

biological factors influencing placental RNA levels in maternal plasma. In addition, transcripts that are expressed and released by non-placental tissues in response to pregnancy could not be identified by this method. A sensitive and high-throughput methodology that allows the direct profiling of the maternal plasma transcriptome would therefore be very desirable.

- 5 [0004] Similarly, direct plasma RNA profiling may be useful in other scenarios where there is a mixture of RNA molecules from two individuals, such as for organ transplantation. The circulation of transplantation recipients contains nucleic acid molecules from both the donor and recipient. A change in the relative profile of RNA molecules contributed by the donor or the recipient may reveal pathologies in the transplanted organ or recipient, such as graft rejection.

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SUMMARY

- [0004a] In one aspect, the present disclosure provides for ~~the use of a method~~ for diagnosing a pregnancy-associated disorder in a female subject pregnant with a fetus, the method comprising: measuring an expression level of a gene in a blood sample obtained from the female subject by: receiving a plurality of reads, wherein the reads are obtained from sequencing RNA molecules
 15 obtained from the blood sample, identifying, by a computer system, locations of the reads in a reference sequence, and counting the reads located at the gene; and by comparing an the
 expression level of the gene with a control value determined from one or more other female subjects, each pregnant with a healthy fetus, wherein the gene is LGALS14, STAT1, CGA, GBP1, HSD17B1, KRT8, KRT18, HPGD, GADD45G, HSD3B1, KRT19, GDF15,
 20 CYP19A1, PSG4, PSG3, CRYAB, HSPB8, PKIB, PGF, CYP11A1, PSG5, PSG2, VGLL3, KRT7, TMEM54, PRKCZ, SDC1, LGALS13, EFHD1, CAPN6, XAGE3, EBI3, PAGE4, ALPP, LOC100505659, FBLN1, SEMA3B, GPC3, PLAC2, FN1, NOS3, LOC100506655, PSG11, SPTLC3, EXPH5, HSPA2, PSG6, TACC2, PRPF40B, LOC388948, GBP1P1, CLDN4, C2orf72, PAPPA2, HIS2H3A, HIST2H3C, TCL6, MFSD2A, ZFAT-AS1, INSL4,
 25 DHRS2, HES2, WLS, PLCXD3, LOC100505483, C1orf130, FOSB, TRPV6, TFAP2A, MMP11, TUSC3, HMGCR, CCK, LOC100129935, C8orf39, GLDN, PGAP3, MSX2P1, GH1, SVEP1, PPP1R32, PSG8, ENDOU, EGFR, DUSP4, PHYHIPL, CTSF, TRIM29, RCN3, SPIRE2, LOC100216001, FAM176A, SCIN, ZNF500, PRR16, LOC100128054, OLR1, SLC30A2, LOC285972, HESX1, TMEM139, ZNF727, TM4SF19, EFS, TIMD4,
 30 ALDH3B2, KRT81, MUC15, PRSS8, SH2D5, LOC728175, GRHL2, PABPN1L, CORO6, ADAM9, AGBL5, APOBR, APOL2, APP, ASAH1, ATP5I, ATP6V0E1, B2M, BCAP31, BRK1, C12orf76, C19orf59, C19orf79, C1orf151-NBL1, C21orf7, C7orf53, CARD16, CD97, CEBPD, CTSA, CYB5R1, DDX11L10, DUSP1, DYNLRB1, EMP3, ENKUR, GALM, GDI1, HIST1H2AC, HIST1H3H, HIST1H4A, HIST1H4B, HIST1H4E, HIST1H4H,
 35 HIST1H4L, HLA-C, HLA-L, HRC, HSPA1A, IFI6, ISG20, JAM3, KLF6, LEPR, LEPROT, LILRA5, LOC146336, LRRC32, LY6E, MEIS1, MLH3, MYADM, NCF1, NCF1B, NDUFA1, NES, NFAM1, NGFRAP1, NPTN, NT5C3, OST4, PARK7, PARP10, PDGFA, PF4, PGRMC1, PRIC285, PSMB9, RAB32, RABAC1,

CLAIMS:

