

What is claimed is:

1. A method of detecting preeclampsia and/or determining an increased risk for preeclampsia in a pregnant female, the method comprising:

identifying in a biosample obtained from the pregnant women a plurality of circulating RNA (C-RNA) molecules;

wherein the identification of a plurality of C-RNA molecules is selected from:

(a) a plurality of C-RNA molecules encoding a coding region of a protein selected from any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, any twenty two or more, any twenty three or more, any twenty four or more, any twenty five or more, any fifty or more, or all seventy of ARRDC2, JUN, SKIL, ATP13A3, PDE8B, GSTA3, TIPARP, RGP1, USP54, CLEC4C, MRPS35, ARHGEF25, CUX2, HEATR9, FSTL3, DDI2, ZMYM6, ST6GALNAC3, GBP2, NES, ETV3, ADAM17, ATOH8, SLC4A3, TRAF3IP1, TTC21A, HEG1, ASTE1, TMEM108, ENC1, SCAMP1, ARRDC3, SLC26A2, SLIT3, CLIC5, TNFRSF21, PPP1R17, TPST1, GATSL2, SPDYE5, HIPK2, MTRNR2L6, CLCN1, GINS4, C10orf2, TRUB1, ACY3, FAR2, CD63, CKAP4, TPCN1, RNF6, THTPA, FOS, PARN, ORAI3, ELMO3, SMPD3, SERPINF1, TMEM11, PSMD11, CLEC4M, CCDC151, CPAMD8, CNFN, LILRA4, ADA, C22orf39, PI4KAP1, and ARFGAP3; or

(b) a plurality of C-RNA molecules encoding a coding region of a protein selected from any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, or all twenty two of TIMP4, FLG, HTRA4,

AMPH, LCN6, TEAD4, ARMS2, SEMA3G, ADAMTS1, ALOX15B, SLC9A3R2, IGFBP5, HSPA12B, CLEC4C, KRT5, PRX, ARHGEF25, ADAMTS2, DAAM2, FAM107A, NES, and VSIG4; or

(c) a plurality of C-RNA molecules encoding a coding region of a protein selected from any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, any twenty two or more, any twenty three or more, any twenty four or more, any twenty five or more, any fifty or more, any seventy-five or more, any one hundred or more, or all of CYP26B1, IRF6, MYH14, PODXL, PPP1R3C, SH3RF2, TMC7, ZNF366, ADCY1, C6, FAM219A, HAO2, IGIP, IL1R2, NTRK2, SH3PXD2A, SSUH2, SULT2A1, FMO3, FSTL3, GATA5, HTRA1, C8B, MN1, NFE2L1, PRDM16, AP3B2, EMP1, FLNC, STAG3, CPB2, TENC1, RP1L1, A1CF, NPR1, TEK, ERFF1, ARHGEF15, CD34, RSPO3, ALPK3, SAMD4A, ZCCHC24, LEAP2, MYL2, NRG3, ZBTB16, SERPINA3, AQP7, SRPX, UACA, ANO1, FKBP5, SCN5A, PTPN21, CACNA1C, ERG, SOX17, WWTR1, AIF1L, CA3, HRG, TAT, AQP7P1, ADRA2C, SYNPO, GPR116, KRT17, AZGP1, BCL6B, KIF1C, CLIC5, GPR4, GJA5, OLAH, C14orf37, ZEB1, JAG2, KIF26A, APOLD1, PNMT, MYOM3, PITPNM3, TIMP4, HTRA4, AMPH, LCN6, TEAD4, ARMS2, SEMA3G, ADAMTS1, ALOX15B, SLC9A3R2, IGFBP5, HSPA12B, PRX, ARHGEF25, ADAMTS2, DAAM2, FAM107A, NES, VSIG4, HBG2, CADM2, LAMP5, PTGDR2, NOMO1, NXF3, PLD4, BPIFB3, PACSIN1, CUX2, FLG, CLEC4C, and KRT5; or

(d) a plurality of C-RNA molecules encoding a coding region of a protein selected from any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more,

any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty-one or more, any twenty-two or more, any twenty-three or more, any twenty-four or more, or all twenty-five of VSIG4, ADAMTS2, NES, FAM107A, DAAM2, ARHGEF25, , PRX, ALOX15B, HSPA12B, IGFBP5, CLEC4C, SLC9A3R2, ADAMTS1, SEMA3G, KRT5, AMPH, TEAD4, PITPNM3, TIMP4, PNMT, ZEB1, APOLD1, PLD4, CUX2, and HTRA4; or

