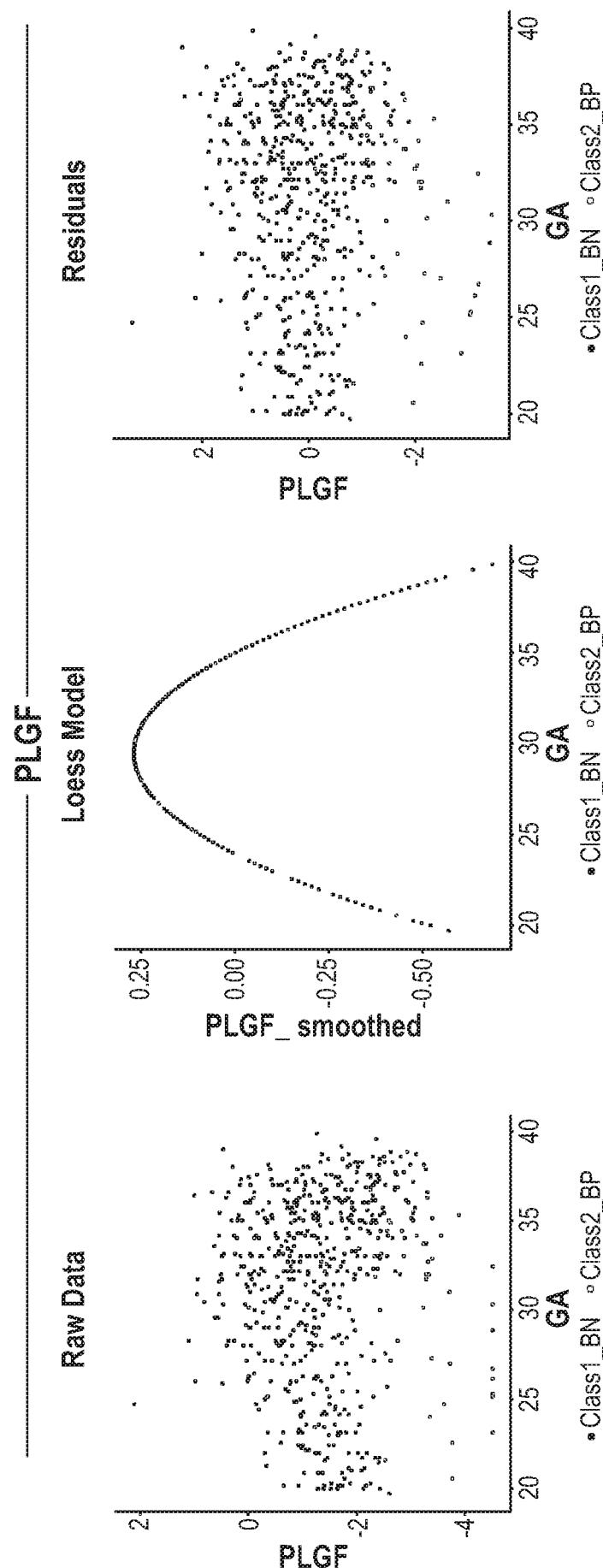


FIG. 14

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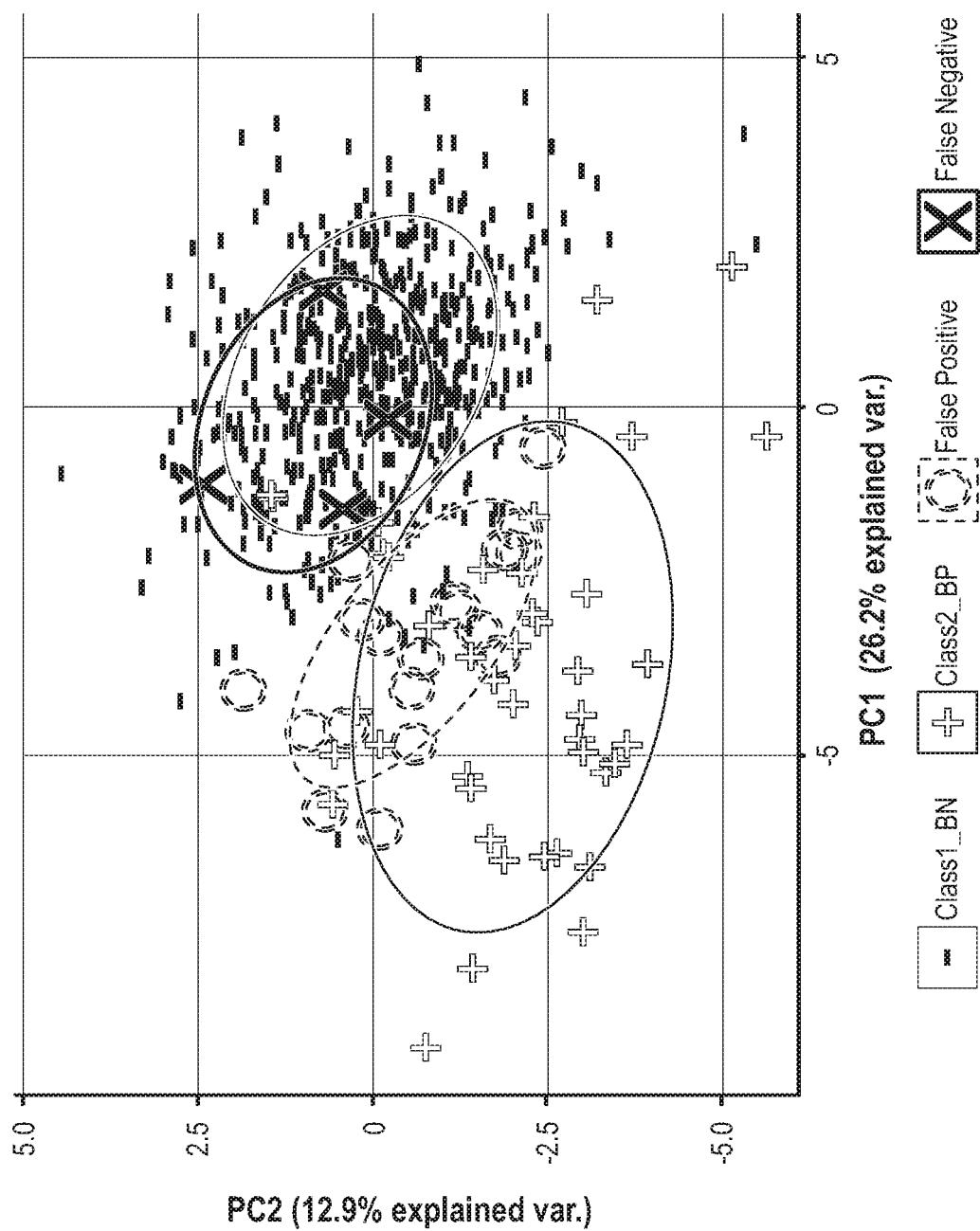