1. Use of a gene-A method for diagnosing a pregnancy-associated disorder in a female subject pregnant with a fetus, the method comprising:
measuring an expression level of a gene in a blood sample obtained from the female subject by:
receiving a plurality of reads, wherein the reads are obtained from sequencing RNA molecules obtained from the blood sample,
identifying, by a computer system, locations of the reads in a reference sequence, and
counting the reads located at the gene; and
by comparing ~~an~~ the expression level of the gene with a control value determined from one or more other female subjects, each pregnant with a healthy fetus, wherein the gene is LGALS14, STAT1, CGA, GBP1, HSD17B1, KRT8, KRT18, HPGD, GADD45G, HSD3B1, KRT19, GDF15, CYP19A1, PSG4, PSG3, CRYAB, HSPB8, PKIB, PGF, CYP11A1, PSG5, PSG2, VGLL3, KRT7, TMEM54, PRKCZ, SDC1, LGALS13, EFHD1, CAPN6, XAGE3, EBI3, PAGE4, ALPP, LOC100505659, FBLN1, SEMA3B, GPC3, PLAC2, FN1, NOS3, LOC100506655, PSG11, SPTLC3, EXPH5, HSPA2, PSG6, TACC2, PRPF40B, LOC388948, GBP1P1, CLDN4, C2orf72, PAPP2, HIS2H3A, HIST2H3C, TCL6, MFSD2A, ZFAT-AS1, INSL4, DHRS2, HES2, WLS, PLCXD3, LOC100505483, C1orf130, FOSB, TRPV6, TFAP2A, MMP11, TUSC3, HMGCR, CCK, LOC100129935, C8orf39, GLDN, PGAP3, MSX2P1, GH1, SVEP1, PPP1R32, PSG8, ENDOU, EGFR, DUSP4, PHYHIPL, CTSF, TRIM29, RCN3, SPIRE2, LOC100216001, FAM176A, SCIN, ZNF500, PRR16, LOC100128054, OLR1, SLC30A2, LOC285972, HESX1, TMEM139, ZNF727, TM4SF19, EFS, TIMD4, ALDH3B2, KRT81, MUC15, PRSS8, SH2D5, LOC728175, GRHL2, PABPN1L, CORO6, ADAM9, AGBL5, APOBR, APOL2, APP, ASAH1, ATP5I, ATP6V0E1, B2M, BCAP31, BRK1, C12orf76, C19orf59, C19orf79, C1orf151-NBL1, C21orf7, C7orf53, CARD16, CD97, CEBPD, CTSA, CYB5R1, DDX11L10, DUSP1, DYNLRB1, EMP3, ENKUR, GALM, GDI1, HIST1H2AC, HIST1H3H, HIST1H4A, HIST1H4B, HIST1H4E, HIST1H4H, HIST1H4L, HLA-C, HLA-L, HRC, HSPA1A, IFI6, ISG20, JAM3, KLF6, LEPR, LEPROT, LILRA5, LOC146336, LRRC32, LY6E, MEIS1, MLH3, MYADM, NCF1, NCF1B, NDUFA1, NES, NFAM1, NGFRAP1, NPTN, NT5C3, OST4, PARK7, PARP10, PDGFA, PF4, PGRMC1, PRIC285,

PSMB9, RAB32, RABAC1, RBX1, RNF213, RPPH1, S100P, S1PR3, SAT1, SEPT3, SERF2, SHISA5, SIGLEC1, SIGLEC14, SNN, SOD2, SPARC, TIMP1, TMEM140, TMEM185A, TMEM50A, TRIM22, TSC22D3, UBE2L6, VKORC1L1, VTRNA1-1, YIF1B, YPEL3, YWHAH, or ZNF485.

2. The ~~use~~method of claim 1, wherein the pregnancy-associated disorder is associated with the female subject.

3. The ~~use~~method of claim 1, wherein the pregnancy-associated disorder is associated with the fetus.

4. The ~~use~~method of claim 3, wherein the pregnancy-associated disorder is ~~pre-eclampsia or pre-term birth~~.

~~5. The method of claim 1, wherein the pregnancy-associated disorder is pre-eclampsia.~~

~~56.~~ The ~~use~~method of claim 1, wherein the pregnancy-associated disorder is diagnosed if the expression level exceeds the control value.

~~67.~~ The ~~use~~method of claim 1, wherein the pregnancy-associated disorder is diagnosed if the expression level is below the control value.

~~78.~~ The ~~use~~method of claim 1, wherein the female subject exhibits an elevated expression level of the gene while pregnant as compared with after delivery.

~~8. The use of claim 1, wherein the expression level of the gene in a female subject is measured by receiving a plurality of reads, wherein the reads are obtained from an analysis of RNA molecules obtained from a sample, wherein the sample is a blood sample obtained from the female subject; identifying, by a computer system, locations of the reads in a reference sequence; and counting the reads located at the gene.~~

9. The ~~use~~method of claim 1, wherein the gene is CGA, HSD17B1, LGALS14, HSD3B1, PSG4, PSG3, PSG5, PSG2, LGALS13, or CAPN6.

10. The ~~use~~method of claim 1, wherein the gene is ASAH1, C12orf76, C19orf59, C19orf79, C21orf7, C7orf53, CEBPD, DDX11L10, DUSP1, ENKUR, GALM, HIST1H2AC, HIST1H3H, HIST1H4A, HIST1H4B, HIST1H4H, HIST1H4L, HLA-L, HRC, IFI6, ISG20, MEIS1, MLH3, MYADM, NCF1B, NES, NGFRAP1, OST4, PF4, PGRMC1, PRIC285, RABAC1, RPPH1, S100P, S1PR3, SIGLEC1, SIGLEC14, SPARC, TMEM140, TMEM185A, TMEM50A, TSC22D3, UBE2L6, or VTRNA1-1.

11. The method of claim 1, wherein the gene is ASAH1, TSC22D3, MYADM, and C7orf53.

~~11~~12. The ~~use~~method of claim 1, wherein the pregnancy-associated disorder is intrauterine growth restriction, invasive placentation, hemolytic disease of the newborn, placental insufficiency, hydrops fetalis, fetal malformation, HELLP syndrome, or systemic lupus erythematosus.

~~12~~13. The ~~use~~method of claim 1, wherein:
the expression level of the gene is the expression level of the gene in a biological sample, and
the biological sample is a blood, plasma, serum, urine, or saliva sample.