(e) a plurality of C-RNA molecules encoding a coding region of a protein selected from any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty-one or more, any twenty-two or more, or all twenty-three or more, any twenty-four or more, any twenty-five or more, or all twenty-six of ADAMTS1, ADAMTS2, ALOX15B, AMPH, ARHGEF25, CELF4, DAAM2, FAM107A, HSPA12B, HTRA4, IGFBP5, KCNA5, KRT5, LCN6, LRRC26, NES, OLAH, PACSIN1, PRX, PTGDR2, SEMA3G, SLC9A3R2, and VSIG4; or

(f) a plurality of C-RNA molecules encoding a coding region of a protein selected from any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, or all twenty of ADAMTS1, ADAMTS2, ALOX15B, ARHGEF25, CELF4, DAAM2, FAM107A, HTRA4, IGFBP5, KCNA5, KRT5, LCN6, LRRC26, NES, OLAH, PRX, PTGDR2, SEMA3G, SLC9A3R2, and VSIG4; or

(g) a plurality of C-RNA molecules encoding a coding region of a protein selected from any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, or all eight of

CLEC4C, ARHGEF25, ADAMTS2, ARRDC2, SKIL, VSIG4, ARRDC4, and NES; or

(h) a plurality of C-RNA molecules encoding a coding region of a protein selected from any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, or all twenty-one of KCNA5, ADAMTS2, MYOM3, ATP13A3, ARHGEF25, ADA, HTRA4, NES, ACY3, PLD4, SCT, NOX4, PACSIN1, SERPINF1, SKIL, SEMA3G, TIPARP, LRRC26, PHEX, LILRA4, and PER1, is indicative of preeclampsia and/or an increased risk for preeclampsia in the pregnant women.

2. A method of detecting preeclampsia and/or determining an increased risk for preeclampsia in a pregnant female, the method comprising:

purifying a population of circulating RNA (C-RNA) molecules from a biosample obtained from the pregnant female;

identifying protein coding sequences encoded by the C-RNA molecules within the purified population of C-RNA molecules;

wherein the identification of protein coding sequences encoded by the C-RNA molecules encoding a coding region of a protein selected from:

(a) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, any twenty two or more, any twenty three or more, any twenty four or more, any twenty five or more, any fifty or more, or all of ARRDC2, JUN, SKIL, ATP13A3, PDE8B, GSTA3, TIPARP, RGP1, USP54,

CLEC4C, MRPS35, ARHGEF25, CUX2, HEATR9, FSTL3, DDI2, ZMYM6, ST6GALNAC3, GBP2, NES, ETV3, ADAM17, ATOH8, SLC4A3, TRAF3IP1, TTC21A, HEG1, ASTE1, TMEM108, ENC1, SCAMP1, ARRDC3, SLC26A2, SLIT3, CLIC5, TNFRSF21, PPP1R17, TPST1, GATSL2, SPDYE5, HIPK2, MTRNR2L6, CLCN1, GINS4, C10orf2, TRUB1, ACY3, FAR2, CD63, CKAP4, TPCN1, RNF6, THTPA, FOS, PARN, ORAI3, ELMO3, SMPD3, SERPINF1, TMEM11, PSMD11, CLEC4M, CCDC151, CPAMD8, CNFN, LILRA4, ADA, C22orf39, PI4KAP1, and ARFGAP3; or

(b) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, any twenty two or more, or all twenty three of TIMP4, FLG, HTRA4, AMPH, LCN6, TEAD4, ARMS2, SEMA3G, ADAMTS1, ALOX15B, SLC9A3R2, IGFBP5, HSPA12B, CLEC4C, KRT5, PRX, ARHGEF25, ADAMTS2, DAAM2, FAM107A, NES, and VSIG4; or