FIG. 15

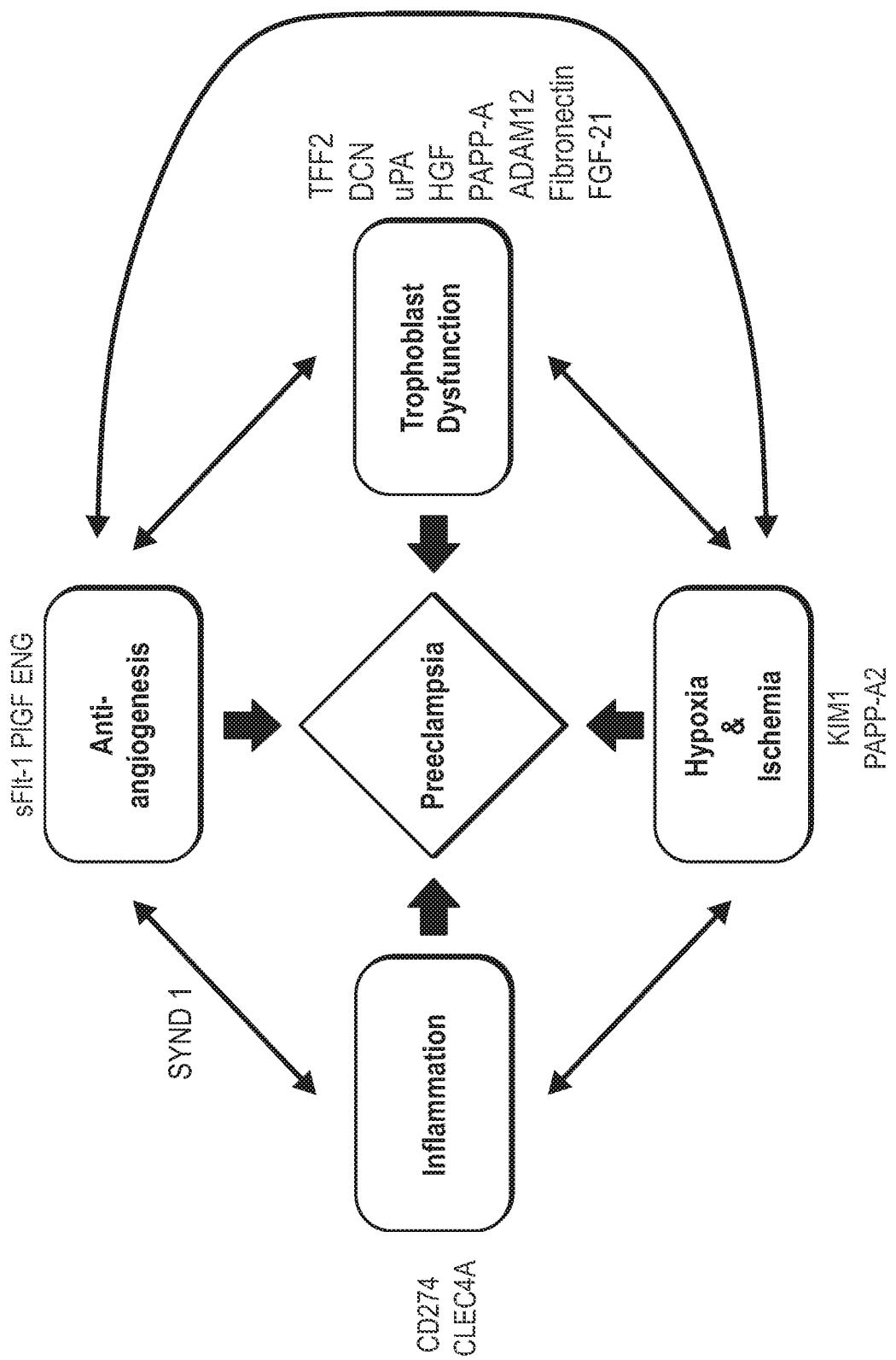


FIG. 16

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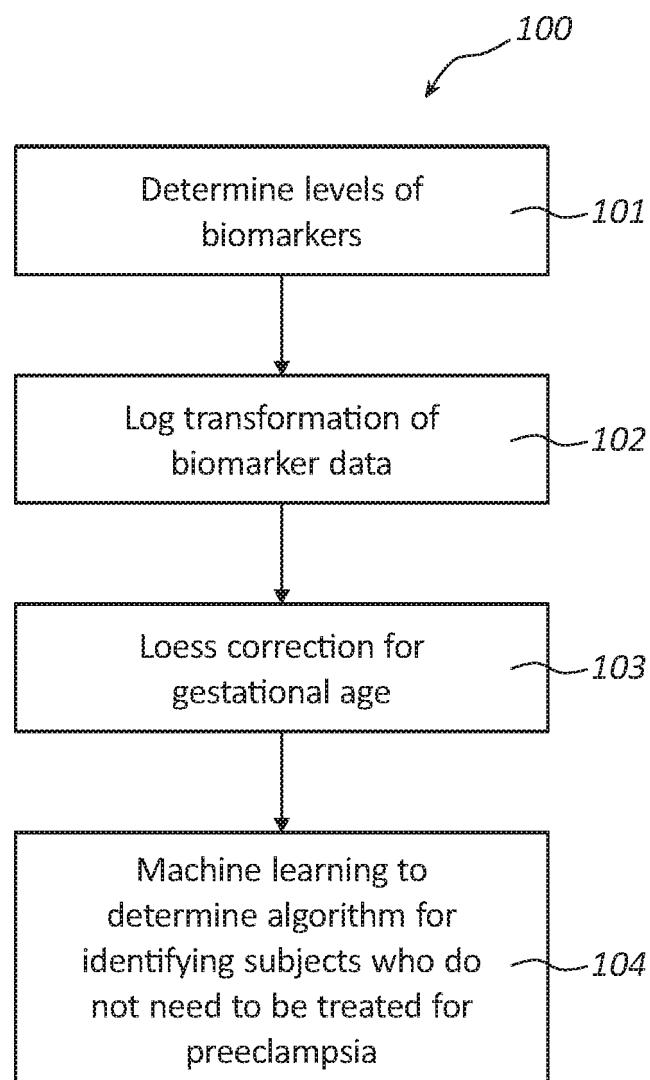


FIG. 17

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
CD274	CST	13684	PD-L1 (E1L3N®) XP® Rabbit mAb	Rabbit	Human	Mono	E1L3N
CD274	CST	29122	PD-L1 (405.9 A11) Mouse mAb	Mouse	Human	Mono	405.9A11
CD274	CST	15165	PD-L1 (Extracellular Domain Specific) (E1J2J™) Rabbit mAb	Rabbit	Human	Mono	E1J2J
CD274	CST	86744	PD-L1 (Extracellular Domain Specific) (D8T4X) Rabbit mAb	Rabbit	Human	Mono	D8T4X
CD274	Abcam	ab205921	Anti-PD-L1 antibody [28-8]	Rabbit	Human	Mono	28-8
CD274	Abcam	ab209889	Anti-PD-L1 antibody [28-8] - Low endotoxin, Azide free	Rabbit	Human	Mono	28-8

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
CD274	Abcam	ab228415	Anti-PD-L1 antibody [73-10]. Clone 73-10 is also known as clone MKP1A 07310. Clone 73-10 has been tested within Blueprint Phase 2 project	Rabbit	Human	Mono	73-10
CD274	Abcam	ab226766	Anti-PD-L1 antibody [73-10] - BSA and Azide free	Rabbit	Human	Mono	73-10
CD274	Abcam	ab213524	Anti-PD-L1 antibody [EPR19759]	Rabbit	Human	Mono	EPR19759
CD274	Abcam	ab221612	Anti-PD-L1 antibody	Rabbit	Human	Mono	EPR19759

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			[EPR19759] - BSA and Azide free				
CD274	Abcam	ab228462	Anti-PD-L1 antibody [SP142] - C-terminal	Rabbit	Human	Mono	SP142
CD274	Abcam	ab236238	Anti-PD-L1 antibody [SP142] - BSA and Azide free	Rabbit	Human	Mono	SP142
CD274	Abcam	ab210931	Anti-PD-L1 antibody [ABM4E54]	Mouse	Human	Mono	ABM4E54
CD274	Abcam	ab233482	Anti-PD-L1 antibody	Rabbit	Human, Mouse, Pig	Poly	NA
CD274	R&D Systems	AF156	Human PD-L1/B7-H1 Antibody	Goat	Human	Poly	NA
CD274	R&D Systems	MAB1561	Human PD-L1/B7-H1	Mouse	Human	Mono	130021

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			Antibody				
HGF	LSBio	LS-C400788	HGF / Hepato cyte Growth Factor Antibody	Rabbit	Human, Mouse, Rat	Poly	NA
HGF	LSBio	LS-C404040	HGF / Hepato cyte Growth Factor Antibody	Rabbit	Human, Mouse, Rat	Poly	NA
HGF	LSBio	LS-C742971	HGF / Hepato cyte Growth Factor Antibody	Rabbit	Human	Poly	NA
HGF	LSBio	LS-C486536	HGF / Hepato cyte Growth Factor Antibody	Rabbit	Human	Poly	NA
HGF	LSBio	LS-C486538	HGF / Hepato cyte Growth Factor Antibody	Rabbit	Human	Poly	NA
HGF	LSBio	LS-C486540	HGF / Hepato cyte Growth Factor Antibody	Rabbit	Human	Poly	NA

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			y				
TFF2	R&D Systems	MAB4077	Human TFF2 Antibody y Works in direct ELISA	Mouse	Human	Mono	366508
TFF2	Novus	NBP2-50334	TFF2 Antibody (HSP GE16C)	Mouse	Human	Mono	HSP GE16C
TFF2	Novus	H00007032	TFF2 Antibody y (2A10) ELISA	Mouse	Human	Mono	2A10
TFF2	ThermoFisher		Only polyAbs				
TFF2	LSBio	LS-C669220	TFF2 / SP Antibody y (clone 4G7C3) ELISA	Mouse	Human	Mono	4G7C3
TFF2	OriGene	TA353503L	Spasmolytic Polypeptide(TFF2) Mouse Monoclonal Antibody [Clone ID: HSP	Mouse	Human	Mono	HSP GE16C

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			GE16C 1				
Decorin (DCN)	Abcam	ab18145 6	Anti-Decorin antibody [5E8E7 1]	Mouse	Human (Hu)	Monoclonal	5E8E7
Decorin (DCN)	Abcam	ab17540 4	Anti-Decorin antibody	Rabbit	Hu, Ms, Rat	Polyclonal	na
Decorin (DCN)	Abcam	ab31614	Anti-Decorin antibody	Sheep	Chk, Cow, Hu	Polyclonal	na
Decorin (DCN)	Abcam	ab15198 8	Anti-Decorin antibody	Rabbit	Hu	Polyclonal	na
Decorin (DCN)	Abcam	ab35378	Anti-Decorin antibody	Sheep	Chk, Cow, Hu	Polyclonal	na
Decorin (DCN)	Abcam	ab18936 4	Anti-Decorin antibody	Goat	Hu	Polyclonal	na
Decorin (DCN)	Abcam	ab18907 1	Anti-Decorin antibody - N-terminal	Sheep	Hu	Polyclonal	na
Decorin (DCN)	Abcam	ab13750 8	Decorin antibody	Rabbit	Mouse, Human	Polyclonal	na
Decorin (DCN)	Abcam	ab90425	Decorin antibody	Goat	Human	Polyclonal	na
Decorin (DCN)	antibodies-online	ABIN199 5977	anti-DCN (Decorin)	Rabbit	Human (Hu)	Monoclonal	4

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			n) antibod y				
Decorin (DCN)	antibodies- online	ABIN197 8290	anti- DCN (Decorin) antibod y	Mouse	Human (Hu)	Monoclon al	1G4C5
Decorin (DCN)	antibodies- online	ABIN225 2143	anti- DCN (Decorin) antibod y	Mouse	Human (Hu)	Monoclon al	9j121
Decorin (DCN)	Biorbyt	orb89581	Decorin antibod y	Mouse	Human (Hu)	Monoclon al	?
Decorin (DCN)	Biorbyt	orb15349 3	DCN antibod y	Mouse	Human (Hu)	Monoclon al	1G4C5
Decorin (DCN)	Creative Diagnostics	DMABT- H13567	Anti- DCN monocl onal antibod y, clone 4I5- 2G5	Mouse	Human (Hu)	monoclon al	4I5-2G5
Decorin (DCN)	Creative Diagnostics	DCABY- 4107	Anti- DCN monocl onal antibod y, clone 226535	Mouse	Human (Hu)	monoclon al	226535
Decorin (DCN)	GeneTex	GTX5269 5	Anti- Decorin antibod y [6Z1]	Mouse	Human (Hu)	Monoclon al	6Z1
Decorin (DCN)	Invitrogen Antibodies	PA1- 1744	Decorin Polycl onal	Rabbit	Bovine, Human, Mouse	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			Antibody				
Decorin (DCN)	Invitrogen Antibodies	PA5-19151	Decorin Polyclonal Antibody	Goat	Human	Polyclonal	na
Decorin (DCN)	Invitrogen Antibodies	PA5-27370	Decorin Polyclonal Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	Invitrogen Antibodies	PA5-13538	Decorin Polyclonal Antibody	Rabbit	Human, Mouse	Polyclonal	na
Decorin (DCN)	Invitrogen Antibodies	PA1-85833	Decorin Polyclonal Antibody	Sheep	Bovine, Chicken, Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioScience s	LS-C285837-100	Anti-DCN / Decorin Antibody (aa263-324, clone 1G4C5 )	Mouse	Human (Hu)	Monoclonal	1G4C5
Decorin (DCN)	LifeSpan BioScience s	LS-C36148-500	Anti-DCN / Decorin Antibody	Mouse	Human (Hu)	Monoclonal	?
Decorin (DCN)	..	LS-B4312-50	Anti-DCN / Decorin Antibody (clone	Mouse	Human (Hu)	Monoclonal	3H4-1F4

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
	LifeSpan BioScience s		3H4-1F4) IHC-plus™				
Decorin (DCN)	LifeSpan BioScience s	LS-C46802-100	Anti-DCN / Decorin Antibody (C-Terminus)	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioScience s	LS-B33-50	Anti-DCN / Decorin Antibody IHC-plus™	Sheep	Chicken, Bovine, Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioScience s	LS-C81179-50	Anti-DCN / Decorin Antibody (C-Terminus)	Rabbit	Zebrafish, Pig, Horse, Bat, Mouse, Goat, Dog, Guinea pig, Hamster, Human, Monkey	Polyclonal	na
Decorin (DCN)	LifeSpan BioScience s	LS-B8177-50	Anti-DCN / Decorin Antibody IHC-plus™	Rabbit	Rabbit, Mouse, Rat, Pig, Human	Polyclonal	na

FIG. 18 (Cont'd)

<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
Decorin (DCN)	LifeSpan BioScience s	LS-C99324-400	Anti-DCN / Decorin Antibody (aa122-150)	Rabbit	Mouse, Human	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS690954	Mouse Anti-Human Decorin	Mouse	Human (Hu)	Monoclonal	(#6Z1)
Decorin (DCN)	MyBioSource.com	MBS2543875	Rabbit Anti-Decorin Antibody	Rabbit	Human (Hu)	Monoclonal	?
Decorin (DCN)	Novus Biologicals	NBP2-37336	Decorin Antibody (1G4C5)	Mouse	Human (Hu)	Monoclonal	1G4C5
Decorin (DCN)	Novus Biologicals	NBP2-37333	Decorin Antibody (5E8E7)	Mouse	Human (Hu)	Monoclonal	5E8E7
Decorin (DCN)	Origene Technologies	AM20879 PU-N	anti Decorin (full length)	Mouse	Human (Hu)	Monoclonal	3H4-1F4
Decorin (DCN)	ProSci, Inc	51-449	Decorin Antibody [3H4-1F4]	Mouse	Human (Hu)	Monoclonal	[3H4-1F4]
Decorin (DCN)	R&D Systems	MAB1432	Decorin Antibody	Mouse	Human (Hu)	Monoclonal	115424
Decorin (DCN)	R&D Systems	MAB143	Decorin Antibody	Mouse	Human (Hu)	Monoclonal	115402
Decorin (DCN)	R&D Systems	AF143	Decorin Antibody	Goat	Human	Polyclonal	na

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
Decorin (DCN)	Santa Cruz Biotechnology, Inc.	sc-517271	Decorin (1G4C 5) Antibody	mouse	Human (Hu)	monoclonal	1G4C5
Decorin (DCN)	Santa Cruz Biotechnology, Inc.	sc-73896	Decorin (9XX)	mouse	Human (Hu)	monoclonal	9XX
Decorin (DCN)	Sino Biological, Inc.	10189-R004	Decorin / DCN / SLRR1 B Antibody, Rabbit MAb	Rabbit	Human (Hu)	Monoclonal	4
Decorin (DCN)	United States Biological	D1875-06-500ug	Mouse Anti-Decorin Antibody	mouse	Human (Hu)	Monoclonal	9j121
Decorin (DCN)	United States Biological	D1875-06D-50ug	Mouse Anti-Decorin Antibody	mouse	Human (Hu)	Monoclonal	3H4-1F4
Decorin (DCN)	United States Biological	216445-100ug	Mab Mo x human DCN (Decorin) Antibody	mouse	Human (Hu)	Monoclonal	14L349
Decorin (DCN)	ABclonal	A1669	DCN Antibody	Rabbit	Human, Mouse, Rat	Polyclonal	na
Decorin (DCN)	Abnova Corporation	PAB18704	DCN polyclonal antibody	Goat	Human	Polyclonal	na
Decorin	Abnova	H000016	DCN	Mouse	Human,	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
(DCN)	Corporation	34-B01	MaxPa b mouse polyclonal antibody (B01)		Human, Rat		
Decorin (DCN)	Abnova Corporation	PAB9509	DCN polyclonal antibody	Rabbit	Human, Mouse, Pig, Rabbit, Rat, Human	Polyclonal	na
Decorin (DCN)	Abnova Corporation	PAB9510	DCN polyclonal antibody	Rabbit	Human, Mouse, Pig, Rabbit, Rat, Human	Polyclonal	na
Decorin (DCN)	Abnova Corporation	H000016 34-A01	DCN polyclonal antibody (A01)	Mouse	Human	Polyclonal	na
Decorin (DCN)	Abnova Corporation	H000016 34-B01P	DCN purified MaxPa b mouse polyclonal antibody (B01P)	Mouse	Human, Human, Rat	Polyclonal	na
Decorin (DCN)	Abnova Corporation	H000016 34-D01P	DCN purified MaxPa b rabbit polyclonal antibody (D01P)	Rabbit	Human	Polyclonal	na
Decorin (DCN)	Abnova Corporation	PAB3085 1	DCN polyclonal	Rabbit	Human	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			nal antibody				
Decorin (DCN)	Biorbyt	orb18168	Decorin antibody	Rabbit	Human, Rat	Polyclonal	na
Decorin (DCN)	Biorbyt	orb241575	Decorin antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	Biorbyt	orb86456	Decorin antibody	Sheep	Human	Polyclonal	na
Decorin (DCN)	Biorbyt	orb10520	Decorin antibody	Rabbit	Human, Mouse, Rat, Guinea Pig	Polyclonal	na
Decorin (DCN)	Biorbyt	orb36745	Decorin antibody	Rabbit	Human, Mouse	Polyclonal	na
Decorin (DCN)	Biorbyt	orb96420	Decorin antibody	Goat	Human, Monkey	Polyclonal	na
Decorin (DCN)	Biorbyt	orb386318	DCN antibody	Rabbit	Human, Mouse	Polyclonal	na
Decorin (DCN)	Biorbyt	orb386292	DCN antibody	Rabbit	Human, Mouse	Polyclonal	na
Decorin (DCN)	Biorbyt	orb386294	DCN antibody	Rabbit	Human, Mouse	Polyclonal	na
Decorin (DCN)	Biorbyt	orb192289	DCN antibody	Rabbit	Human, Mouse, Rat	Polyclonal	na
Decorin (DCN)	Biorbyt	orb215928	DCN antibody	Rabbit	Human, Rat	Polyclonal	na
Decorin (DCN)	Biorbyt	orb221233	DCN antibody	Rabbit	Human, Rat	Polyclonal	na
Decorin (DCN)	Biorbyt	orb375309	DCN antibody	Rabbit	Human, Mouse,	Polyclonal	na

FIG. 18 (Cont'd)

<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			y		Rat, Pig		
Decorin (DCN)	Biorbyt	orb375243	DCN antibody	Rabbit	Human, Mouse, Rat, Pig	Polyclonal	na
Decorin (DCN)	Biorbyt	orb48349	DCN antibody	Rabbit	Human, Mouse, Rat	Polyclonal	na
Decorin (DCN)	Biorbyt	orb20265	DCN antibody	Goat	Human	Polyclonal	na
Decorin (DCN)	Biorbyt	orb228678	DCN antibody	Rabbit	Human, Mouse, Rat	Polyclonal	na
Decorin (DCN)	Biorbyt	orb378026	DCN antibody	Rabbit	Human, Mouse, Rat	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-B8312-50	Anti-DCN / Decorin Antibody (aa232-246) IHC-plus™	Goat	Human, Monkey	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-B8745-50	Anti-DCN / Decorin Antibody IHC-plus™	Rabbit	Rabbit, Mouse, Rat, Pig, Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C192752-100	Anti-DCN / Decorin Antibody	Rabbit	Mouse, Rat, Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C307208-50	Anti-DCN / Decorin Antibody	Mouse	Rat, Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioScience	LS-C310119	Anti-DCN /	Rabbit	Human	Polyclonal	na

<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
	s	-100	Decorin Antibody				
Decorin (DCN)	LifeSpan BioSciences	LS-C331624-50	Anti-DCN / Decorin Antibody	Rabbit	Mouse, Rat, Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C403953-120	Anti-DCN / Decorin Antibody	Rabbit	Hu, Ms, Rt	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C331624-200	Anti-DCN / Decorin Antibody	Rabbit	Hu, Ms, Rt	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C331624-100	Anti-DCN / Decorin Antibody	Rabbit	Hu, Ms, Rt	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C393203-100	Anti-DCN / Decorin Antibody	Rabbit	Hu, Ms, Rt	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C403953-60	Anti-DCN / Decorin Antibody	Rabbit	Hu, Ms, Rt	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C403953-200	Anti-DCN / Decorin Antibody	Rabbit	Hu, Ms, Rt	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C128548-100	Anti-DCN / Decorin Antibody (C-)	Rabbit	Hu, Ms, Rt	Polyclonal	na

<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			Terminus)				
Decorin (DCN)	LifeSpan BioSciences	LS-C171988-100	Anti-DCN / Decorin Antibody (C-Terminus)	Rabbit	Hu, Ms, Rt	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C403953-20	Anti-DCN / Decorin Antibody	Rabbit	Hu, Ms, Rt	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-B14959-50	Anti-DCN / Decorin Antibody (aa 20-359) IHC-plus™	Rabbit	Human (Hu)	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C344032-100	Anti-DCN / Decorin Antibody (aa31-359)	Rabbit	Rat, Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C293647-100	Anti-DCN / Decorin Antibody (aa31-359)	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C293652-100	Anti-DCN / Decorin Antibody (aa45-152)	Rabbit	Human	Polyclonal	na