(c) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, any twenty two or more, any twenty three or more, any twenty four or more, any twenty five or more, any fifty or more, any seventy-five or more, any one hundred or more, or all of CYP26B1, IRF6, MYH14, PODXL, PPP1R3C, SH3RF2, TMC7, ZNF366, ADCY1, C6, FAM219A, HAO2, IGIP, IL1R2, NTRK2, SH3PXD2A, SSUH2, SULT2A1, FMO3, FSTL3, GATA5, HTRA1, C8B, MN1, NFE2L1, PRDM16, AP3B2, EMP1, FLNC, STAG3, CPB2, TENC1, RP1L1, A1CF, NPR1, TEK, ERFFI1, ARHGEF15, CD34, RSPO3, ALPK3, SAMD4A, ZCCHC24, LEAP2, MYL2, NRG3, ZBTB16, SERPINA3,

AQP7, SRPX, UACA, ANO1, FKBP5, SCN5A, PTPN21, CACNA1C, ERG, SOX17, WWTR1, AIF1L, CA3, HRG, TAT, AQP7P1, ADRA2C, SYNPO, GPR116, KRT17, AZGP1, BCL6B, KIF1C, CLIC5, GPR4, GJA5, OLAH, C14orf37, ZEB1, JAG2, KIF26A, APOLD1, PNMT, MYOM3, PITPNM3, TIMP4, HTRA4, AMPH, LCN6, TEAD4, ARMS2, PAPP2, SEMA3G, ADAMTS1, ALOX15B, SLC9A3R2, TIMP3, IGFBP5, HSPA12B, PRX, ARHGEF25, ADAMTS2, DAAM2, FAM107A, NES, VSIG4, HBG2, CADM2, LAMP5, PTGDR2, NOMO1, NXF3, PLD4, BPIFB3, PACSIN1, CUX2, FLG, CLEC4C, and KRT5; or

(d) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any
5 seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty-one or more, any twenty-two or more, any twenty-three or more, any twenty-four or more, or all twenty-five of VSIG4, ADAMTS2, NES, FAM107A, DAAM2, ARHGEF25, PRX, ALOX15B, HSPA12B, IGFBP5, CLEC4C, SLC9A3R2, ADAMTS1, SEMA3G, KRT5, AMPH, TEAD4,
10 PITPNM3, TIMP4, PNMT, ZEB1, APOLD1, PLD4, CUX2, and HTRA4; or

(e) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any
15 seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty-one or more, any twenty-two or more, or all of ADAMTS1, ADAMTS2, ALOX15B, AMPH, ARHGEF25, CELF4, DAAM2, FAM107A, HSPA12B, HTRA4, IGFBP5, KCNA5, KRT5, LCN6, LRRC26, NES, OLAH, PACSIN1, PRX, PTGDR2, SEMA3G, SLC9A3R2, and VSIG4; or

(f) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or

more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, or all twenty of ADAMTS1, ADAMTS2, ALOX15B, ARHGEF25, CELF4, DAAM2, FAM107A, HTRA4, IGFBP5, KCNA5, KRT5, LCN6, LRRC26, NES, OLAH, PRX, PTGDR2, SEMA3G, SLC9A3R2, and VSIG4; or

5 (g) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, or all eight of CLEC4C, ARHGEF25, ADAMTS2, ARRDC2, SKIL, VSIG4, ARRDC4, and NES; or

10 (h) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, or all twenty-one of KCNA5, ADAMTS2, MYOM3, ATP13A3,

15 ARHGEF25, ADA, HTRA4, NES, ACY3, PLD4, SCT, NOX4, PACSIN1, SERPINF1, SKIL, SEMA3G, TIPARP, LRRC26, PHEX, LILRA4, and PER1, is indicative of preeclampsia and/or an increased risk for preeclampsia in the pregnant women.

3. The method of claim 2, wherein identifying the plurality of C-RNA molecules or identifying protein coding sequences encoded by C-RNA molecules within the biosample comprises hybridization, reverse transcriptase PCR, microarray chip analysis, or sequencing.

4. The method of claim 3, wherein sequencing optionally comprises:
 a) massively parallel sequencing of clonally amplified molecules; or
 b) RNA sequencing.

5. The method of claim any one of claims 1 to 4, further comprising:
 removing intact cells from the biosample;
 treating the biosample with a deoxynuclease (DNase) to remove cell free DNA (cfDNA);

synthesizing complementary DNA (cDNA) from C-RNA molecules in the biosample;
and/or

enriching the cDNA sequences for DNA sequences that encode proteins by exome
enrichment;

prior to identifying protein coding sequence encoded by the circulating RNA (C-RNA)
molecules.