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
Decorin (DCN)	LifeSpan BioSciences	LS-C485845-100	Anti-DCN / Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C485844-400	Anti-DCN / Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C485843-100	Anti-DCN / Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C485843-200	Anti-DCN / Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C485843-50	Anti-DCN / Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C485845-50	Anti-DCN / Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C660230-100	Anti-DCN / Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-B6704-50	Anti-DCN / Decorin Antibody (aa36-85) IHC-	Rabbit	Rabbit, Dog, Guinea pig, Hamster, Pig, Horse, Human,	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			plus™		Monkey		
Decorin (DCN)	LifeSpan BioSciences	LS-C22770-1000	Anti-DCN / Decorin Antibody (aa316-329)	Sheep	Mouse, Dog, Guinea pig, Hamster, Pig, Horse, Bat, Human, Monkey	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C388351-100	Anti-DCN / Decorin Antibody (aa343-359)	Rabbit	Mouse, Dog, Guinea pig, Rat, Hamster, Pig, Horse, Bat, Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C293647-200	Anti-DCN / Decorin Antibody (aa31-359)	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C293652-20	Anti-DCN / Decorin Antibody (aa45-152)	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C293647-20	Anti-DCN / Decorin Antibody (aa31-359)	Rabbit	Human	Polyclonal	na
Decorin (DCN)	LifeSpan BioSciences	LS-C293652	Anti-DCN /	Rabbit	Human	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
	s	-200	Decorin Antibody (aa45-152)				
Decorin (DCN)	MyBioSource.com	MBS175 601	Anti-Decorin antibody	Rabbit	Human, Mouse, Rat	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS177 488	Anti-Decorin Antibody	Rabbit	Human, Rat	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS840 859	Decorin Antibody	Rabbit	Human, Mouse, Rat, Rabbit, Pig	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS840 644	Decorin Antibody	Rabbit	Human, Mouse, Rat, Rabbit, Pig	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS421 985	Goat anti-Decorin Antibody	Goat	Human, Cow, Pig, Cavia	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS716 239	Rabbit anti-human decorin polyclonal Antibody	Rabbit	Human, Mouse, Rat	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS149 0929	Rabbit anti-human Decorin polyclonal Antibody	Rabbit	Human	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			y				
Decorin (DCN)	MyBioSource.com	MBS221 111	SHEEP ANTI HUMAN DECORIN (aa36-49)	Sheep	Bovine, Chicken	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS622 492	Sheep Anti-Decorin Antibody	Sheep	Bovine, Chicken, Human	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS768 553	Decorin Rabbit Polyclonal	Rabbit	Human, Mouse, Rat	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS244 947	Goat Polyclonal to Human DCN / Decorin	Goat	Gibbon, Chimpanzee, Gorilla, Human, Monkey	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS200 4983	Polyclonal Antibody to Decorin (DCN)	Rabbit	Human	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS200 7005	Polyclonal Antibody to Decorin (DCN)	Rabbit	Human	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS418 093	Anti-DCN (decorin isoform d) Antibody	Rabbit	Human	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			y				
Decorin (DCN)	MyBioSource.com	MBS127 148	DCN Polyclonal Antibody	Rabbit	Human, Mouse, Rat	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS251 6635	DCN Polyclonal Antibody	Rabbit	Human, Mouse, Rat	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS625 596	Rabbit Anti-DCN Antibody	Rabbit	Human, Mouse	Polyclonal	na
Decorin (DCN)	MyBioSource.com	MBS920 9128	DCN Antibody (Center)	Rabbit	Human, mouse (Predicted Reactivity: Bovine, Pig)	Polyclonal	na
Decorin (DCN)	Novus Biologicals	NBP1-84970	Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	Novus Biologicals	NB100-74403	Decorin Neo Antibody	Rabbit	Human, Mouse, Bovine	Polyclonal	na
Decorin (DCN)	Novus Biologicals	NBP1-51962	Decorin Antibody	Goat	Human	Polyclonal	na
Decorin (DCN)	Novus Biologicals	NBP1-32270	Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	Novus Biologicals	NBP1-57923	Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	Novus Biologicals	NBP1-57944	Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin	Novus	NBP1-	Decorin	Sheep	Human	Polyclonal	na

FIG. 18 (Cont'd)

<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
(DCN)	Biologicals	02605	Antibody				
Decorin (DCN)	Novus Biologicals	2354000 2-0.1mg	Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	Novus Biologicals	NBP2-56346	Decorin Antibody	Rabbit	Human	Polyclonal	na
Decorin (DCN)	Novus Biologicals	NB100-65669	Proteoglycan 2 Precursors or Antibody	Sheep	Human	Polyclonal	na
Decorin (DCN)	United States Biological	D1875-06C-100ug	Goat Anti-Decorin Antibody	goat	Hu	Polyclonal	na
Decorin (DCN)	United States Biological	313262-100ug	Pab Rb x human Decorin Antibody	rabbit	Hu, Mo	Polyclonal	na
Decorin (DCN)	United States Biological	350594-100ug	Pab Rb x human Decorin (DCN) Antibody	rabbit	Hu, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	313264-150ul	Pab Rb x human Decorin Antibody	rabbit	Hu, Mo, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	313262-50ug	Pab Rb x human Decorin	rabbit	Hu, Mo	Polyclonal	na

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			Antibody				
Decorin (DCN)	United States Biological	313264-50ul	Pab Rb x human Decorin Antibody	rabbit	Hu, Mo, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	144446-100ug	Rabbit Anti-Decorin Antibody	rabbit	Hu, Mo, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	215275-100ug	Rabbit Anti-Decorin Antibody	rabbit	Hu, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	210444-100ul	Rabbit Anti-Decorin Antibody	rabbit	Hu, Mo, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	125752-50ug	Mouse Anti-Decorin Antibody	mouse	Hu, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	D1875-06F-100ug	Rabbit Anti-Decorin Antibody	rabbit	Hu, Mo, Po, Rb, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	D1875-06E-100ug	Rabbit Anti-Decorin Antibody	rabbit	Hu, Mo, Po, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	125753-100ug	Rabbit Anti-Decorin Antibody	rabbit	Hu	Polyclonal	na

FIG. 18 (Cont'd)

<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
Decorin (DCN)	United States Biological	140029-50ug	Rabbit Anti-Decorin Antibody	rabbit	Hu	Polyclonal	na
Decorin (DCN)	United States Biological	140030-50ug	Rabbit Anti-Decorin Antibody	rabbit	Hu	Polyclonal	na
Decorin (DCN)	United States Biological	140029-100ug	Rabbit Anti-Decorin Antibody	rabbit	Hu	Polyclonal	na
Decorin (DCN)	United States Biological	D1875-05C-50ug	Sheep Anti-Decorin Antibody	sheep	Hu	Polyclonal	na
Decorin (DCN)	United States Biological	D1875-05B-100ug	Rabbit Anti-Decorin Antibody	rabbit	Hu, Mo, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	140030-100ug	Rabbit Anti-Decorin Antibody	rabbit	Hu	Polyclonal	na
Decorin (DCN)	United States Biological	D1875-500ul	Sheep Anti-Decorin Antibody	sheep	Bo, Ch, Hu	Polyclonal	na
Decorin (DCN)	United States Biological	D1875-100ul	Sheep Anti-Decorin Antibody	sheep	Bo, Ch, Hu	Polyclonal	na
Decorin (DCN)	United States Biological	D1875-05-1ml	Sheep Anti-Decorin	sheep	Bo, Ch, Hu	Polyclonal	na

<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			, CT, aa316-329 Antibody				
Decorin (DCN)	United States Biological	D1875-1ml	Sheep Anti-Decorin Antibody	sheep	Bo, Ch, Hu	Polyclonal	na
Decorin (DCN)	United States Biological	245215-50ul	Mouse Anti-DCN Antibody	mouse	Hu	Polyclonal	na
Decorin (DCN)	United States Biological	222107-100ul	Rabbit Anti-DCN Antibody	rabbit	Hu, Mo, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	222107-50ul	Rabbit Anti-DCN Antibody	rabbit	Hu, Mo, Rt	Polyclonal	na
Decorin (DCN)	United States Biological	313103-100ul	Pab Rb x human DCN Antibody	rabbit	Hu, Mo, Rt	Polyclonal	na
KIM1	R&D Systems	MAB1750	Human TIM-1/KIM-1/HAV CR Antibody	Mouse	Human	Mono	219211
KIM1	R&D Systems	MAB17502	Human TIM-1/KIM-1/HAV CR	Mouse	Human	Mono	526114R

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			Antibody				
KIM1	Novus	NBP2-11925	TIM-1/KIM-1/HAV CR Antibody (MM0570-6D21)	Mouse	Human	Mono	MM0570-6D21
KIM1	Novus	H000267-62	TIM-1/KIM-1/HAV CR Antibody ELISA	Mouse	Human	Mono	2G11
KIM1	Novus	H000267-62-M02	TIM-1/KIM-1/HAV CR Antibody ELISA	Mouse	Human	Mono	2B9
KIM1	Novus	H000267-62-M04	TIM-1/KIM-1/HAV CR Antibody ELISA	Mouse	Human	Mono	1G1
KIM1	Novus	NBP2-32775	TIM-1/KIM-1/HAV CR Antibody ELISA	Mouse	Human	Mono	KIM70
KIM1	Novus	NBP2-32776	TIM-1/KIM-1/HAV CR	Mouse	Human	Mono	KIM75

FIG. 18 (Cont'd)

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Antigen	Company	Cat. No.	Name	Species	Reacts with	Mono- or Polyclonal	Clone #
			Antibody ELISA				
KIM1	CST	14971	TIM-1 (E1R9 N) Rabbit mAb #14971	Rabbit	Human	Mono	E1R9N
KIM1	Enzo	ADI-905-905-0100	KIM-1 (human) monoclonal antibody (3E3) ELISA	Mouse	Human	Mono	3E3
KIM1	Creative Diagnostics	DCAB-TJ219	Magic™ Anti-KIM-1 monoclonal antibody, clone C2695 N (DCAB-TJ219)	Mouse	Human	Mono	C2695N
KIM1	Creative Diagnostics	DCAB-TJ218	Magic™ Anti-KIM-1 monoclonal antibody, clone C2694 N (DCAB-TJ218)	Mouse	Human	Mono	C2694N
KIM1	Abcam	ab233714	Anti-TIM 1 antibody	Mouse	Human	Mono	[3A12E10]

FIG. 18 (Cont'd)

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Antigen	Company	Cat. No.	Name	Species	Reacts with	Mono- or Polyclonal	Clone #
			[3A12E 10] (ab233 714)				
KIM1	Abcam	ab23372 0	Anti-TIM 1 antibody [3D9F5 1] (ab233 720)	Mouse	Human	Mono	[3D9F5]
ADAM12	Abcam	ab39155	Anti-ADAM1 2 antibody - Amino terminal end	Rabbit	Hu, Ms, Rt, Pg	Polyclonal	na
ADAM12	Abcam	ab28747	Anti-ADAM1 2 antibody	Goat	Human (Hu)	Polyclonal	na
ADAM12	Abcam	ab11520 3	Anti-ADAM1 2 antibody	Goat	Human (Hu)	Polyclonal	na
ADAM12	Abcam	ab22347 6	Anti-ADAM1 2	Goat	Mouse, Rat, Human, Pig	Polyclonal	na
ADAM12	Abcam	ab22374 5	Anti-ADAM1 2	rabbit	human	Polyclonal	na
ADAM12	Abcam	ab23418 9	Anti-ADAM1 2	mouse	human	Monoclonal	24F.10C 12
ADAM12	Invitrogen Antibodies	MA5-24285	ADAM1 2 Monocl	Mouse	Human (Hu)	Monoclonal	632525