6. A method of detecting preeclampsia and/or determining an increased risk for
preeclampsia in a pregnant female, the method comprising:

removing intact cells from a biosample obtained from the pregnant female;
treating the biosample with a deoxynuclease (DNase) to remove cell free DNA (cfDNA);
synthesizing complementary DNA (cDNA) from RNA molecules in the biosample;
enriching the cDNA sequences for DNA sequences that encode proteins (exome
enrichment);

sequencing the resulting enriched cDNA sequences; and

identifying protein coding sequences encoded by enriched C-RNA molecules;

wherein the identification of protein coding sequences encoded by the C-RNA molecules
encoding a coding region of a protein selected from:

(a) any one or more, any two or more, any three or more, any four or more,
any five or more, any six or more, any seven or more, any eight or more, any nine
or more, any ten or more, any eleven or more, any twelve, any thirteen or more,
any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or
more, any eighteen or more, any nineteen or more, any twenty or more, any
twenty one or more, any twenty two or more, any twenty three or more, any
twenty four or more, any twenty five or more, any fifty or more, or all seventy of
ARRDC2, JUN, SKIL, ATP13A3, PDE8B, GSTA3, TIPARP, RGP1, USP54,
CLEC4C, MRPS35, ARHGEF25, CUX2, HEATR9, FSTL3, DDI2, ZMYM6,
ST6GALNAC3, GBP2, NES, ETV3, ADAM17, ATOH8, SLC4A3, TRAF3IP1,
TTC21A, HEG1, ASTE1, TMEM108, ENC1, SCAMP1, ARRDC3, SLC26A2,
SLIT3, CLIC5, TNFRSF21, PPP1R17, TPST1, GATSL2, SPDYE5, HIPK2,
MTRNR2L6, CLCN1, GINS4, C10orf2, TRUB1, ACY3, FAR2, CD63, CKAP4,

TPCN1, RNF6, THTPA, FOS, PARN, ORAI3, ELMO3, SMPD3, SERPINF1, TMEM11, PSMD11, CLEC4M, CCDC151, CPAMD8, CNFN, LILRA4, ADA, C22orf39, PI4KAP1, and ARFGAP3; or

(b) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, or all twenty two of TIMP4, FLG, HTRA4, AMPH, LCN6, TEAD4, ARMS2, SEMA3G, ADAMTS1, ALOX15B, SLC9A3R2, IGFBP5, HSPA12B, CLEC4C, KRT5, PRX, ARHGEF25, ADAMTS2, DAAM2, FAM107A, NES, and VSIG4; or

(c) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, any twenty two or more, any twenty three or more, any twenty four or more, any twenty five or more, any fifty or more, any seventy-five or more, any one hundred or more, or all of CYP26B1, IRF6, MYH14, PODXL, PPP1R3C, SH3RF2, TMC7, ZNF366, ADCY1, C6, FAM219A, HAO2, IGIP, IL1R2, NTRK2, SH3PXD2A, SSUH2, SULT2A1, FMO3, FSTL3, GATA5, HTRA1, C8B, MN1, NFE2L1, PRDM16, AP3B2, EMP1, FLNC, STAG3, CPB2, TENC1, RP1L1, A1CF, NPR1, TEK, ERFFI1, ARHGEF15, CD34, RSPO3, ALPK3, SAMD4A, ZCCHC24, LEAP2, MYL2, NRG3, ZBTB16, SERPINA3, AQP7, SRPX, UACA, ANO1, FKBP5, SCN5A, PTPN21, CACNA1C, ERG, SOX17, WWTR1, AIF1L, CA3, HRG, TAT, AQP7P1, ADRA2C, SYNPO, GPR116, KRT17, AZGP1, BCL6B, KIF1C, CLIC5, GPR4, GJA5, OLAH, C14orf37, ZEB1, JAG2, KIF26A, APOLD1, PNMT, MYOM3, PITPNM3, TIMP4, HTRA4, AMPH, LCN6, TEAD4, ARMS2, SEMA3G, ADAMTS1,