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			onal Antibod y (63252 5)				
ADAM12	Invitrogen Antibodies	PA5-46950	ADAM1 2 Polyclonal Antibod y	Sheep	Human (Hu)	Polyclonal	na
ADAM12	Invitrogen Antibodies	PA1-20301	ADAM1 2 Polyclonal Antibod y	Rabbit	Human (Hu)	Polyclonal	na
ADAM12	Invitrogen Antibodies	PA5-18314	ADAM1 2 Polyclonal Antibod y	Goat	Human (Hu)	Polyclonal	na
ADAM12	Invitrogen Antibodies	PA5-50594	ADAM1 2 Polyclonal Antibod y	Rabbit	Hu, Ms	Polyclonal	na
ADAM12	Invitrogen Antibodies	PA5-75796	ADAM1 2 Polyclonal Antibod y	Rabbit	Hu, Ms, Rt	Polyclonal	na
ADAM12	MilliporeSigma	SAB2100046	Anti-ADAM1 2	rabbit	horse, rabbit, bovine, guinea pig, mouse, human, rat	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
ADAM12	MilliporeSigma	HPA030867	Anti-ADAM12	rabbit	human	Polyclonal	na
ADAM12	MilliporeSigma	HPA030866	Anti-ADAM12	rabbit	human	Polyclonal	na
ADAM12	MilliporeSigma	HPA030868	Anti-ADAM12	rabbit	human	Polyclonal	na
ADAM12	MilliporeSigma	MABT1330	ADAM12 Antibody	Mouse	Human	mono	8F8
ADAM12	MilliporeSigma	MABT1331	ADAM12 Antibody	Mouse	Human	mono	6E6
ADAM12	Novus	NB300-889	ADAM12 Antibody	Goat	Human (Hu)	Polyclonal	na
ADAM12	Novus	NBP1-82791	ADAM12 Antibody	Rabbit	Human (Hu)	Polyclonal	na
ADAM12	Novus	NBP2-	ADAM1	Rabbit	Human	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
		33939	2 Antibody		(Hu)		
ADAM12	Novus	NBP2-33940	ADAM12 Antibody	Rabbit	Human (Hu)	Polyclonal	na
ADAM12	Novus	MAB44161	ADAM12 Antibody	Mouse	Human (Hu)	mono	632525
ADAM12	Novus	AF4416	ADAM12 Antibody	Sheep	Human (Hu)	Polyclonal	na
ADAM12	Novus	NBP1-59142	ADAM12 Antibody	Rabbit	Human (Hu)	Polyclonal	na
ADAM12	Novus	H00008038-D01P	ADAM12 Antibody	Rabbit	Human (Hu)	Polyclonal	na
ADAM12	Novus	H00008038-M01	ADAM12 Antibody	Mouse	Human (Hu)	mono	IG3
ADAM12	R&D Systems	MAB44161	ADAM12 Antibody	Mouse	Human (Hu)	Monoclonal	632525
ADAM12	R&D Systems	AF4416	ADAM12 Antibody	Sheep	Human (Hu)	Polyclonal	na
ADAM12	Raybiotech, Inc.	119-13202	Goat Anti-Human ADAM12 (N-Terminus)	Goat	Human (Hu)	Polyclonal	na
ADAM12	Sino	10896-	ADAM1	Rabbit	Human	Monoclonal	737

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
	Biological, Inc.	R737	2 Antibody, Rabbit MAb		(Hu)	al	
ADAM12	Sino Biological, Inc.	10896-MM10	ADAM12 / MLTN Antibody, Mouse MAb	Mouse	Human (Hu)	Monoclonal	3G1B10 B9
ADAM12	Sino Biological, Inc.	10896-RP02	ADAM12 / MLTN Antibody, Rabbit PAb, Antigen Affinity Purified	Rabbit	Human (Hu)	Polyclonal	na
ADAM12	Sino Biological, Inc.	10896-R001	ADAM12 / MLTN Antibody, Rabbit MAb	Rabbit	Human (Hu)	Monoclonal	1
ADAM12	Sino Biological, Inc.	10896-RP01	ADAM12 / MLTN Antibody, Rabbit PAb	Rabbit	Human (Hu)	Polyclonal	na
ENDOGLIN (ENG)	CST	14606	Endoglin (3A9) Mouse mAb	Mouse	Human	Mono	3A9
ENDOGLIN (ENG)	CST	4335	Endoglin (3A9) Mouse	Rabbit	Human	Mono	D50G1

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			mAb				
ENDOGLIN (ENG)	R&D Systems	MAB1097	Human Endoglin/CD105 Antibody	Mouse	Human	Mono	166709
ENDOGLIN (ENG)	R&D Systems	MAB10971	Human Endoglin/CD105 Antibody	Mouse	Human	Mono	166707
ENDOGLIN (ENG)	R&D Systems	MAB10972	Human Endoglin/CD105 Antibody	Mouse	Human	Mono	166713
ENDOGLIN (ENG)	R&D Systems	AF1097	Human Endoglin/CD105 Antibody	Goat	Human	Poly	NA
ENDOGLIN (ENG)	Novus	NBP2-34493	Endoglin/CD105 Antibody (CL1912)	Mouse	Human	Mono	CL1912
ENDOGLIN (ENG)	Novus	NBP1-91212	Endoglin/CD105 Antibody	Rabbit	Human	Poly	NA
ENDOGLIN (ENG)	Novus	NBP2-49516	Endoglin/CD105 Antibody	Rabbit	Human	Poly	NA
ENDOGL	Novus	NBP2-	Endogli	Mouse	Human	Mono	ENG/132

FIG. 18 (Cont'd)

<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
IN (ENG)		53327	n/CD105 Antibody (ENG/1326)				6
ENDOGLIN (ENG)	Novus	NBP1-35471	Endoglin/CD105 Antibody	Rabbit	Human	Poly	NA
ENDOGLIN (ENG)	22 Abcam (13mono; 9 poly)						
ENDOGLIN (ENG)	Abcam	ab11414	Anti-CD105 antibody [SN6]	Mouse	Human, Rat	Mono	SN6
ENDOGLIN (ENG)	Abcam	ab169545	Anti-CD105 antibody [EPR10145-12]	Rabbit	Human	Mono	EPR10145-12
ENDOGLIN (ENG)	Abcam	ab156756	Anti-CD105 antibody [OTI8A1]	Mouse	Mouse, Rat, Dog, Human, Monkey	Mono	OTI8A1
ENDOGLIN (ENG)	Abcam	ab107595	Anti-CD105 antibody	Rabbit	Human, Mouse, Rat*	Poly	NA
ENDOGLIN (ENG)	Abcam	ab2529	Anti-CD105 antibody [MEM-226]	Mouse	Human, Rat	Mono	MEM-226
ENDOGLIN (ENG)	Abcam	ab114052	Anti-CD105 antibody	Mouse	Human	Mono	3A9

<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			y [3A9]				
ENDOGLIN (ENG)	Abcam	ab49228	Anti-CD105 antibody	Rabbit	Human, Mouse*	Poly	NA
ENDOGLIN (ENG)	Abcam	ab44967	Anti-CD105 antibody [105C02]	Mouse	Human	Mono	105C02
ENDOGLIN (ENG)	Abcam	ab135528	Anti-CD105 antibody	Rabbit	Human, Mouse	Poly	NA
ENDOGLIN (ENG)	Abcam	ab27422	Anti-CD105 antibody, prediluted	Rabbit	Human	Poly	NA
ENDOGLIN (ENG)	Abcam	ab69772	Anti-CD105 antibody [MEM-229]	Mouse	Human, Pig	Mono	MEM-229
ENDOGLIN (ENG)	Abcam	ab170943	Anti-CD105 antibody [EPR10145-10]	Rabbit	Human	Mono	EPR10145-10
ENDOGLIN (ENG)	Abcam	ab21224	Anti-CD105 antibody	Rabbit	Human	Poly	NA
ENDOGLIN (ENG)	Abcam	ab206419	Anti-CD105 antibody [EPR19911]	Rabbit	Human	Mono	EPR19911

Antigen	Company	Cat. No.	Name	Species	Reacts with	Mono- or Polyclonal	Clone #
ENDOGLIN (ENG)	Abcam	ab137389	Anti-CD105 antibody	Rabbit	Human	Poly	NA
ENDOGLIN (ENG)	Abcam	ab219362	Anti-CD105 antibody [EPR10145-12] - Low endotoxin, Azide free	Rabbit	Human	Mono	EPR10145-10
ENDOGLIN (ENG)	Abcam	ab85956	Anti-CD105 antibody	Rabbit	Human, Orangutan*	Poly	NA
ENDOGLIN (ENG)	Abcam	ab124610	Anti-CD105 antibody	Rabbit	Human; Chimpanzee*, Macaque monkey*, Gorilla*	Poly	NA
ENDOGLIN (ENG)	Abcam	ab74462	Anti-CD105 antibody	Rabbit	Human	Poly	NA
ENDOGLIN (ENG)	Abcam	ab218387	Anti-CD105 antibody [ENG/1327]	Mouse	Human	Mono	ENG/1327
ENDOGLIN (ENG)	Abcam	ab218855	Anti-CD105 antibody [ENG/1327] - BSA and	Mouse	Human	Mono	ENG/1327

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Antigen	Company	Cat. No.	Name	Species	Reacts with	Mono- or Polyclonal	Clone #
			Azide free				
ENDOGLIN (ENG)	Abcam	ab171225	Anti-CD105 antibody [SN6] - Low endotoxin, Azide free	Mouse	Human, Rat	Mono	SN6
ENDOGLIN (ENG)	ThermoFisher					Mono	SN6
ENDOGLIN (ENG)	ThermoFisher					Mono	SN6h
ENDOGLIN (ENG)	ThermoFisher					Mono	MEM-226
ENDOGLIN (ENG)	ThermoFisher					Mono	MEM-229
ENDOGLIN (ENG)	ThermoFisher					Mono	3A9
ENDOGLIN (ENG)	Biolegend	323202	Purified anti-human CD105 Antibody	Mouse	Human	Mono	43A3
ENDOGLIN (ENG)	Biolegend	800501	Purified anti-human CD105 Antibody	Mouse	Human	Mono	SN6h
ENDOGLIN (ENG)	Biolegend	684102	Purified anti-human CD105 Antibody	Mouse	Human	Mono	099E5
ENDOGLIN (ENG)	Hycult Biotech	HM2140	Endoglin, Human	Mouse	Not stated	Not stated	Not stated

FIG. 18 (Cont'd)

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Antigen	Company	Cat. No.	Name	Species	Reacts with	Mono- or Polyclonal	Clone #
			, mAb E9				
ENDOGLIN (ENG)	Bosterbio	M02997	Anti-Endoglin / CD105 (Angiogenesis Marker) Monoclonal Antibody	Mouse	Human	Mono	ENG/1327
PLGF	R&D Systems	MAB264	Human pIGF Antibody	Mouse	Human	Mono	IgG1 Clone # 37203
PLGF	R&D Systems	MAB264 R	Human pIGF Antibody	Mouse	Human	Mono	IgG1 Clone # 37203R
PLGF	R&D Systems	MAB264 2	Human pIGF Antibody	Rat	Human	Mono	IgG2A Clone # 358905
PLGF	R&D Systems	AF-264-PB	Human pIGF Antibody	Goat	Human	Poly	NA
PLGF	R&D Systems	AF6837	Human pIGF Antibody	Sheep	Human	Poly	NA
PLGF	R&D Systems	AB-264-PB	Human pIGF Antibody	Goat	Human	Poly	NA
PLGF	Abcam	ab140639	Anti-PLGF antibody [EPR2802(2)]	Rabbit	Human	Mono	EPR2802(2)