ALOX15B, SLC9A3R2, IGFBP5, HSPA12B, PRX, ARHGEF25, ADAMTS2, DAAM2, FAM107A, NES, VSIG4, HBG2, CADM2, LAMP5, PTGDR2, NOMO1, NXF3, PLD4, BPIFB3, PACSIN1, CUX2, FLG, CLEC4C, and KRT5; or

(d) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any
5 seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty-one or more, any twenty-two or more, any twenty-three or more, any twenty-four or more, or all twenty-five of VSIG4, ADAMTS2, NES, FAM107A, DAAM2, ARHGEF25, PRX, ALOX15B, HSPA12B, IGFBP5, CLEC4C, SLC9A3R2, ADAMTS1, SEMA3G, KRT5, AMPH, TEAD4,
10 PITPNM3, TIMP4, PNMT, ZEB1, APOLD1, PLD4, CUX2, and HTRA4; or

(e) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any
15 seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty-one or more, any twenty-two or more, or all twenty-three of ADAMTS1, ADAMTS2, ALOX15B, AMPH, ARHGEF25, CELF4, DAAM2, FAM107A, HSPA12B, HTRA4, IGFBP5, KCNA5, KRT5, LCN6, LRRC26, NES, OLAH, PACSIN1, PRX, PTGDR2, SEMA3G, SLC9A3R2, and VSIG4; or

(f) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any
20 seventeen or more, any eighteen or more, any nineteen or more, or all twenty of ADAMTS1, ADAMTS2, ALOX15B, ARHGEF25, CELF4, DAAM2, FAM107A, HTRA4, IGFBP5, KCNA5, KRT5, LCN6, LRRC26, NES, OLAH, PRX, PTGDR2, SEMA3G, SLC9A3R2, and VSIG4; or
25

(g) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, or all eight of CLEC4C, ARHGEF25, ADAMTS2, ARRDC2, SKIL, VSIG4, ARRDC4, and NES; or

5 (h) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any
10 seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, or all twenty-one of KCNA5, ADAMTS2, MYOM3, ATP13A3, ARHGEF25, ADA, HTRA4, NES, ACY3, PLD4, SCT, NOX4, PACSIN1, SERPINF1, SKIL, SEMA3G, TIPARP, LRRC26, PHEX, LILRA4, and PER1, is indicative of preeclampsia and/or an increased risk for preeclampsia in the pregnant women.

15

7. A method of identifying a circulating RNA signature associated with an increased risk of preeclampsia, the method comprising:

removing intact cells from a biosample obtained from the pregnant female;
treating the biosample with a deoxynuclease (DNase) to remove cell free DNA (cfDNA);
synthesizing complementary DNA (cDNA) from RNA molecules in the biosample;
enriching the cDNA sequences for DNA sequences that encode proteins (exome enrichment);
sequencing the resulting enriched cDNA sequences; and
identifying protein coding sequences encoded by enriched C-RNA molecules.

8. A method comprising:

removing intact cells from a biosample obtained from the pregnant female;
treating the biosample with a deoxynuclease (DNase) to remove cell free DNA (cfDNA);
synthesizing complementary DNA (cDNA) from RNA molecules in the biosample;
enriching the cDNA sequences for DNA sequences that encode proteins (exome enrichment);

sequencing the resulting enriched cDNA sequences; and
identifying protein coding sequences encoded by the enriched C-RNA molecules;
wherein protein coding sequences encoded by the C-RNA molecules includes a coding
region of a protein are selected from:

- (a) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, any twenty two or more, any twenty three or more, any twenty four or more, any twenty five or more, any fifty or more, or all seventy of ARRDC2, JUN, SKIL, ATP13A3, PDE8B, GSTA3TIPARP, RGP1, USP54, CLEC4C, MRPS35, ARHGEF25, CUX2, HEATR9, FSTL3, DDI2, ZMYM6, ST6GALNAC3, GBP2, NES, ETV3, ADAM17, ATOH8, SLC4A3, TRAF3IP1, TTC21A, HEG1, ASTE1, TMEM108, ENC1, SCAMP1, ARRDC3, SLC26A2, SLIT3, CLIC5, TNFRSF21, PPP1R17, TPST1, GATSL2, SPDYE5, HIPK2, MTRNR2L6, CLCN1, GINS4, C10orf2, TRUB1, ACY3, FAR2, CD63, CKAP4, TPCN1, RNF6, THTPA, FOS, PARN, ORAI3, ELMO3, SMPD3, SERPINF1, TMEM11, PSMD11, CLEC4M, CCDC151, CPAMD8, CNFN, LILRA4, ADA, C22orf39, PI4KAP1, and ARFGAP3; or
- (b) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, or all twenty two of TIMP4, FLG, HTRA4, AMPH, LCN6, TEAD4, ARMS2, SEMA3G, ADAMTS1, ALOX15B, SLC9A3R2, IGFBP5, HSPA12B, CLEC4C, KRT5, PRX, ARHGEF25, ADAMTS2, DAAM2, FAM107A, NES, and VSIG4;

(c) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, any twenty two or more, any twenty three or more, any twenty four or more, any twenty five or more, any fifty or more, any seventy-five or more, any one hundred or more, or all of CYP26B1, IRF6, MYH14, PODXL, PPP1R3C, SH3RF2, TMC7, ZNF366, ADCY1, C6, FAM219A, HAO2, IGIP, IL1R2, NTRK2, SH3PXD2A, SSUH2, SULT2A1, FMO3, FSTL3, GATA5, HTRA1, C8B, MN1, NFE2L1, PRDM16, AP3B2, EMP1, FLNC, STAG3, CPB2, TENC1, RP1L1, A1CF, NPR1, TEK, ERFFI1, ARHGEF15, CD34, RSPO3, ALPK3, SAMD4A, ZCCHC24, LEAP2, MYL2, NRG3, ZBTB16, SERPINA3, AQP7, SRPX, UACA, ANO1, FKBP5, SCN5A, PTPN21, CACNA1C, ERG, SOX17, WWTR1, AIF1L, CA3, HRG, TAT, AQP7P1, ADRA2C, SYNPO, GPR116, KRT17, AZGP1, BCL6B, KIF1C, CLIC5, GPR4, GJA5, OLAH, C14orf37, ZEB1, JAG2, KIF26A, APOLD1, PNMT, MYOM3, PITPNM3, TIMP4, HTRA4, AMPH, LCN6, CRH, TEAD4, ARMS2, SEMA3G, ADAMTS1, ALOX15B, SLC9A3R2, IGFBP5, HSPA12B, PRX, ARHGEF25, ADAMTS2, DAAM2, FAM107A, NES, VSIG4, HBG2, CADM2, LAMP5, PTGDR2, NOMO1, NXF3, PLD4, BPIFB3, PACSIN1, CUX2, FLG, CLEC4C, and KRT5; or

(d) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty-one or more, any twenty-two or more, any twenty-three or more, any twenty-four or more, or all twenty-five of VSIG4, ADAMTS2, NES, FAM107A, DAAM2, ARHGEF25, PRX, ALOX15B, HSPA12B, IGFBP5,

CLEC4C, SLC9A3R2, ADAMTS1, SEMA3G, KRT5, AMPH, TEAD4, PITPNM3, TIMP4, PNMT, ZEB1, APOLD1, PLD4, CUX2, and HTRA4; or

(e) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty-one or more, any twenty-two or more, or all twenty-three of ADAMTS1, ADAMTS2, ALOX15B, AMPH, ARHGEF25, CELF4, DAAM2, FAM107A, HSPA12B, HTRA4, IGFBP5, KCNA5, KRT5, LCN6, , LRRC26, NES, OLAH, PACSIN1, PRX, PTGDR2, SEMA3G, SLC9A3R2, and VSIG4; or

(f) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, or all twenty of ADAMTS1, ADAMTS2, ALOX15B, ARHGEF25, CELF4, DAAM2, FAM107A, HTRA4, IGFBP5, KCNA5, KRT5, LCN6, LRRC26, NES, OLAH, PRX, PTGDR2, SEMA3G, SLC9A3R2, and VSIG4; or

(g) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, or all eight of CLEC4C, ARHGEF25, ADAMTS2, ARRDC2, SKIL, VSIG4, ARRDC4, and NES; or

(h) any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, or all twenty-one of KCNA5, ADAMTS2, MYOM3, ATP13A3, ARHGEF25, ADA, HTRA4, NES, ACY3, PLD4, SCT, NOX4, PACSIN1, SERPINF1, SKIL, SEMA3G, TIPARP, LRRC26, PHEX, LILRA4, and PER1.