FIG. 18 (Cont'd)

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Antigen	Company	Cat. No.	Name	Species	Reacts with	Mono- or Polyclonal	Clone #
PLGF	Abcam	ab10966	Anti-PLGF antibody [37203.111]	Mouse	Human	Mono	[37203.111]
PLGF	Abcam	ab190717	Anti-PLGF antibody [PLGF94]	Mouse	Human	Mono	[PLGF94]
PLGF	Abcam	ab212717	Anti-PLGF antibody [PLGF/94] - BSA and Azide free	Mouse	Human	Mono	[PLGF/94]
PLGF	Abcam	ab9542	Anti-PLGF antibody - N-terminal	Rabbit	Human, Mouse	Poly	NA
PLGF	Abcam	ab196666	Anti-PLGF antibody	Rabbit	Human, Mouse, Rat	Poly	NA
PLGF	Abcam	ab99250	Anti-PLGF antibody	Goat	Human	Poly	NA
PLGF	Abcam	ab11938	Anti-PIGF Antibody	Rabbit	Human	Poly	NA
PLGF	Abcam	ab83906	Anti-PLGF antibody	Rabbit	Human	Poly	NA

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			y				
PLGF	Abcam	ab21700 1	Anti- PIGF Antibod y	Rabbit	Human	Poly	NA
PLGF	Abcam	ab21491 7	Anti- PIGF Antibod y	Sheep	Human	Poly	NA
PLGF	EMD/Millipore	MABF24 1	Anti- PLGF Antibod y	Mouse	Human	Mono	216-17
PLGF	LSBio	LS- C91984- 100	Anti- PLGF Antibod y	Mouse	Human	Mono	Not indicated
PLGF	LSBio	LS- C343156 -100	PGF / PLGF Antibod y (clone 3G6-F5 -F4)	Mouse	Human	Mono	3G6-F5- F4
PLGF	LSBio	LS- C343158 -100	PGF / PLGF Antibod y (clone 2H8-E2 -G11)	Mouse	Human	Mono	2H8-E2- G11
PLGF	LSBio	LS- C343168 -100	PGF / PLGF Antibod y (clone 5E9-C7 -G7-F7)	Mouse	Human	Mono	5E9-C7- G7-F7
PLGF	LSBio	LS- C358022 -100	PGF / PLGF Antibod y (clone	Mouse	Human	Mono	PLGF94

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			PLGF9 (4)				
PLGF	LSBio	LS-C391649 -100	PGF / PLGF Antibod y (clone PLGF/9 3)	Mouse	Human	Mono	PLGF/93
PLGF	OriGene	DM3524	PLGF( PGF) Mouse Monocl onal Antibod y [Clone ID: 342/3B 10]	Mouse	Human	Mono	342/3B10
PLGF	OriGene	DM3525	PLGF( PGF) Mouse Monocl onal Antibod y [Clone ID: 178/G1 0]	Mouse	Human	Mono	178/G10
PLGF	OriGene	DM3526	PLGF( PGF) Mouse Monocl onal Antibod y [Clone ID: 331/H1 2]	Mouse	Human	Mono	331/H12
PLGF	OriGene	AM50307	PLGF(	Mouse	Human	Mono	PLGF94

*FIG. 18 (Cont'd)*

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
		PU-S	PGF) Mouse Monoclonal Antibody [Clone ID: PLGF94]				
PLGF	Novus	NB110-60976	PLGF Antibody (MM0010-2D93)	Mouse	Human	Mono	MM0010-2D93
PLGF	RayBiotech	188-10153-SAF	Mouse anti-Human PLGF Antibody [Sodium Azide Free]	Mouse	Human	Mono	Not stated
PLGF	ThermoFisher	MA1-188	PGF Monoclonal Antibody (24G3)	Mouse	Human	Mono	24G3
PLGF	CreativeBioLabs	HOM-19431	Recombinant Human Anti-Human PLGF Monoclonal Antibody	Mouse	Human	Mono	Not stated
PLGF	USBio	216895	216895	Mouse	Human	Mono	14L799

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			Mouse Anti-PLGF				
PLGF	USBio	P4273-01B	P4273-01B Mouse Anti-PLGF	Mouse	Human	Mono	9A373
PAPP-A	Novus	NB100-73060	Pappalysin-1/PAPP-A Antibody	Mouse	Human	Monoclonal	7A6
PAPP-A	Novus	NB200-404	Pappalysin-1/PAPP-A Antibody	Mouse	Human	Monoclonal	10H9
PAPP-A	Novus	NB120-8346	Pappalysin-1/PAPP-A Antibody	Mouse	Human	Monoclonal	10E1
PAPP-A	Novus	NB110-8423	Pappalysin-1/PAPP-A Antibody	Mouse	Human	Monoclonal	5H9
PAPP-A	Novus	NB100-73059	Pappalysin-1/PAPP-A Antibody	Mouse	Human	Monoclonal	18A10
PAPP-A	R&D Systems	AF2487	Pappalysin-1 / PAPP-A Antibod	Goat	Human	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			y				
FGF21	Abbexa Ltd	abx2702 92	Fibroblast Growth Factor 21 (FGF21 )	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Abcam	ab17194 1	Recombinant FGF21 [EPR83 14(2)]	Rabbit	Hu, Ms, Rt	Monoclonal	na
FGF21	Abcam	ab77692	Anti-FGF21	Goat	Human (Hu)	Polyclonal	na
FGF21	Abcam	ab66564	Anti-FGF21	Rabbit	Hu, Ms	Polyclonal	na
FGF21	Abcam	ab64857	Anti-FGF21	Rabbit	Human, Mouse	Polyclonal	na
FGF21	Abcam	ab21936 8	Anti-FGF21	Rabbit	Human, Mouse, Rat	Monoclonal	EPR8314 (2)
FGF21	Abcam	ab13771 5	Anti-FGF21	Rabbit	Human	Polyclonal	na
FGF21	ABclonal	A10368	FGF21	Rabbit	Hu, Ms	Polyclonal	na
FGF21	Abnova Corporation	PAB1988 3	FGF21 polyclonal	Rabbit	Human (Hu)	Polyclonal	na
FGF21	antibodies-online	ABIN595 091	anti-FGF21 (Fibroblast Growth Factor 21)	Rabbit	Hu, Ms, Mu	Polyclonal	na
FGF21	antibodies-online	ABIN595 090	anti-FGF21 (Fibroblast Growth Factor 21)	Sheep	Human (Hu)	Polyclonal	na
FGF21	AssayPro	13018-	Human	Rabbit	Human	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
		05011	Fibroblast Growth Factor 21 (FGF-21)		(Hu)		
FGF21	Atlas Antibodies	HPA061286	Anti-FGF21	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Atlas Antibodies	AMAb91421	Anti-FGF21	Mouse	Human (Hu)	Monoclonal	CL6491
FGF21	Biomatik	CAC07045	FGF21 Polyclonal	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Biorbyt	orb76187	FGF21	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Biorbyt	orb381065	FGF21	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Bioss Inc.	bs-2318R	FGF21	Rabbit	Hu, Rt	Polyclonal	na
FGF21	BosterBio	PA1673	Anti-FGF21	Rabbit	Hu, Ms, Rt	Polyclonal	na
FGF21	BosterBio	PB10063	Anti-FGF21 Picoband	Rabbit	Hu, Ms, Rt	Polyclonal	na
FGF21	BosterBio	M00802	Anti-FGF21 Rabbit Monoclonal	Rabbit	Hu, Ms, Rt	Monoclonal	AG-6
FGF21	Creative Diagnostics	DPABH-24921	Anti-FGF21 (N-terminal) polyclonal	Rabbit	Human (Hu)	polyclonal	na
FGF21	Creative Diagnostics	DPABH-00759	Anti-FGF21 (aa 99-193) polyclonal	Rabbit	Human (Hu)	polyclonal	na

FIG. 18 (Cont'd)

<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
FGF21	EpiGentek	A52640	FGF21 Polyclonal	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Fitzgerald Industries International	10R-4111	FGF21	Mouse	Human (Hu)	monoclonal	4B4
FGF21	Fitzgerald Industries International	10R-4112	FGF21	Mouse	Human (Hu)	monoclonal	1B4
FGF21	GeneTex	GTX64384	Anti-FGF21	Rabbit	Hu, Ms	Polyclonal	na
FGF21	GeneTex	GTX111877	Anti-FGF21 [N3C3]	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Invitrogen Antibodies	PA5-18811	FGF21 Polyclonal	Goat	Human (Hu)	Polyclonal	na
FGF21	Invitrogen Antibodies	PA5-29386	FGF21 Polyclonal	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Invitrogen Antibodies	PA5-44325	FGF21 Polyclonal	Rabbit	Hu, Ms, Rb, Rt, Bv, Ca, GP, Hr	Polyclonal	na
FGF21	Invitrogen Antibodies	MA5-25522	FGF21 Monoclonal (OTI4B2)	Mouse	Human (Hu)	Monoclonal	OTI4B2
FGF21	Invitrogen Antibodies	MA5-25558	FGF21 Monoclonal (OTI1H4)	Mouse	Human (Hu)	Monoclonal	OTI1H4
FGF21	LifeSpan BioScience s	LS-C61737-100	Anti-FGF21 (aa103-115)	Goat	Hu, Mk	Polyclonal	na
FGF21	LifeSpan BioScience s	LS-C190802-200	Anti-FGF21 (aa184-	Rabbit	Human (Hu)	Polyclonal	na

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			209)				
FGF21	LifeSpan BioSciences	LS-C190801-200	Anti-FGF21 (aa26-47)	Rabbit	Human (Hu)	Polyclonal	na
FGF21	MyBioSource.com	MBS940 6788	FGF21	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Novus Biologicals	NBP1-31368	FGF-21	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Novus Biologicals	NBP2-00645	FGF-21 (OTI2F 10)	Mouse	Human (Hu)	Monoclonal	OTI2F10
FGF21	NSJ Bioreagents	R30758	FGF21	Rabbit	Hu, Ms, Rt	Polyclonal (rabbit origin)	na
FGF21	NSJ Bioreagents	R32531	FGF21	Rabbit	Human (Hu)	Polyclonal (rabbit origin)	na
FGF21	Proteintech Group Inc	26272-1-AP	FGF21	Rabbit	Human (Hu)	Polyclonal	na
FGF21	R&D Systems	AF2539	FGF-21	Goat	Human (Hu)	Polyclonal	na
FGF21	R&D Systems	MAB253 72	FGF-21	Mouse	Human (Hu)	Monoclonal	461804
FGF21	R&D Systems	MAB253 71	FGF-21	Mouse	Hu, Ms	Monoclonal	315901
FGF21	R&D Systems	MAB253 7	FGF-21	Mouse	Human (Hu)	Monoclonal	315914
FGF21	R&D Systems	MAB253 73	FGF-21	Goat	Human (Hu)	Monoclonal	40020A
FGF21	Santa Cruz Biotechnology, Inc.	sc-81946	FGF-21 (Y-16)	mouse	Human (Hu)	monoclonal	Y-16
FGF21	Signalway Antibody LLC	36478	FGF21	Rabbit	Human (Hu)	Polyclonal	na
FGF21	Signalway Antibody LLC	42458	Fibroblast growth factor 21 Polyclonal	Rabbit	Human (Hu)	Polyclonal	na