9. The method of any one of claims 1 to 7, wherein the biosample comprises plasma and/ or, wherein the biosample is obtained from a pregnant female: at less than 16 weeks gestation; at less than 20 weeks gestation; or at greater than 20 weeks gestation.

10. A circulating RNA (C-RNA) signature for an elevated risk of preeclampsia, the C-RNA signature comprising any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, any twenty two or more, any twenty three or more, any twenty four or more, any twenty five or more, any fifty or more, or all seventy of ARRDC2, JUN, SKIL, ATP13A3, PDE8B, GSTA3, TIPARP, RGP1, USP54, CLEC4C, MRPS35, ARHGEF25, CUX2, HEATR9, FSTL3, DDI2, ZMYM6, ST6GALNAC3, GBP2, NES, ETV3, ADAM17, ATOH8, SLC4A3, TRAF3IP1, TTC21A, HEG1, ASTE1, TMEM108, ENC1, SCAMP1, ARRDC3, SLC26A2, SLIT3, CLIC5, TNFRSF21, PPP1R17, TPST1, GATSL2, SPDYE5, HIPK2, MTRNR2L6, CLCN1, GINS4, C10orf2, TRUB1, ACY3, FAR2, CD63, CKAP4, TPCN1, RNF6, THTPA, FOS, PARN, ORAI3, ELMO3, SMPD3, SERPINF1, TMEM11, PSMD11, CLEC4M, CCDC151, CPAMD8, CNFN, LILRA4, ADA, C22orf39, PI4KAP1, and ARFGAP3.

11. A circulating RNA (C-RNA) signature for an elevated risk of preeclampsia, the C-RNA signature comprising any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty one or more, or all twenty two of more, or all twenty-seven of TIMP4, FLG, HTRA4, AMPH, LCN6, TEAD4, ARMS2, SEMA3G, ADAMTS1, ALOX15B, SLC9A3R2, IGFBP5, HSPA12B, CLEC4C, KRT5, PRX, ARHGEF25, ADAMTS2, DAAM2, FAM107A, NES, and VSIG4.

12. A circulating RNA (C-RNA) signature for an elevated risk of preeclampsia, the C-RNA signature comprising a plurality of CYP26B1, IRF6, MYH14, PODXL, PPP1R3C, SH3RF2, TMC7, ZNF366, ADCY1, C6, FAM219A, HAO2, IGIP, IL1R2, NTRK2, SH3PXD2A, SSUH2, SULT2A1, FMO3, FSTL3, GATA5, HTRA1, C8B, MN1, NFE2L1, PRDM16, AP3B2, EMP1, FLNC, STAG3, CPB2, TENC1, RP1L1, A1CF, NPR1, TEK, ERRF1, ARHGEF15, CD34, RSPO3, ALPK3, SAMD4A, ZCCHC24, LEAP2, MYL2, NRG3, ZBTB16, SERPINA3, AQP7, SRPX, UACA, ANO1, FKBP5, SCN5A, PTPN21, CACNA1C, ERG, SOX17, WWTR1, AIF1L, CA3, HRG, TAT, AQP7P1, ADRA2C, SYNPO, GPR116, KRT17, AZGP1, BCL6B, KIF1C, CLIC5, GPR4, GJA5, OLAH, C14orf37, ZEB1, JAG2, KIF26A, APOLD1, PNMT, MYOM3, PITPNM3, TIMP4, HTRA4, AMPH, LCN6, TEAD4, ARMS2, SEMA3G, ADAMTS1, ALOX15B, SLC9A3R2, IGFBP5, HSPA12B, PRX, ARHGEF25, ADAMTS2, DAAM2, FAM107A, NES, VSIG4, HBG2, CADM2, LAMP5, PTGDR2, NOMO1, NXF3, PLD4, BPIFB3, PACSIN1, CUX2, FLG, CLEC4C, and KRT5.

13. A circulating RNA (C-RNA) signature for an elevated risk of preeclampsia, the C-RNA signature comprising any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty-one or more, any twenty-two or more, any twenty-three or more, any twenty-four or more, or all twenty-five of VSIG4, ADAMTS2, NES, FAM107A, DAAM2, ARHGEF25, PRX, ALOX15B, HSPA12B, IGFBP5, CLEC4C, SLC9A3R2, ADAMTS1, SEMA3G, KRT5, AMPH, TEAD4, PITPNM3, TIMP4, PNMT, ZEB1, APOLD1, PLD4, CUX2, and HTRA4.