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
FGF21	St John's Laboratory	STJ1124 05	Anti-FGF21	Rabbit	Hu, Ms	Polyclonal	na
FGF21	United States Biological	126777	Mouse Anti-FGF21	mouse	Hu, Rt	Polyclonal	na
FGF21	United States Biological	315928	Pab Rb x human FGF21	rabbit	Hu, Ms	Polyclonal	na
SFLT1	ThermoFisher	14-5936-82	VEGF Receptor 1 (Flt1) Monoclonal Antibody (7A6), eBioscience™	Rat	Human	Mono	7A6
SFLT1	ThermoFisher	BMS196	VEGF Receptor 1 (Flt1) Monoclonal Antibody (Flt-19), eBioscience™	Mouse	Human	Mono	FLT-19
SFLT1	ThermoFisher	MA5-15550	VEGF Receptor 1 Monoclonal Antibody (3D10)	Mouse	Human	Mono	3D10
SFLT1	ThermoFisher	36-1100	VEGF Receptor 1 (solubl)	Rabbit	Human	Poly	NA

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			e) Polyclonal Antibody				
SFLT1	Abgent	AJ1814a	VEGFR -1 Antibody (N-term) Rabbit Monoclonal Antibody	Rabbit	Human, Mouse	Mono	Y103
SFLT1	LSBio	LS-B9103	FLT1 / VEGFR 1 Antibody (N-Ter minus) IHC-plu s™ LS-A94 05 (this antibod y replace s LS- C7679 2)	Rabbit	Human, Rat	Poly	NA
SFLT1	LSBio	LS- A9405	FLT1 / VEGFR 1 Antibody (N-Ter minus) IHC-plu s™ LS-B91 03	Rabbit	Human, Monkey*, Dog*, Horse*	Poly	NA

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			(This antibody replaces LS-C1328 67)				
SFLT1	LSBio	LS-C144 953	FLT1 / VEGFR 1 Antibody (N-Ter minus)	Rabbit	Human	Poly	NA
SFLT1	Epitomics/ Abcam	1303-1; ab32152	Anti-VEGF Receptor 1 antibody y [Y103]	Rabbit	Human, Mouse, Rat, Hamster	Mono	Y103
SFLT1	Abcam	ab18478 4	Anti-VEGF Receptor 1 antibody y [Y103] - Low endotoxin, Azide free	Rabbit	Human, Mouse, Rat, Hamster	Mono	Y103
SFLT1	Abcam	ab56300	Anti-VEGF Receptor 1 antibody y [AP-MAB0702]	Mouse	Human, Mouse	Mono	AP-MAB0702
SFLT1	Sigma	V4262	Monoclonal	Mouse	Human	Mono	FLT-11

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			Anti-Vascular Endothelial Growth Factor Receptor-1 antibody produced in mouse				
SFLT1	Creative Biolabs	TAB-177	Anti-Human VEGFR-1 Therapeutic Antibody (Icrucumab)	Human	Human	Mono	
SFLT1	Active Bioscience	2029.650 .200	Anti-human Flt-1 / VEGFR-1 Agonistic (MAB)	Mouse	Human	Mono	
SFLT1	Cell Sciences	CMV125	Mouse Anti-human VEGFR-1 Agonistic mAb	Mouse	Human	Mono	
SFLT1	Novus	NB110-60964	VEGFR-1/Flt-1 Antibody	Mouse	Human	Mono	MM0001-7G96

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			(MM00 01- 7G96)				
SFLT1	Novus	NBP2-21963	VEGFR 1/Flt-1 Antibody (MAB0702)	Mouse	Human, Mouse	Mono	MAB0702
SFLT1	R&D Systems	AF321	Human VEGF R1/Flt-1 Antibody	Goat	Human	Poly	
SFLT1	R&D Systems	MAB321	Human VEGF R1/Flt-1 Antibody	Mouse	Human	Mono	49560
SFLT1	Sino	10136-MM03	Anti-FLT1 antibody	Mouse	Human	Mono	5A4D2
SFLT1	Sino	10136-R111	Anti-FLT1 antibody	Rabbit	Human	Mono	111
SFLT1	Sino	10136-H08H	FLT1 Protein, Human, Recombinant (His Tag)				
PAPP-A2	R&D Systems	MAB1668	Human Pappalysin-2/PAPP-A2 Antibody	Mouse	Human	Mono	242011

FIG. 18 (Cont'd)

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Antigen	Company	Cat. No.	Name	Species	Reacts with	Mono- or Polyclonal	Clone #
			y				
PAPP-A2	Abcam	ab89899	Anti-PAPP A2 antibody y [MM05 07- 8M12]	Mouse	Human	Mono	[MM0507-8M12]
PAPP-A2	Abcam	ab22843 4	Share by email Anti-PAPP A2 antibody y [ABM4 C62] (ab228 434)	Mouse	Human	Mono	[ABM4C6 2]
PAPP-A2	USBiologics	216877	216877 Mouse Anti-PAPPA 2 (Pappalysin-2, Pregnancy-associated Plasma Protein A2, PAPP-A2, Pregnancy-associated Plasma Protein	Mouse	Human	Mono	14L781

FIG. 18 (Cont'd)

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<u>Antigen</u>	<u>Company</u>	<u>Cat. No.</u>	<u>Name</u>	<u>Species</u>	<u>Reacts with</u>	<u>Mono- or Polyclonal</u>	<u>Clone #</u>
			E1)				
uPA	Novus	NBP2-23502	u-Plasminogen Activator/Urokinase Antibody	Mouse	Human	Monoclonal	U-12
uPA	Novus	NBP1-05160	u-Plasminogen Activator/Urokinase Antibody	Mouse	Human	Monoclonal	U-16
uPA	Sino Biological	10815-MM05	Anti-Urokinase / uPA Antibody	Mouse	Human	Monoclonal	05
uPA	Sino Biological	10815-T16	Anti-Urokinase / uPA Antibody	Rabbit	Human	Polyclonal	na
uPA	Sino Biological	10815-MM03	Anti-Urokinase / uPA Antibody	Mouse	Human	Monoclonal	1D3F2B11
uPA	Sino Biological	10815-MM02	Anti-Urokinase / uPA Antibody	Mouse	Human	Monoclonal	1A2G4G11
uPA	RayBiotech	MD-15-0102	Anti-Human	Rabbit	Human	?	?
			Urokinase (uPA) / PLAU				

FIG. 18 (Cont'd)

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Antigen	Company	Cat. No.	Name	Species	Reacts with	Monoclonal or Polyclonal	Clone #
Fibronectin	R&D Systems	MAB1918	Human Fibronectin Antibody	Mouse	Human	Mono	P1H11
Fibronectin	R&D Systems	MAB19182	Human Fibronectin Antibody	Mouse	Human	Mono	960642
Fibronectin	R&D Systems	MAB19181	Human Fibronectin Antibody	Mouse	Human	Mono	P1F11
Fibronectin	Novus	NBP2-22113	Fibronectin antibody- ELISA	Mouse	Human	Mono	2F4
Fibronectin	Novus	NBP2-37508	Fibronectin antibody- ELISA	Mouse	Human	Mono	2F4G2
Fibronectin	Novus	NBP1-05056	Fibronectin antibody- ELISA	Mouse	Human	Mono	A35
Fibronectin	Novus	NBP2-23525	Fibronectin antibody- ELISA	Mouse	Human	Mono	A32
Fibronectin	Novus	NBP2-23524	Fibronectin antibody- ELISA	Mouse	Human	Mono	A17
Fibronectin	Novus	NBP1-05068	Fibronectin antibody- ELISA	Mouse	Human	Mono	3D2
Fibronectin	Novus	NBP1-05117	Fibronectin antibody- ELISA	Mouse	Human	Mono	A22
Fibronectin	Novus	7 polyAbs					
Fibronectin	CST	No antibodies					
Fibronectin	Abcam	ab6328	Not suitable ELISA	Mouse	Human	Mono	IST-9
Fibronectin	Abcam	ab154210	Anti-Fibronectin antibody [BC-1] ELIS	Mouse	Human	Mono	BC-1

FIG. 18 (Cont'd)

Antigen	Company	Cat. No.	Name	Species	Reacts with	Monoclonal or Polyclonal	Clone #
Fibronectin	Abcam	ab206928	Anti-Fibronectin antibody [F14]	Rabbit	Human, Mouse, rat	Mono	F14
Fibronectin	Abcam	ab219366	Anti-Fibronectin antibody [F1] - Low endotoxin, Azide free	Rabbit	Human	Mono	F1
Fibronectin	Abcam	ab212371	Anti-Fibronectin antibody [FN7.1]	Mouse	Human	Mono	FN7.1
Fibronectin	Abcam	ab212373	Anti-Fibronectin antibody [TV-1]	Mouse	Human	Mono	TV-1
Fibronectin	Abcam	5 polyAb					
Fibronectin	Thermo		Not suitable		The FN-3 antibody recognizes a determinant on human		FN3
Fibronectin	Thermo	MA1-12597	Fibronectin Monoclonal Antibody (EP5)	Mouse	Human	Mono	EP5
Fibronectin	Origene	CF803784	Fibronectin(FN1) Mouse Monoclonal Antibody	Mouse	Human	Mono	OTI5C1 (formerly 5C1)
Fibronectin	Origene	CF803733	Fibronectin(FN1) Mouse Monoclonal Antibody	Mouse	Human	Mono	OTI1G2
Fibronectin	Origene	CF803782	Fibronectin(FN1) Mouse Monoclonal Antibody	Mouse	Human	Mono	OTI3F9
Fibronectin	Origene	AM50111PU-S	Fibronectin(FN1) Mouse Monoclonal Antibody	Mouse	Human	Mono	SPM539
Fibronectin	Origene	AM50112PU-S	Fibronectin(FN1) Mouse Monoclonal Antibody	Mouse	Human, Mouse, rat, Porcine	Mono	SPM246
Fibronectin	Origene	AM50272PU-S	Fibronectin(FN1) Mouse Monoclonal Antibody	Mouse	Human, Mouse, rat, Porcine	Mono	2755-8
Fibronectin	Origene	AM06755PU-N	Fibronectin(FN1) Mouse Monoclonal Antibody	Mouse	Human	Mono	2F4-G2
Fibronectin	Atlas Antibodies	AMAb91223	Anti-FN1 antibody	Mouse	Human	Mono	CL3730
Fibronectin	SinoBiological	10314-R014	Anti-FN1 antibody ELISA	Rabbit	Human	Mono	014
Fibronectin	SinoBiological	10314-MM02	Anti-FN1 antibody ELISA	Mouse	Human	Mono	9A6D4A7