14. A circulating RNA (C-RNA) signature for an elevated risk of preeclampsia, the C-RNA signature comprising any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, any twenty-one or more, any twenty-two or more, or all

twenty-three of ADAMTS1, ADAMTS2, ALOX15B, AMPH, ARHGEF25, CELF4, DAAM2, FAM107A, HSPA12B, HTRA4, IGFBP5, KCNA5, KRT5, LCN6, LRRC26, NES, OLAH, PACSIN1, PRX, PTGDR2, SEMA3G, SLC9A3R2, , and VSIG4.

15. A circulating RNA (C-RNA) signature for an elevated risk of preeclampsia, the C-RNA signature comprising any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, or all twenty of ADAMTS1, ADAMTS2, ALOX15B, ARHGEF25, CELF4, DAAM2, FAM107A, HTRA4, IGFBP5, KCNA5, KRT5, LCN6, LRRC26, NES, OLAH, PRX, PTGDR2, SEMA3G, SLC9A3R2, and VSIG4.

16. A circulating RNA (C-RNA) signature for an elevated risk of preeclampsia, the C-RNA signature comprising any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, or all eight of CLEC4C, ARHGEF25, ADAMTS2, ARRDC2, SKIL, VSIG4, ARRDC4, and NES.

17. A circulating RNA (C-RNA) signature for an elevated risk of preeclampsia, wherein the C-RNA signature consists of:

ADAMTS2, ARHGEF25, ARRDC2, CLEC4C, LEP, PAPP2, and VSIG4;
ADAMTS2, ARHGEF25, ARRDC2, CLEC4C, LEP, PAPP2, SKIL, and VSIG4;
ADAMTS2, ARHGEF25, ARRDC4, CLEC4C, LEP, NES, SKIL, and VSIG4;
ADAMTS2, ARHGEF25, ARRDC2, ARRDC4, CLEC4C, CRH, LEP, PAPP2, SKIL, and VSIG4;
ADAMTS2, ARHGEF25, ARRDC2, CLEC4C, LEP, and SKIL; or
ADAMTS2, ARHGEF25, ARRDC2, ARRDC4, CLEC4C, LEP, PAPP2, and SKIL.

18. A circulating RNA (C-RNA) signature for an elevated risk of preeclampsia, the C-RNA signature comprising any one or more, any two or more, any three or more, any four or more, any five or more, any six or more, any seven or more, any eight or more, any nine or more, any

ten or more, any eleven or more, any twelve or more, any thirteen or more, any fourteen or more, any fifteen or more, any sixteen or more, any seventeen or more, any eighteen or more, any nineteen or more, any twenty or more, or all twenty- of KCNA5, ADAMTS2, MYOM3, ATP13A3, ARHGEF25, ADA, HTRA4, NES, ACY3, PLD4, SCT, NOX4, PACSIN1, SERPINF1, SKIL, SEMA3G, TIPARP, LRRC26, PHEX, LILRA4, and PER1.

19. A solid support array comprising a plurality of agents complementary to and capable of binding a C-RNA signature of any one of claims 10 to 18.

20. A kit comprising a plurality of probes capable of binding and/or identifying a C-RNA signature of any one of claims 10 to 18.

21. A kit comprising a plurality of primers for selectively amplifying a C-RNA signature of any one of claims 10 to 18.

22. The method of any one of claims 1 to 9, wherein the biosample is a blood sample and the blood sample is collected, shipped, and/or stored in a tube that has cell- and DNA-stabilizing properties prior to processing the blood sample into plasma.

23. The method of claim 22, wherein preferably the tube comprises a Streck Cell-Free DNA BCT[®] blood collection tube.

24. The method of any one of claims 1 to 9, wherein the plurality of C-RNA molecules further comprises CRH, FN1, PAPPA2, TIMP3, LEP, H19, PRG2, and/or EB13.

25. The circulating RNA (C-RNA) signature for an elevated risk of preeclampsia of any one of claims 10 to 18, wherein the C-RNA signature further comprises CRH, FN1, PAPPA2, TIMP3, LEP, H19, PRG2, and/or EB13.