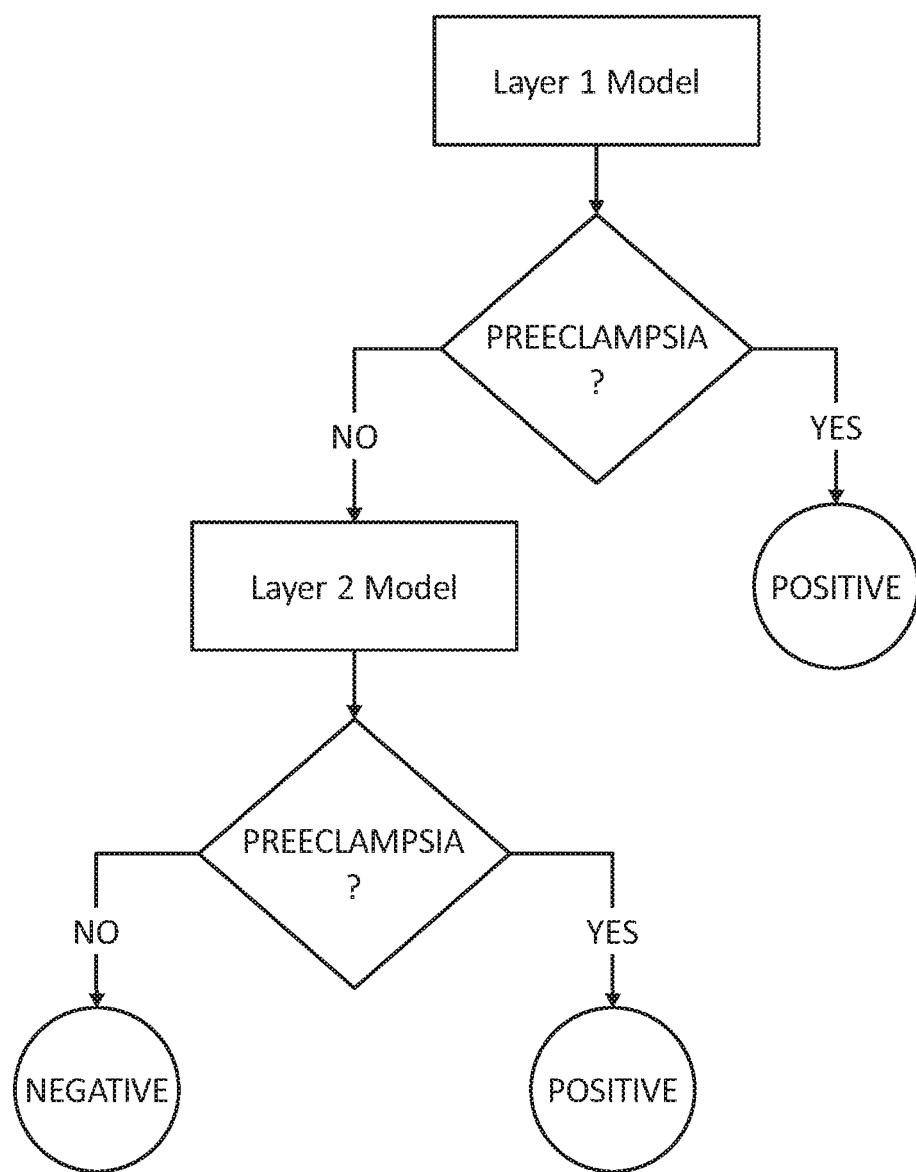
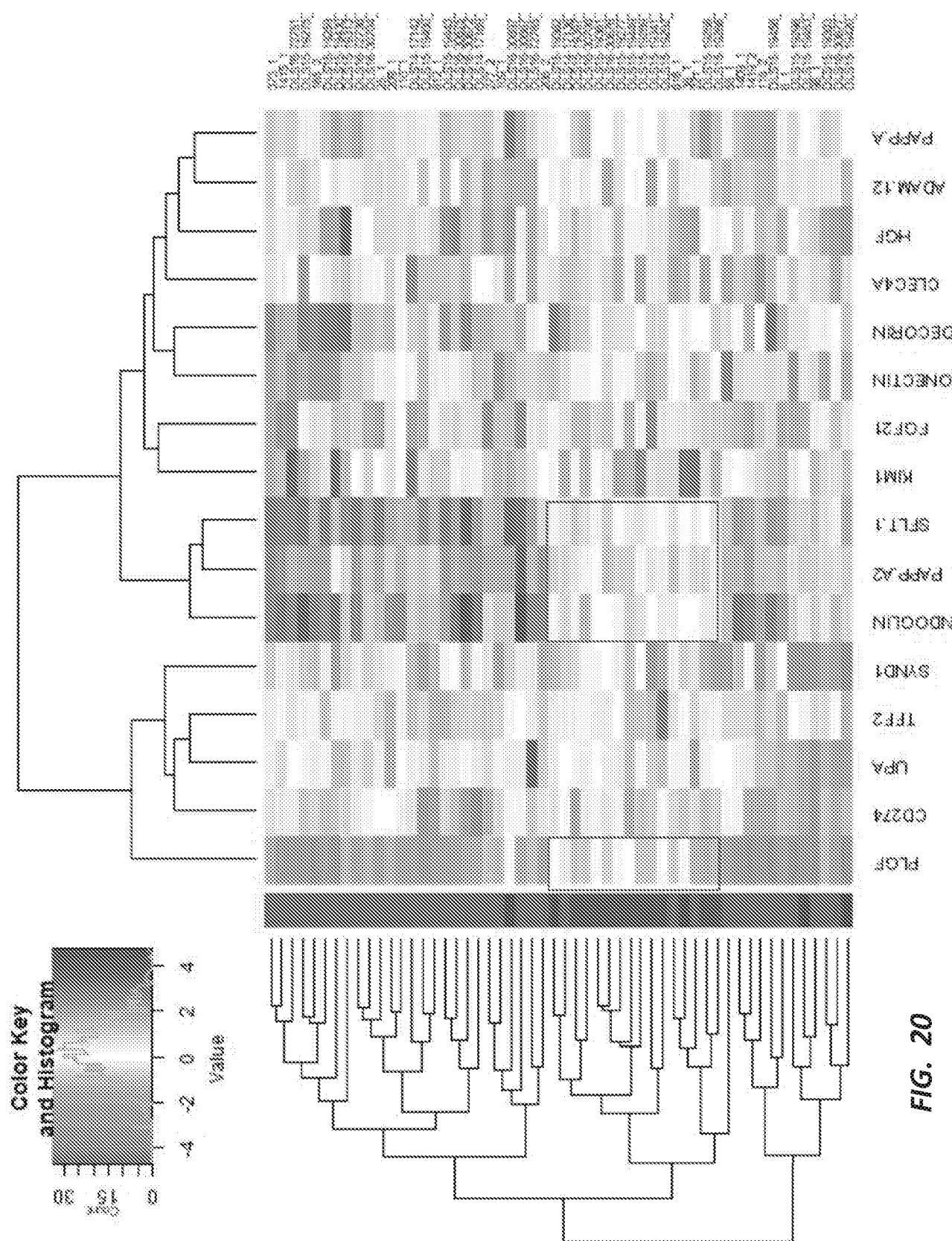


FIG. 19



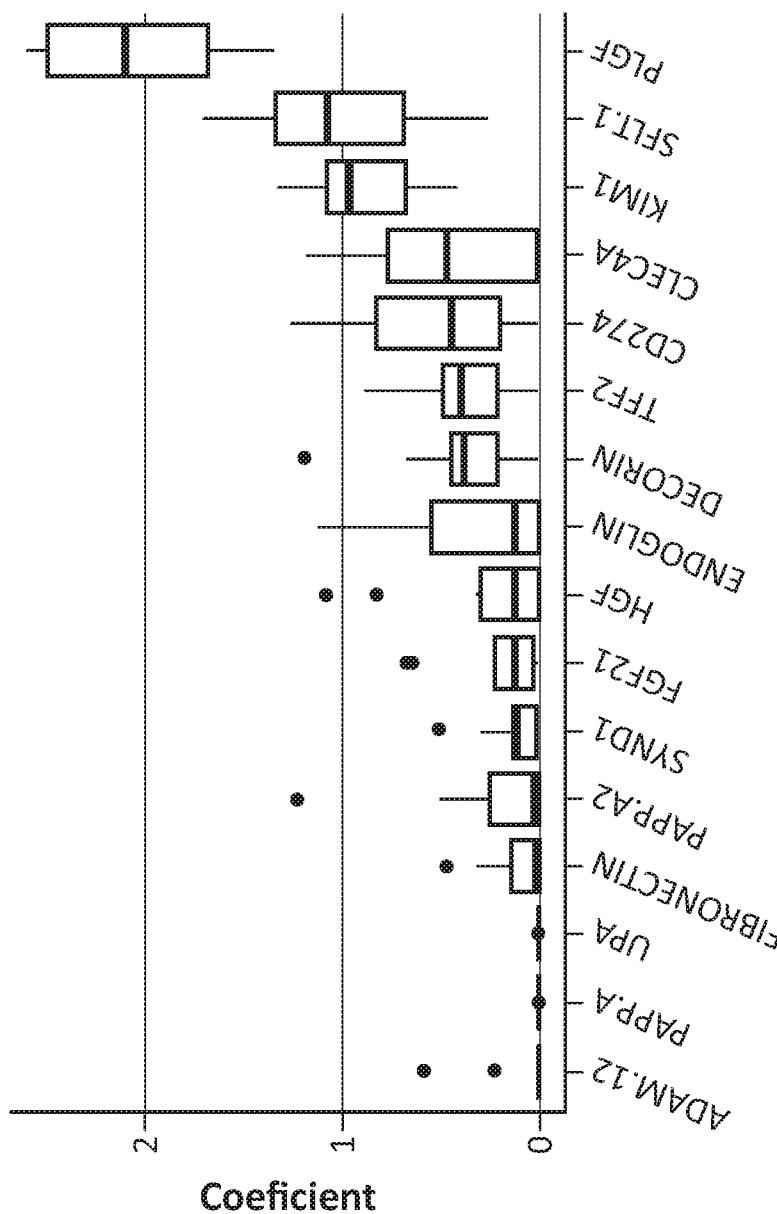


FIG. 21